MINISTRY OF PUBLIC HEALTH OF UKRAINE
NATIONAL UNIVERSITY OF PHARMACY

# TOPICAL ISSUES OF NEW DRUGS DEVELOPMENT

April 23, 2015
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А43



Укладачі: Осьмачко А.П., Мигаль А.В.

**А43** Актуальні питання створення нових лікарських засобів: тези доповідей міжнародної науково-практичної конференції молодих вчених та студентів (23 квітня 2015 р.). – Х.: Вид-во НФаУ, 2015. – 712 с.

Збірка містить матеріали науково-практичної конференції молодих вчених та студентів «Актуальні питання створення нових лікарських засобів». Матеріали згруповано за провідними напрямками науково-дослідної та навчальної роботи Національного фармацевтичного університету. Розглянуто теоретичні та практичні аспекти синтезу біологічно-активних сполук і створення на їх основі лікарських субстанцій; стандартизації ліків, фармацевтичного та хіміко-технологічного аналізу; вивчення рослинної сировини та створення фітопрепаратів; сучасної технології ліків та екстемпоральної рецептури; біотехнології у фармації; досягнень сучасної фармацевтичної мікробіології та імунології; доклінічних досліджень нових лікарських засобів; фармацевтичної опіки рецептурних та безрецептурних лікарських препаратів; доказової медицини; сучасної фармакотерапії, соціально-економічних досліджень у фармації, маркетингового менеджменту та фармакоекономіки на етапах створення, реалізації та використання лікарських засобів; управління якістю у галузі створення, виробництва і обігу лікарських засобів; інформаційниих технологій у фармації та медицині; основ педагогіки та психології; суспільствознавства; філології. Для широкого кола наукових і практичних працівників фармації та медицини.

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**A43** Topical issues of new drugs development: Abstracts of International Scientific And Practical Conference Of Young Scientists And Student (April 23, 2015). – Kh.: Publishing Office NUPh, 2015. – 712 P.

Book of Abstracts includes materials of Scientific and Practical Conference of Young Scientists and Students «Actual questions of development of new drugs». Materials are groupped according to the main directions of scientific, research and educational work of the National University of Pharmacy. Teoretical and practical aspects of the synthesis of biologically active compounds and development of medicinal substances on their basis; standardization of drugs, pharmaceutical and chemical-technological analysis, the study of raw materials and herbal remedies development, modern drug technology and extemporal recipe; biotechnology in pharmacy, modern advances in pharmaceutical microbiology and immunology, clinical trials of new drugs, pharmaceutical care for prescription and OTC-drugs, evidence-based medicine, modern pharmacotherapy, socio-economic studies in pharmacy, marketing management and pharmacoeconomics during the development, implementation and use of drugs, quality management in development, production and traffi cking of drugs; information technologies in pharmacy and medicine; basics of pedagogy and psychology; social science; philology are presented. For a wide audience of scientists and pharmaceutaical and medicinal employees.

**UDC 615.1**

**Dear Students and Young Scientists!**

Welcome to the National University of Pharmacy – the Center of Science and Education! Traditionally we hold the Youth Scientific Forum in spring.

People who like creation, research and discovery of something new are gathered together in this auditorium. We are the colleagues. We have the common mission – science. Making your way in the science is easy and difficult at the same time. Easy – because there are no restrictions in the University and developed all conditions to carry out scientific researches. Difficult – because the science is made by strong personalities and requires perseverance and major efforts from them.

At the beginning of our "scientific path" there were no much information resources: no Internet, no wide access to scientific literature, opportunities to travel abroad, etc. Nowadays we live in a global world where a lot of information is available. We have an opportunity to visit different scientific conferences that are hold in our country and abroad, read a huge number of scientific journals that are published, and use scientometrical databases that are already function. There are also different kinds of state support of the youth. There are many scholarships, government programs, internships (in our country/ national and foreign).

One need only a desire, skills and knowledge of foreign languages for free communication. This is a long-term work. To become a personality in science you must become an expert in your field. Some of the most important criteria of the scientist are the number of publications, patents, followers of scientific school. You must be well-known person in the world and be cited as a reputable researcher.

The highest recognition of the scientist is the introduction of his results into the practice. In pharmacy it is the development of a new medicinal product Nowadays the task of some effective domestic medicinal products development is set to the pharmacists of our country. Such specialists as synthetic chemists, pharmacologists, analysts, technologists, clinicians are required for this purpose. And for the further introduction of the developed drug – organizers, managers, logisticians and economists.

Be ambitious in science, set big goals and achieve them. You are the future of scientific elite. At least for 50 years you will work and develop science, intellectual potential and country's image in the world.

Such conferences help to express yourself as a scientist, represent your scientific work.

I wish you to become Academicians, Honored Workers, State Prize Winners and the Nobel laureate in future. And today I wish you a successful fruitful work, interesting meetings, inspiration, new discoveries and, of course, love.

# SECTION № 1

# SYNTHESIS OF PHYSIOLOGICALLY ACTIVE SUBSTANCES

# DETERMINATION OF BIOLOGICAL ACTIVITY IN A RANGE OF 8-METHYL-2-HYDROXY-4-OXO-4H-PYRIDO [1,2 α] PYRIMIDINE-3-CARBOXYLIC ACID DERIVATIVES

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As it is known, the pharmacological activity of compounds, especially drugs, depend mainly on their interaction with biological matrices or drug targets, such as proteins, which are either receptors or enzymes, nucleic acids and biomembranes (phospholipids and glycolipids).

All these matrices have complex three-dimensional structures, which are capable to recognize specifically the ligand of drug molecule in only one of the many possible arrangements in the three-dimensional space. It is the three-dimensional structure of the drug target that determines which of the potential drug candidate molecules is bound within its cavity and with what affinity.

Nowadays the widely spread procedure for chemist-synthetics in searching potential biologically active compounds is use of software. It helps not only to save time, solvents and make searching cheaper but minimizes application of laboratory animals.

Among the aims of our research were working out techniques of synthesis in the range of 2-hydroxy-4-oxo-4H-pyrido [1,2 α] pyrimidine-3-carboxylic acid derivatives; and making prognosis of probable biological activity in the range of newly synthesized compounds, especially for 8-methyl substituted derivatives of 2-hydroxy-4-oxo-4H-pyrido [1,2α ] pyrimidine-3-carboxylic acid.

For planning and further optimization the synthesis process by us was carried out prediction of the pharmacological activity for the obtained products using the PASS program. Thus for statistical significance in the calculation of activity were used formula of the most affordable radicals in the amide function.

In view of the fact that the starting material may also be of interest as potential biologically active compounds, considered it appropriate to predict their potential pharmacological activity.

Forecast of the expected pharmacological activity for initial 8-methyl amides of 2-hydroxy-4-oxo-4H-pyrido [1,2 α] of pyrimidine-3-carboxylic acid has shown that almost all the compounds are antagonists of leukotriene C, that are potential antispasmodics, and have membrane-stabilizing and hepatoprotective activity types. Quite interesting is the antagonistic activity of the compounds on growth factor.

# SYNTHESIS, PHYSICO-CHEMICAL PROPERTIES AND PHARMACOLOGICAL ACTIVITY OF BIOLOGICALLY ACTIVE SUBSTANCES IN A RANGE OF 7-METHYL-2-HYDROXY-4-OXO-4H-PYRIDO [1,2 α] PYRIMIDINE-3-CARBOXYLIC ACID DERIVATIVES

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The pharmaceutical discovery in the drug-discovery process, which usually begins by focusing on specific diseases and patient needs. Discovery scientists search for biological targets within the body that play a role in a given disease. Targets can be either part of the body (such as a protein, receptor, or gene) or foreign (such as a virus or bacteria). That is why the scientists of the National University of Pharmacy are in the constant search of the new substances, which can have potential biological activity.

The aim of our research is to elaborate the method of synthesis in the range of 2-hydroxy-4-oxo-4H-pyrido [1,2 α] pyrimidine-3-carboxylic acid derivatives; to prove the chemical structure of the synthesized compounds and to study their physical-chemical properties; to carry out research in the range of 7-methyl-2-hydroxy-4-oxo-4H-pyrido [1,2 α] pyrimidine-3-carboxylic acid derivatives on potential biological activity.

For our researches were taken 7-methyl-substituted derivatives of 2-hydroxy-4-oxo-4H-pyrido[1,2 α] pyrimidine-3-carboxylic acid. As substituents in the amide function we have planned radicals, which allow getting the aimed products in this reaction without especial synthetic complications – alkyl, aryl and heterylalkyl. Melting points for the synthesized compounds were determined by capillary method on ПТМ (М). Spectra NMR $^{1}$H has registered on the Varian Mercury-VX-200 (200 MHz).

The forecast of the expected pharmacological activity has shown that almost all the compounds are potential antispasmodics, and have membrane-stabilizing and inhibitors of grows factor activity types.

# BEAUTY OF ORGANIC CHEMISTRY

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Organic chemistry is the main supplier of raw materials for the manufacture of cosmetics. It is impossible to understand a variety of applications of modern cosmetics without knowledge of the basics of this science. The authors set out the task to analyze the way representatives of different classes of organic compounds are being used in cosmetology.

*Saturated hydrocarbons.* Paraffin oil ($C_1$-$C_{15}$), petrolatum ($C_{12}$-$C_{25}$), paraffin ($C_{19}$-$C_{35}$) are obtained by distillation of the crude oil. All these raw materials are widely used in the cosmetic industry. They are good at storage. Despite of the fact of their being not easily absorbed into the skin, they are an excellent basis for cream, cleansing milk, and decorative cosmetics. *Unsaturated hydrocarbons.* The compounds containing vinyl group $H_2C$ = C- (vinyl alcohol, vinyl acetate, vinylpyrrolidone, acrylic acid) have been used in cosmetology. These substances are used as the polyvinyl compounds obtained by polymerization. For example, polyvinyl acetates are used for the hair spray. Polyvinyl alcohol is used as a preservative for a hair styling liquids, as well as in cleansing cream as a grinder substance. *Polyvinylpyrrolidone* is widely used in hand cream and as a means of hair caring and hair dyeing. It is also used in toothpaste and perfume water. *Halogenated hydrocarbons* containing fluorine and chloral are widely used as gas carriers in aerosol containers. Besides, halogenated substances having bacteriostatic or bactericidal action are used in wiping, facial lotions, hair shampoo (hexachlorophene, chlorhexidine, polividoniod). *Quaternary ammonium salts* are used as preservatives as the means for skin care (benzalkonium chloride, methylammonium chloride, polyaminopropyl biguanide). They are used as surfactants (diallyldimethylammonium chloride), emulsifiers, anti-static agents (alkyl benzil dimethyl ammonium chloride, alkyl dimethyl amine oxides) in mouth rinses, hair conditioners and for hair styling. Low molecular alcohol having disinfecting, antiseptic, drying properties are used as components and solvents in perfumes, aerosol deodorants, colognes, lotions, tonics, mouthwashes. *Polyols (cetearyl alcohol)* are used in different kinds of cream. *Polyalcohol* (polyols) are different types of glycol and glycol derivatives, glycerin and all kinds of sugar. Polyols are hygroscopic substances. So they are used in cosmetics and hair care products being

humidifiers (glycerin, propylene glycol, sorbitol, fructose). *Ethers are good solvents.* Glycol ethers are the basis for a variety of cream , cleansing milk and varnish softeners. Anisole (methyl phenyl ether), phenetole (ethyl phenyl ether) are used as odorants in perfumery. *Aldehydes and ketones.* This class of organic compounds is used in perfumery as fragrances: benzaldehyde (the smell of bitter almonds). Hexen-2-al is a "leaf aldehyde" (the smell of freshness and greenery). Caprylic aldehyde (octanal) is used to simulate the smell of lemon oil and orange. Pelargonic aldehyde (nonanal) is used to simulate the smell of rose. 2.6 nonadien-1-al is used to simulate the aldehyde of violet leaves. *Carboxylic acid* is contained practically in all cosmetics. *Alfa-Hydroxy* (fruit acids) are BAS natural that contribute to slowing the aging process of the skin (hyaluronic, orotic acid), soften dry skin (lactic acid, sorbic acid). It cleanses the pores, skin and tones (galacturonic acid). It makes the impact on oily skin with acne (azelaic, salicylic acid). It depigments age spots and freckles (glycolic acid, oxalic acid, azelaic acid). *Amino acids* improve water and protein balance of the skin and promote healing and biostimulation. Only amino acid is used in its pure form in some cosmetic formulations of intensive care. They are usually used in the form of protein hydrolysates. *Fatty acids* (higher-acid), are contained in animal or vegetable fats. They are prepared synthetically by the oxidation of paraffins. They are the main raw materials in the production of soap (stearic acid, palmitic acid) as well as in the preparation of surfactants. Adipic, glutamic, formic acid and thioglycolic are used as the means for hair care. Para-aminobenzoic, phenylbenzimidazole-sulfonic acids are used as a means of suntan. Boric, benzoic, salicylic acids are used as preservatives. *Esters* (product acid compound and an alcohol with the elimination of water). Fats, oil, lanolin wax belong to esters. They are used as emulsifiers, plasticizers, stabilizers. *Polysaccharides* (alginates, amylose, dextrin, chitosan) as emulsifiers and thickeners are used as the means for skin care. They are used as air conditioners in shampoos. They are used as protective and moisturizing additives in hand creams and lotions. They are used as structural components in different kinds of toothpaste. *Terpenes* are used in various cosmetic products as preservatives, fragrances and dietary supplements. They are contained in essential oils (Ylang Ylang oil contains geraniol, linalool. Lavender oil contains linalool, terpinen-4-ol. Lemon oil contains limonene, β-pinene, citral. Rose oil contains geraniol and nerol. Rosemary oil contains cineole, camphor, borneol, linalool). Thus, representatives of all classes of organic compounds are used in cosmetics.

# SYNTHESIS, STRUCTURE, AND ANALGESIC ACTIVITY OF 1-R-4-HYDROXY-2,2-DIOXO-1*H*-2λ$^6$,1-BENZOTHIAZINE-3-CARBOXYLATES

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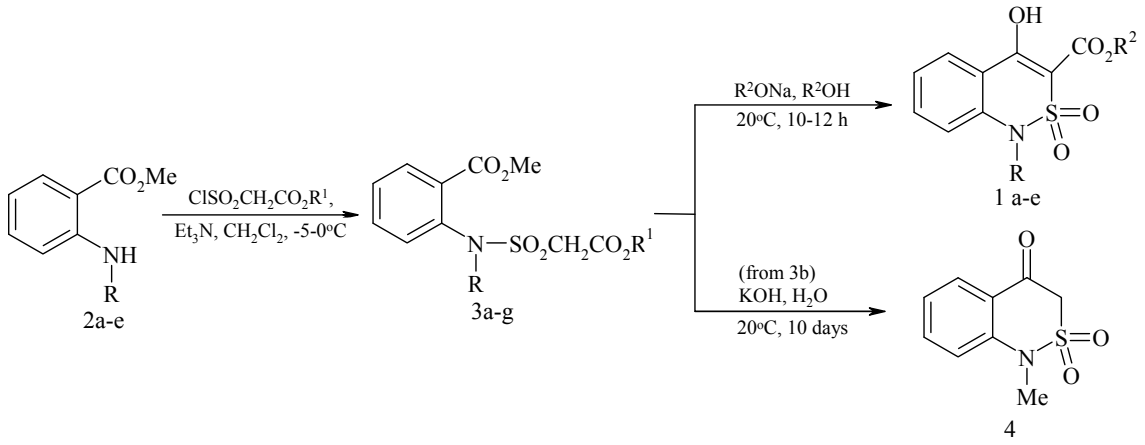
Chemical modification is the simplest and the most widely applied way of improving the pharmacological and pharmaceutical properties of biologically active substances. An interesting extension of the studies in this direction is the replacement of carbonyl in position 2 by a sulfonyl group in the molecules of oxicams to obtain 4-hydroxy-2,1-benzothiazine 2,2-dioxides and to study their analgesic activity. The results of our investigation, devoted to 1-R-4-hydroxy-2,2-dioxo-1*H*-2λ$^6$,1-benzothiazine-3-carboxylates **1**, are given in the present communication.

The synthesis of the desired alkyl-2,1-benzothiazine-3- carboxylic acids **1** was achieved by a route analogous to the preparation of the quinoline analogs , with only difference that upon acylation of methyl anthranilates **2** we used alkyl chlorosulfonylacetates instead of alkyl malonyl chlorides.




**1**–**3 a, 3f**,**g** R = H; **1**–**3 b** R = Me; **1**–**3 c** R = Et, **1**–**3 d** R = All, **1**–**3 e** R = Ph; **3 a** $R^1$ = Et, **b**,**d**–**f** $R^1$ = Me, **c**,**g** $R^1$ = *i*-Pr; **1 a** $R^2$ = Et, **b**–**e** $R^2$ = Me

The structures of the synthesized compounds were confirmed by $^1$H and $^{13}$C NMR spectroscopy. Screening investigations of the analgesic properties of esters **1a-e** were carried out on the standard model of heat-induced pain (tail-flick test) enabling judgment of the central effect on the nociceptive system.

The highest activity of all the groups of the substances studied was revealed by methyl 1-allyl-4-hydroxy-2,2-dioxo-1*H*-2λ$^6$,1-benzo-thiazine-3-carboxylate (**1d**), the analgesic effect of which (+71.1%) exceeded that of all the reference compounds used in the experiment.

# SYNTHESIS OF ARYLAMINOPOHIDNYH BASED ON THE 6-METYLTIOURATSYL

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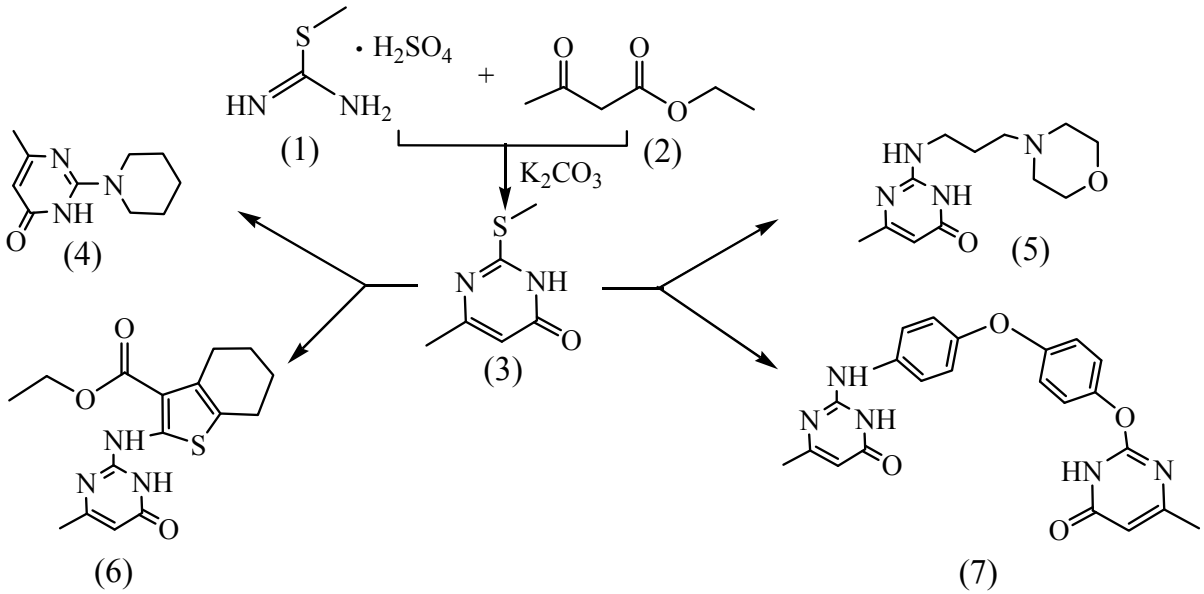
Derivatives of pyrimidine are widely distributed in nature. They are involved in many important biological processes such as nucleotides, vitamins, coenzymes, antibiotics, etc. Therefore, the synthesis of new derivatives of pyrimidine has not only scientific but also practical interest.

Synthesis of new aminopirimidonov and research of its practically useful properties is the aim of our study.

By condensation of sulfate S-methyl-iso-thiourea (1) with acetoacetic ester (2) in an aqueous solution of potassium carbonate in mild conditions obtained by us with high yield of 2-methylthio-6-metilpirimidon 4 (3).

It is shown that during melting of the last with amines by the temperature of 160–180 °C nucleophilic substitution of metyltiogroup on the fragment of corresponding amine with formation of derivatives is occurring (4–7) by the scheme:




The composition and structure of the compounds (3–7) was confirmed by elemental analysis and ЯМР $^1$H spectroscopy method.

Modeling of pharmacological activity of the synthesized compounds we have conducted with a help of computer program PASS (Prediction of Activity spectra for Substances) by v. 1.703 version.

Found that synthesized compounds can be used as building-blocks for creation of new pharmaceuticals.

# ORGANIC CHEMISTRY AS A MIRROR OF A PERSON'S LIFE

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The importance of organic chemistry in human life is very difficult to overestimate, because these processes are everywhere around us: from basic cooking and finishing to biological processes in the body.

Organic chemistry is intimately connected with medicine. Important role in medicine play a synthetic polymeric materials. They help to produce many things: from disposable syringes to artificial heart valves,various prostheses internal organs - blood vessels, esophagus, bile ducts, heart valves, etc. Plastics correct some defects of the face (replace part of the nose, the ear, the eye-sockets).

In everyday life oxalic and citric acids are often used. Oxalic acid is a part of many household chemicals that are designed to remove rust from metal or enameled surfaces. The fact that the oxalate ions $(C_2O_4)^{2-}$ - form a colorless, durable and highly soluble complexes with cations of iron. Citric acid is used as a flavouring substance in order to give the right flavor to drinks or confectionery products.

Organic chemistry also serves as a source of beauty. In the composition of cosmetic lotions, in addition to water, comprises up to 40% ethyl alcohol, and various inorganic and organic additives. Organic chemistry has already found application in the food industry. People often use essential oils, esters, some alcohols, aldehydes, ketones, hydrocarbons and various organic acids (acetic, citric, lactic, adipic, malic). In sausages monosodium salt of glutamic acid, to improve the taste is added.

Some scientists believe that the origin of life on our planet occurred in an environment consisting of carbon dioxide, ammonia, water and methane, and the first organisms get the energy for life, decomposing molecules without oxidation. Thus, the chemistry in human life is the cure for diseases, and weapons, and the economy, and cooking, and, of course, life itself.

# DE NOVO DESIGN DRUG-LIKE MOLECULES WITH POTENCIAL ANTI- ALZHEIMER'S DISEASE PROPERTIES USING METHODS CHEMINFORMATICS

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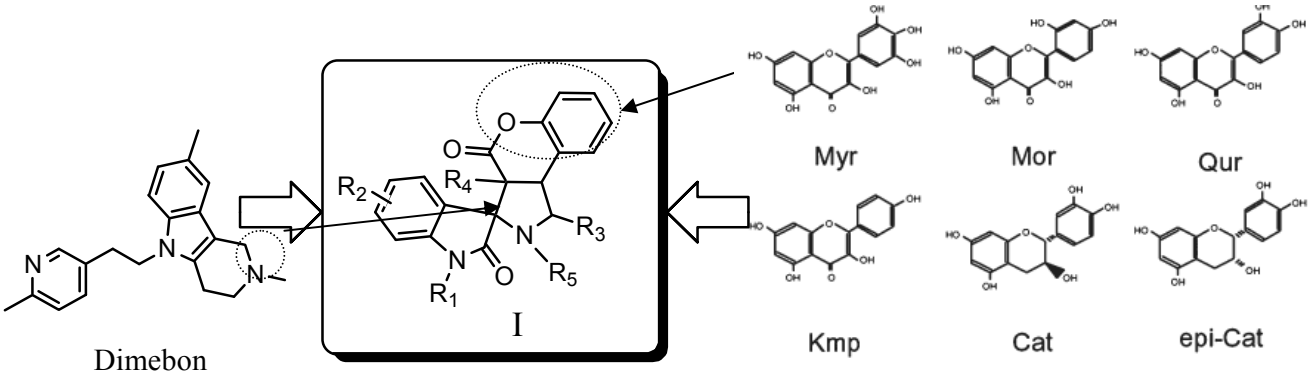
Alzheimer's disease (AD) is a progressive neurodegenerative disorder characterized by the deterioration of cognitive function and behavioral changes. Two main disease mechanism-based approaches are based on the involvement of two proteins, amyloid-β protein (Aβ) and tau. Aβ is the main constituent of senile plaques, and tau- is the main component of neurofibrillary tangles. Impairment of neuronal functions and loss of neurons Aβ is generated from APP by two proteases, β-secretase and γ-secretase. A third protease, α-secretase, which competes with β-secretase for the APP substrate, interferes with the production of Aβ. Therefore, three strategies to reduce Aβ have been proposed: inhibition of β-secretase, inhibition of γ-secretase and stimulation of α-secretase.




Recently, several studies have suggested that many kinds of natural polyphenols (myricetin (Myr), morin (Mor), quercetin (Qur), kaempferol (Kmp), (+)-catechin (Cat) and (-)-epicatechin (epi-Cat)) may have anti-amyloidogenic effects. Another promising molecule approved by the FDA for the treatment of Alzheimer's disease is known earlier $H_1$-histamine blockers Dimebon. We have tried to construct de novo drug-like molecules with potencial anti-Alzheimer's disease properties, containing both the indole moiety and the benzopyran nucleus, like natural compounds. In the first stage, we studied the QSAR for a known set of natural polyphenols using computational platform Molinspiration Cheminformatics, which allowed us to construct the correlation model to a number of molecular descriptors. In the second step, for focus screening libraries (I) in silico, predicted high anti protease activity to compounds (I) with over then 5 points of randomisation. More sensitive point is $R_5$, when $R_5$ is $CONH_2$. Thus, the proposed structures deserve attention for further research for potential anti-Alzheimer's drugs.

# SYNTHESIS AND PROPERTIES OF ASYMMETRIC UREA BASED ON THE LINURON

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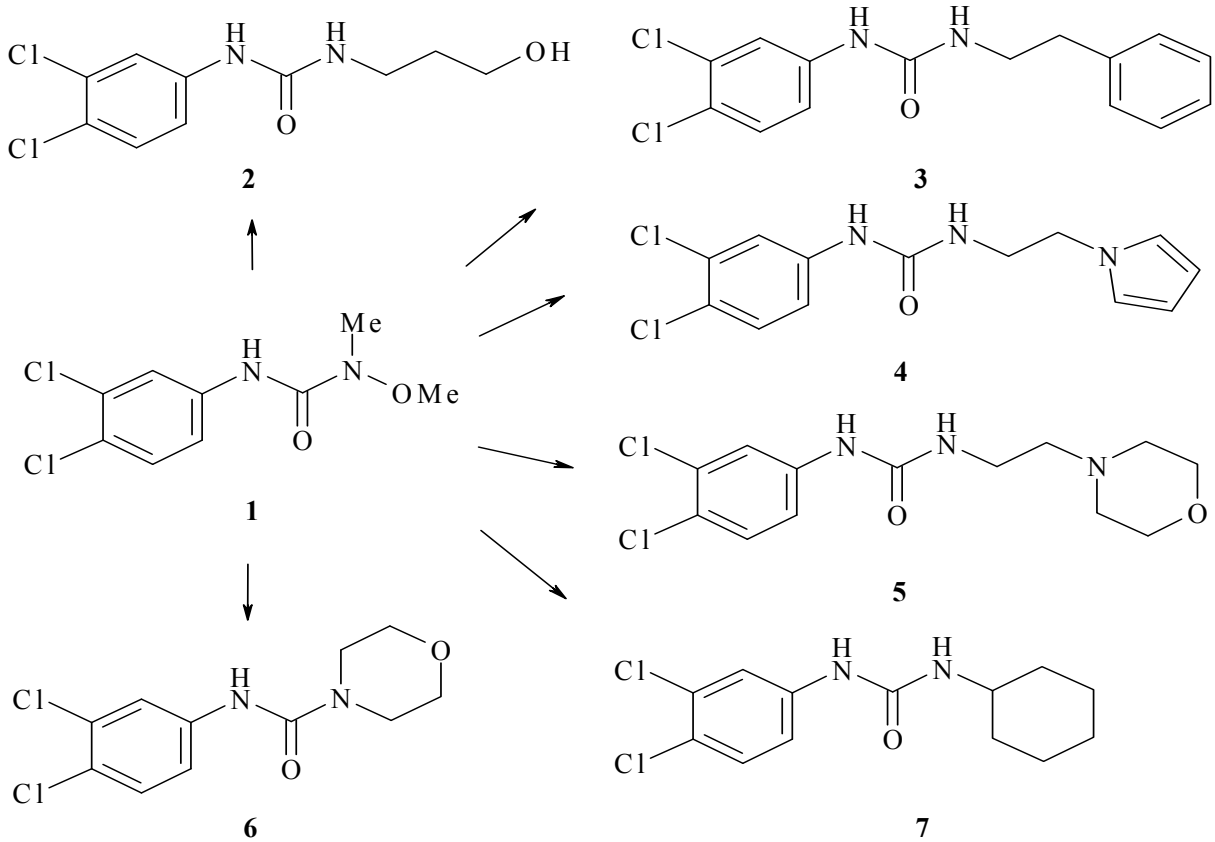
1-Methyl-1-methoxy-3-(3,4-dichlorophenyl) urea is an active substance of linuron herbicide (1). Disposal of this herbicide at the end of its shelf life requires a lot of resources. Therefore, removal of the active ingredient of the drug and its use as a feedstock to produce new biologically active compounds is a promising area of chemical research.

We have shown that these compounds (1) can react with nucleophilic substitution of primary and secondary amines with the formation of asymmetric urea (2-7) with 63-89% yields.



The composition and structure of the compounds (2–7) was confirmed by elemental analysis and ЯМР $^1$H spectroscopy method.

Modeling of pharmacological activity of the synthesized compounds we have conducted with a help of computer program PASS (Prediction of Activity spectra for Substances) by v. 1.703 version.

It is established synthesized urea can exhibit a pharmacological activity and therefore promising as building-blocks for new pharmaceuticals.

# INHIBITORS OF HISTONE DEACETYLASE (HDAC) – PROSPECTIVE EPIGENETIC DRUGS. RATIONAL DESIGN OF NEW HDAC INHIBITORS WITH 2-OXINDOLE NUCLEI AND THE FRAGMENTS OF A DICARBOXYLIC ACID USING METHODS CHEMINFORMATICS

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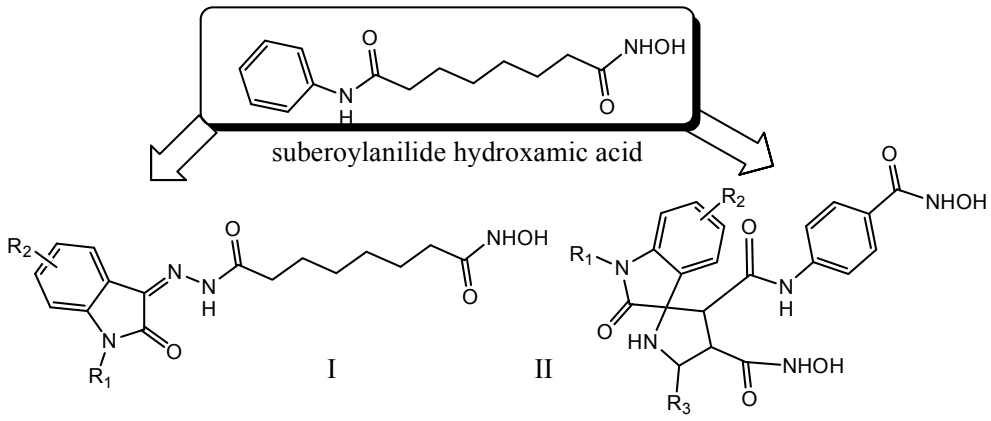
Histone deacetylase (HDAC) inhibitors are a prospective class of therapeutics with potential as anticancer drugs. The rationale for developing and de novo design HDAC inhibitors as anticancer therapies arose from the understanding that in addition to contribute to neoplastic growth. The family of HDAC inhibitors includes a range of naturally occurring and synthetic compounds. HDAC inhibitors have multiple cell type-specific effects *in vitro* and *in vivo*, such as growth arrest, cell differentiation, and apoptosis in malignant cells. Currently, there are two HDAC inhibitors that have received approval from the US FDA for the treatment of cutaneous T-cell lymphoma: vorinostat (suberoylanilide hydroxamic acid, Zolinza) and depsipeptide (romidepsin, Istodax). The aim of our work is the rational design of new HDAC inhibitors with the nuclei of 2-oxindole and dicarboxylic acid residues using techniques Cheminformatics, in particular the design of computer platforms Molinspiration Cheminformatics (University of Bratislava, Slovakia). As a promising class for the construction of new HDAC inhibitors us consider hydroxamates (e.g. suberoylanilide hydroxamic acid, Zolinza). Pharmacofore based approach as potential HDAC inhibitors we have proposed structure based on 3-N-acyl (suberoyl-, glutaroyl-, succinoyl-) hydrazones of 2-oxindole hydroxamic acid (I) and spiropyrrolidino-2-oxindoles (II). In the first stage, we studied the QSAR for a known set of hydroxamates using computational platform Molinspiration Cheminformatics, which allowed us to construct the correlation model to a number of molecular descriptors. In the second phase, two focus screening libraries I, II in silico, showed high sensitivity to compounds II. Thus, the proposed structures deserve attention for further research for potential HDAC inhibitors.



# ANTIMOCROBIAL ACTIVITY OF ETHYL 4-(ALKYLTHIO)-5-METHYLTHIENO[2,3-*d*]PYRIMIDINE-6-CARBOXYLATES

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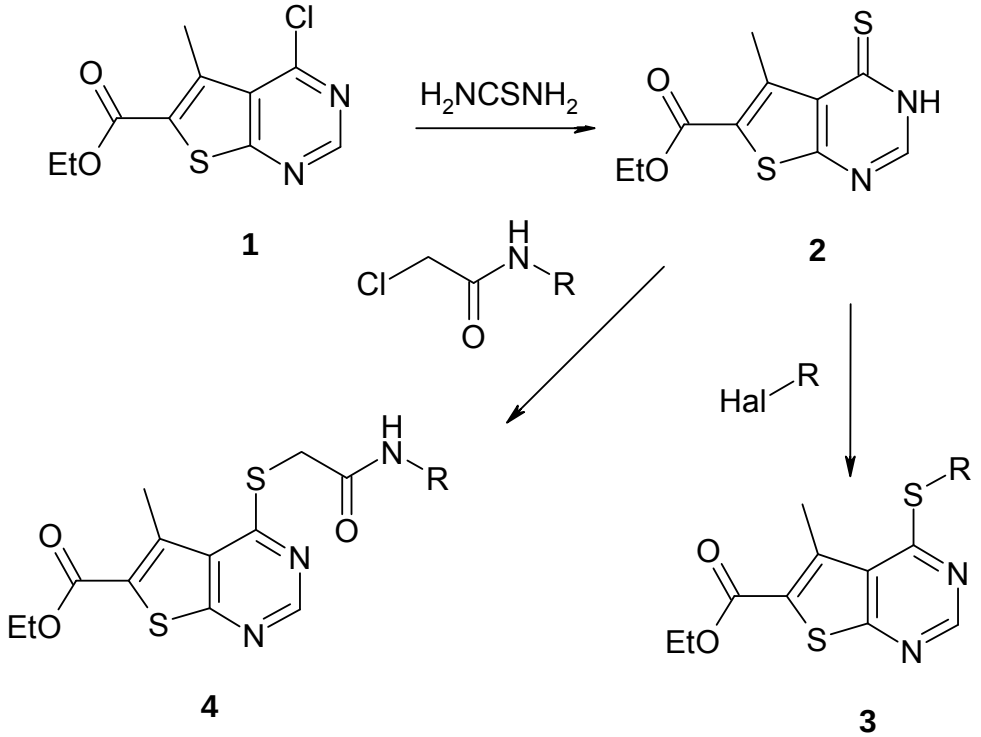
The derivatives of thieno[2,3-*d*]pyrimindine with thiol substituents are known as the compounds with antimicrobial activity. Therefore, study of antimicrobial properties for the compounds of this class is a promising approach for obtaining of novel antimicrobials. The target molecules were prepared by interaction of ethyl 5-methyl-4-chlorothieno[2,3-*d*]pyrimidine-6-carboxylate with thiourea to give the intermediate thione **2**. Further modification of the compound 2 was performed by its reaction with corresponding halides in DMF using triethylamine as the base. Then the derivatives of ethyl 4-(alkylthio)-5-methylthieno[2,3-*d*]pyrimidine-6-carboxylates **3** and **4** were studied for antimicrobial activity.




Antimicrobial activity screening was performed by agar-well diffusion method. The screening study showed that the compounds **3** and **4** are active against *Bacillus subtilis* and *Candida albicans* fungi. It was determined that the presence of benzyl radical at the position 4 sulphur atom increases antimicrobial activity of ethyl 4-(alkylthio)-5-methylthieno[2,3-*d*]pyrimidine-6-carboxylates against *Proteus vulgaris*, while the derivatives of mercaptoacetic acid at position 4 appeared to be active against the strain *Staphylococcus aureus.*

# SYNTHESIS OF 3-HYDROXYINDOLINE-2-ONES

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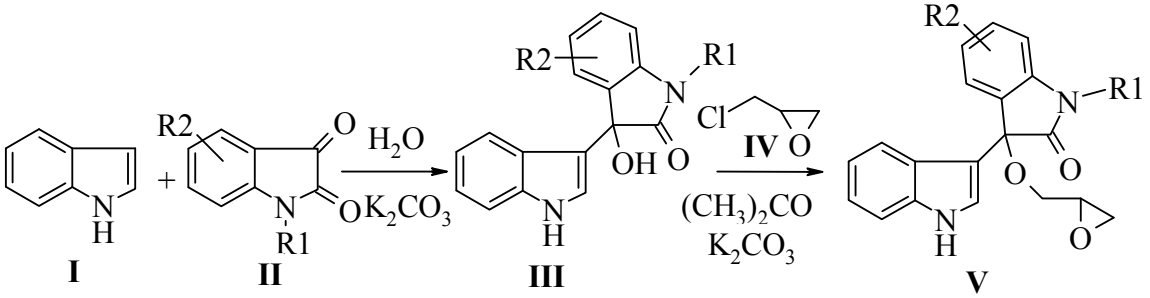
Indole core is common for wide variety of biologically active compounds. Oxindoles are particularly well-known among them due to their broad spectrum of bioactivity. Thus, oxindoles reveal antibacterial, antifungal, antitumor, analgesic, antihypoxic and other types of activities. Therefore scientists are interested in the development of new efficient ways to synthesize oxindole derivatives.

Nowadays isatin is one of lead molecules for designing oxindoles. Its' reactive keto-carbonyl group readily undergoes condensation reactions under mild conditions. Such properties give useful opportunities for developing safe and economical green chemistry methods.

To synthesize 3-hydroxyindoline-2-one the reaction of isatin (I) and indole (II) (the molar ratio 1:1) was used. As a solvent we used water. Potassium carbonate was added to the reaction mixture in a molar equivalent. The reaction proceeded under reflux (50 – 60°C) and with stirring for 4 hours.




The reaction product (III) – a light yellow amorphous precipitate – was recrystallized from water. On the average 80% yield was obtained.

Prolongation of the reaction time did not increase the yield.

Obtained 3-hydroxyindoline-2-one can be subsequently used in different kinds of reactions: O-alkylation, C-alkylation, cycloaddition reactions with aldehydes and aminoacids etc.

However the attempt to alkylate 3-hydroxyindoline-2-one with epichlorohydrin (IV) in order to obtain product V wasn't successful. The reaction was carried out under reflux (50 – 60°C), using acetone as a solvent, in the presence of potassium carbonate.

Such difficulties may occur due to the possible competitive N-alkylation reaction in the oxindole core. That's why we are interested in additional research involving N-substituted isatins.

Moreover, according to the last researches in oxindoles area, condensation cycloaddition reactions of 3-hydroxyindoline-2-one give great synthetic opportunities to create spirocyclic compounds, that are expected to possess different types of biological activity.

Consequently, synthesis of 3-hydroxyindoline-2-one derivatives remains the key purpose of our future researches.

# FORMATION OF 1-METHYL[1,2,4]TRIAZOLO[4,3-*a*]QUINAZOLIN-5(4*H*)-ONES BY REACTION OF 2-HYDRAZINOQUINAZOLIN-4(3*H*)-ONES WITH ACETYL ACETONE

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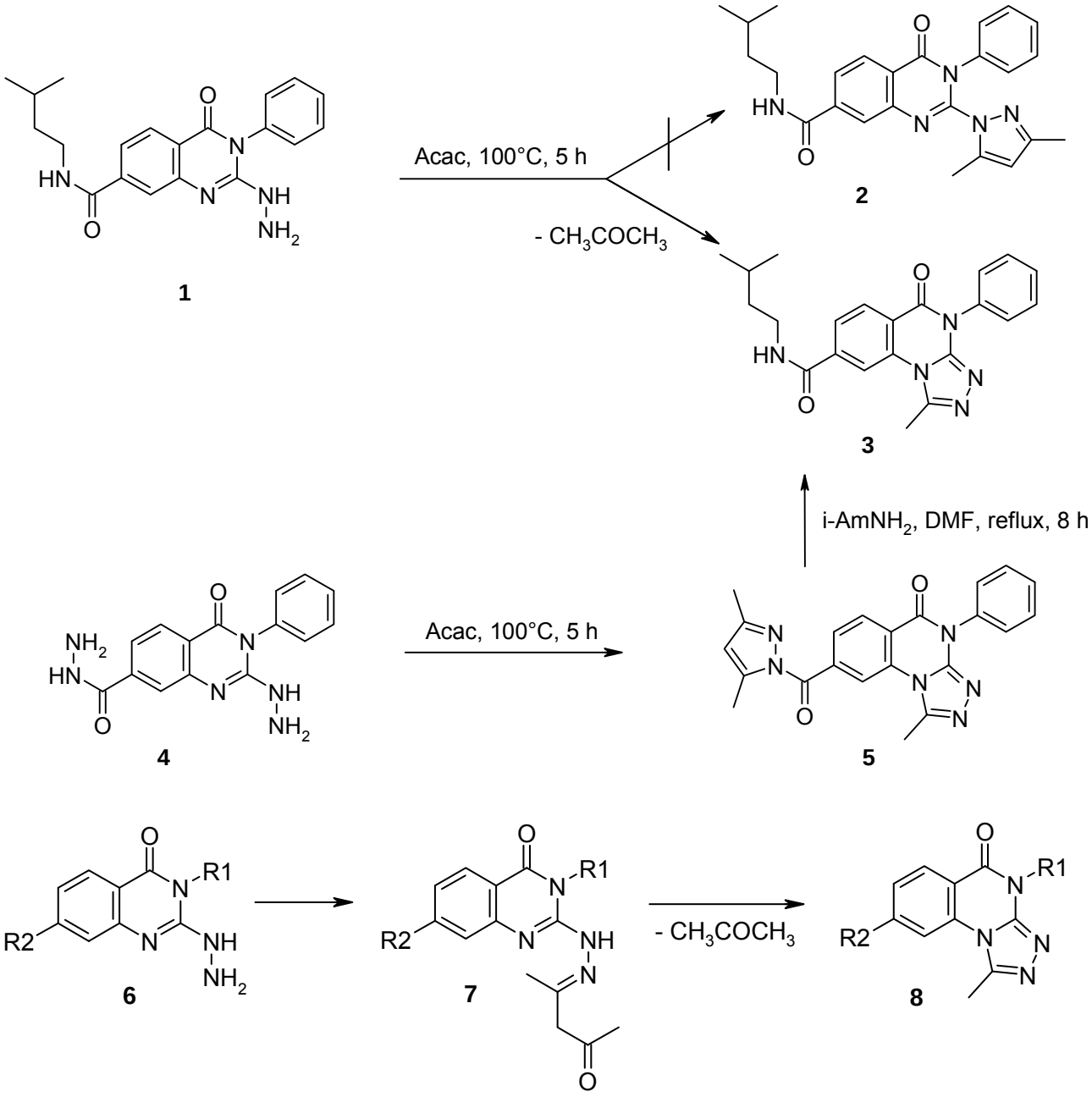
Search for innovative biologically active substances among quinazolin-4-one derivatives has apparent interest, which is due to wide range of their pharmacological properties.

Development of new effective and technological synthetic schemes both improvement of existing schemes for synthesis of various quinazolin-4-one derivatives could be useful for direct synthesis of potentially active pharmaceutical ingredients. However, despite the high practical significance of quinazolin-4-one derivatives, there are known not so much methods for their synthesis, although this class of compounds has every reason to be considered as a source of perspective molecules for applied and fundamental investigations in chemical both pharmaceutical fields.

The aim of our investigations is enhancement of assortment of biologically active substances among [1,2,4]triazolo[4,3-*a*]quinazolin-5(4*H*)-one derivatives – as potential active pharmaceutical ingredients. In continuing of our investigations in this field we studied reaction of 2-hydrazinoquinazolin-4(3*H*)-ones with acetyl acetone.

When 2-hydrazino-*N*-(3-methylbutyl)-4-oxo-3-phenyl-3,4-dihydroquinazoline-7-carboxamide **1** was refluxed in acetyl acetone during 5 hours, we obtained 1-methyl-*N*-(3-methylbutyl)-5-oxo-4-phenyl-4,5-dihydro[1,2,4]triazolo[4,3-*a*]quinazoline-8-carboxamide **3** instead of expected 2-(3,5-dimethyl-1*H*-pyrazol-1-yl)-*N*-(3-methylbutyl)-4-oxo-3-phenyl-3,4-dihydroquinazoline-7-carboxamide **2**. In analogous conditions 2-hydrazino-4-oxo-3-phenyl-3,4-dihydroquinazoline-7-carbohydrazide **4** was changed into 8-[(3,5-dimethyl-1*H*-pyrazol-1-yl)carbonyl]-1-methyl-4-phenyl[1,2,4]triazolo[4,3-*a*]quinazolin-5(4*H*)-one **5**. By reaction of pyrazolide **5** with *i*-amylamine the substitution of pyrazole group occurred with amide **3** formation.

The obtained experimental results can give assumption, that 2-hydrazinoquinazolin-4(3*H*)-ones react with acetyl acetone via acetone removal from intermediate compound **7** with formation of annelated triazole ring but not pyrazole.




The structure and individuality of synthesized compounds has been proven by elemental analysis and 1H NMR spectroscopy data. The structure of 1-methyl-*N*-(3-methylbutyl)-5-oxo-4-phenyl-4,5-dihydro[1,2,4]triazolo[4,3-*a*]quinazoline-8-carboxamide **3** was confirmed by LCMS data in addition.

Our preliminary estimation of biologic activity of their compounds by computer program PASS showed the perspectivity of investigations for searching of new biologically active substances of diversified action with lower toxicity among quinazolin-4-one derivatives with annelated heterocyclic rings.

**SYNTHESIS OF QUATERNARY SALTS ON THE BASIS OF ISONIAZID**

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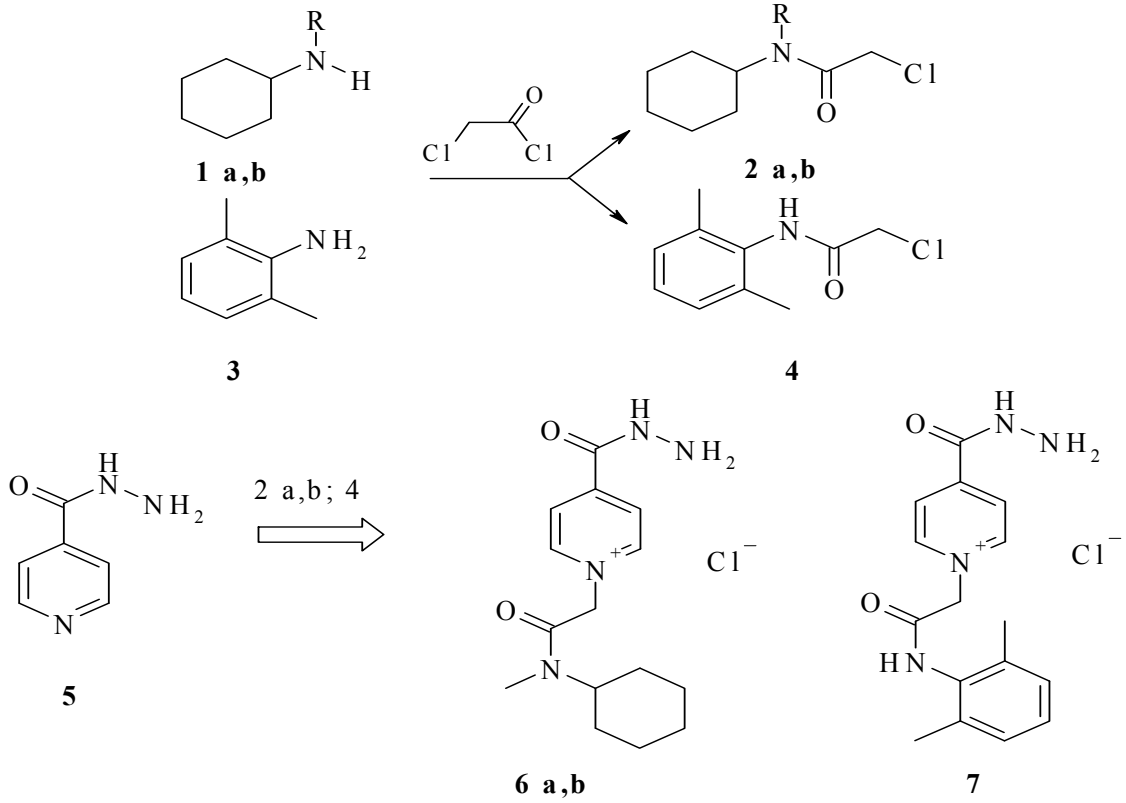
Isoniazid is an effective means for treatment of active tuberculosis. Therefore, the synthesis and study of derivatives of isoniazid is a promising area of research.

By interaction of both aliphatic (1a, b), and aromatic (3) amine with hloratsetylhloryd in the environment of dry ortho-xylene we carried out the synthesis of appropriate hloratsetanilid (2a, b; 4). With the help of condensation of the last with isoniazid in the environment of polar solvents obtained corresponding quaternary salt (6a, b; 7).




The composition and structure of the compounds (2–7) was confirmed by elemental analysis and ЯМР $^{1}$H spectroscopy method.

Conclusion about the direction of the alkylation of pyridine nitrogen atom is done by analyzing the PMR spectra of the reaction products.

Modeling of pharmacological activity of the synthesized compounds we have conducted with a help of computer program PASS (Prediction of Activity spectra for Substances) by v. 1.703 version.

Found that synthesized compounds can be used as building-blocks for creation of new pharmaceuticals.

# OPTIMIZATION OF N-*R*-1*H*-2,1-BENZOTHIAZIN-4(3*H*)-ON 2,2-DIOXIDES SYNTHESIS

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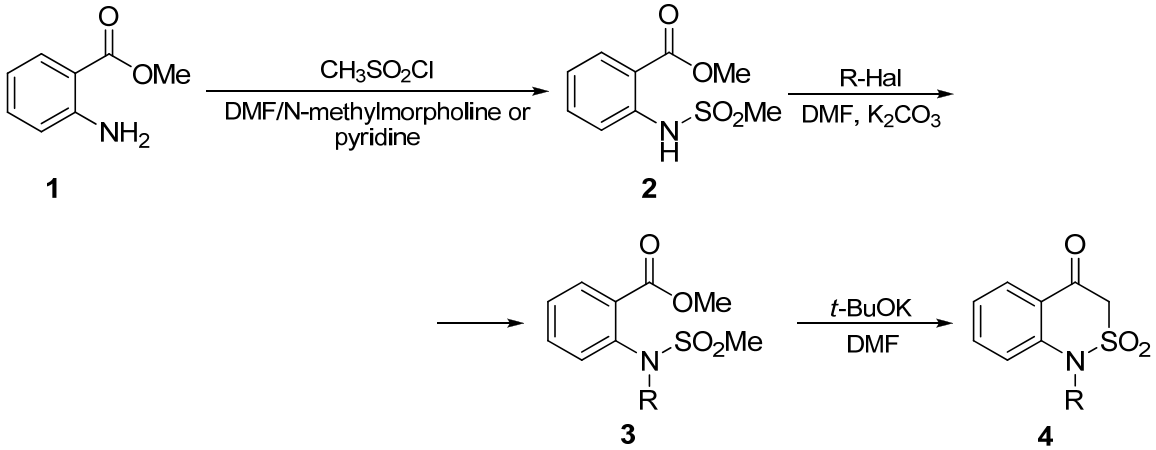
Compounds containing benzo[c][2,1]thiazine-4-on 2,2-dioxide core have attracted a great attention of scientists for a long time. This is due to the fact that among derivatives of this heterocyclic system biologically active compounds (BAC) for the treatment of various diseases (primarily, inflammatory processes, pain syndrome and bacterial infections etc.) were found. Moreover, benzo[c][2,1]thiazine-4-on 2,2-dioxide core is bioisosteric to the benzo[e][1,2]thiazine-4-on 1,1-dioxide one, which is a base of well-known analgesic and anti-inflammatory agents, such as Piroxicam®, Droxicam® and Meloxicam® and its heteroanologues, namely Tenoxicam® and Lornoxicam®.


The techniques, which are used in synthesis of organic compounds, allow to obtain different BAC based on simpler precursors. However, despite of the significance evolution of organic chemistry methods, development of new efficient approaches for synthesis BAC is the actual task of medical chemistry as well as the methodology of organic synthesis.

The synthesis of the initial N-R-*1H*-2,1-benzothiazin-4(*3H*)-on 2,2-dioxides **4** were described in the literature, and included esters of anthranilic acids **1** as initial compounds. We have improved methods which are present in literature. It allowed us to obtain the pure target compounds **4** with better yields in a shorter time.




The structure and purity of target compounds **4** were confirmed using the $^1$H NMR spectra.

# STRATEGY OF SEARCH FOR POTENTIAL ANTIMICROBIAL COMPOUNDS AMONG MAGNESIUM AND ALUMINIUM SALTS OF NITROSUBSTITUTED OF N-PHENYLANTHRANILIC ACIDS

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Recently, a number of publications devoted to the problem of medical complications in the treatment of viral and bacterial diseases of different etiologies. Mainly this associated with the appearance of strains of microorganisms specific resistant to medicines which are presented in a wide range in the pharmaceutical market.

One of the alternative ways to eliminate those described deficiencies is introduction to the structure of substance some biometals, such as copper, magnesium, calcium, zinc, aluminum and others.

Research of many years, carried out by scientist's community of medical and biological departments of National University of Pharmacy, has shown a promising of receiving of potential antimicrobial agents based on derivatives of N-phenylanthranilic acids, which included various pharmacophores. Proposed pharmacophores in many cases exhibit optimization, synergy and expand the range of pharmacological effects of both compounds. This allows us to offer this approach to resolving the issue of possible treatment viral and bacterial diseases.

Based on the experience of previous studies, we have synthesized magnesium and aluminum salts of 5-nitro- and 3,5-dinitro-N-phenylantrhanilic acids.

The synthesized compounds was identified with the methods of $H^1$-, IR-, UV-spectroscopy and thin layer chromatography.

The level of microbiological activity was determined by two-time serial dilutions in meat's broth of neutral medium using the daily culture of these microorganisms: Staphylococcus aureus ATCC 25923, Bacterium subtilis ATCC 66337, Echerichia coli ATCC 25912, Pseudomonas aeruginosa ATCC 78857. As reference preparation using the solutions of ethacridine lactate of different concentrations.

Also for obtained compounds was determined an acute toxicity ($DL_{50}$) by the method of intraperitoneal injection.

The synthesized compounds revealed antimicrobial activity at a concentration of 15.6 - 62.5 mg/ml.

The toxicity of which in experiment was over 2000 mg/kg, and for toxicological classification relating to low-toxic compounds.

# SYNTHESIS, METHODS OF ANALYSIS AND BIOLOGICAL ACTIVITY OF 6-NITRO-N-(2'-CARBOXY-4'-BROMOPHENYL)ANTHRANILIC ACID

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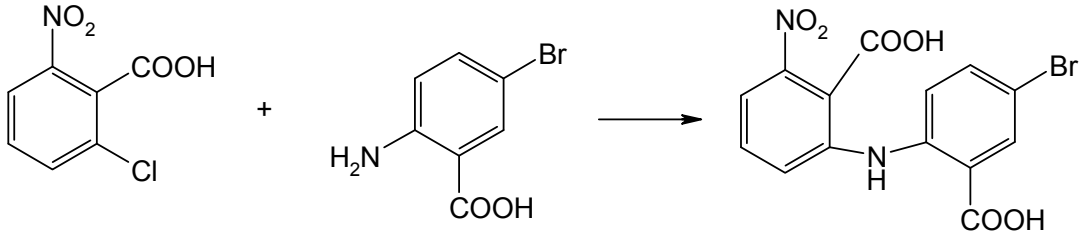
The most important task of pharmacy is to create a highly effective and non-toxic drugs. The group of aromatic acids, in particular N-phenylanthranilic acids and their derivatives, is promissing chemical scaffolds for drugs development; effective medicines have been created on their basis (mefenamic and flufenamic acids, and their salts, diphtorant, antral etc.). Besides the significant biological activity N-phenylanthranilic acids also show a high chemical reactivity due to the presense of carboxyl and secondary amino groups, and it gives possibility to obtain their diverse functional derivatives with new pharmacological properties.

6-Nitro-N-(2'-carboxy-4'-bromophenyl)anthranilic acid has been chosen as an object for our research.

6-Nitro-N-(2'-carboxy-4'-bromophenyl)anthranilic acid (3) has been synthesized by the reaction of 2-chlor-6-nitro-benzoic acid (1) with 5-bromanthranilic acid (2) in the presence of the CuO and $K_2CO_3$ as catalysts and at temperature 180-200$^oC$:

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The structure of the synthesized compound was confirmed by elemental analysis, IR, UV, $^1$H-NMR spectroscopy, and their purity was proved by thin-layer chromatography.

Identification for this substance has been proposed using UV-spectrophotometry and chemical methods. The method of alkalimetry has been chosen for assay of the compound.

It has been found experimentally that the synthesized acid possess anti-inflammatory, analgesic, diuretic, antifungal activities. The substance exhibits low toxicity ($LD_{50}$ in mice > 6500 mg/kg).

The conducted researches show promising results in search of biologically active compounds among derivatives of 6-nitro-N-phenylanthranilic acid.

# SYNTHESIS OF THE NEW DERIVATIVES OF 3-MERCAPTO-4-R-5-R$^1$-METHOXYPHENYL-1,2,4(4*H*)-TRIAZOLE

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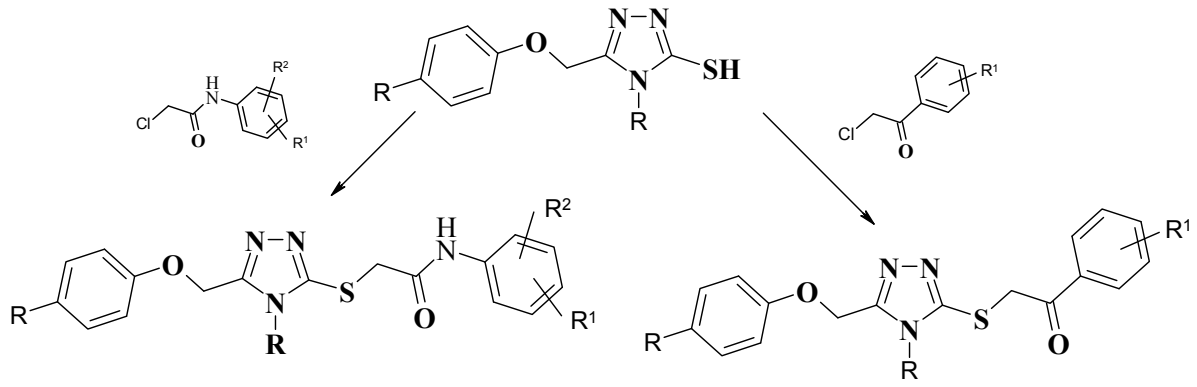
*Purpose*. The work devoted to the synthesis of new compounds the derivatives of 1,2,4(4*H*)-triazole and the study of their antiulcer activity.

*Materials and Methods.* Synthesis of new potential biological active substances on the base of 3-mercapto-4-R-5-R$^1$-methoxyphenyl-1,2,4(4*H*)-triazole has been carried out. Finished products have been obtained by the interaction of 3-mercapto-4-R-5-R$^1$-phenoxymethyl-1,2,4-triazole (4*H*) with corresponding chloroacetanilides or cloroacetophenones at standard alkylation conditions(Scheme 1)

Scheme 1



Target products have been obtained with satisfactory yields. Structure of substances synthesized have been proved by elemental analysis and NMR spectra, the purity was confirmed by the method of thinlayer chromatography. All spectra of the compounds synthesized are characterized by the presence of signals of two methylene groups. The signals of these groups were identified in accordance with the electronegativity of adjacent functional groups: at 5,22-5,32 ppm - $OCH_2$; at 5,13-5,19 ppm - $SCH_2$. The signals of aromatic protons in most cases overlap each other and are in the form of complex multiplets. The computer prognosis of biological activity spectrum of all new compound by program PASS has set that the several acetophenones are able to show the antiulcer activity (activity indexes of compounds are in the range of 0.5 to 0. 7) and antihelicobacter activity (activity indexes of compounds are in the range of 0.6 to 0. 7). Pharmacological screening for antiulcer activity has been carried out.

*Results and conclusions.* New derivatives of 3-mercapto-4-R-5-R1-methoxy-phenyl-1,2,4(4H)-triazole were synthesized. The structure of the compounds obtained was proved by methods NMR-spectroscopy. Prognosis of pharmacological activity has showed high possibility of antiulcer activity for the acetophenones. Data of primary pharmacological screening have proved the computer prognosis data.

# DESIGN AND SYNTHESIS OF NEW TRIAZOLOPYRIDINE DERIVATIVES

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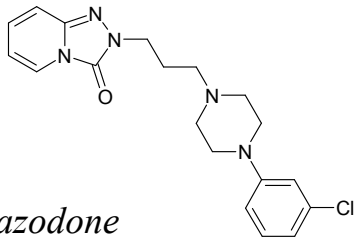
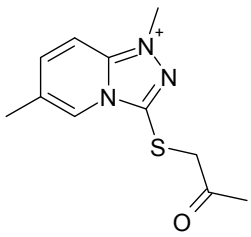
Triazolopyridines have not been studied enough especially concerning their physiological action. However it is known that the compounds with triazolopyridine-fragment possess a wide range of biological activities and are widely used in medicine. There are known analgesic, anti-inflammatory, antibacterial, antiviral, antihypertensive, antitumor, cardiovascular effects. Trazodone (antidepressant drug) is the most well-known representative of compounds which contain 1,2,4-triazolo[4,3-a]pyridine core.

Antidepressant

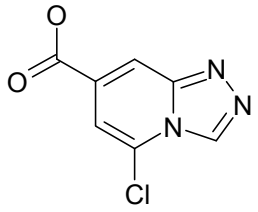


*Trazodone*

Factor XIIIa inhibitors



Mediator Release inhibitors



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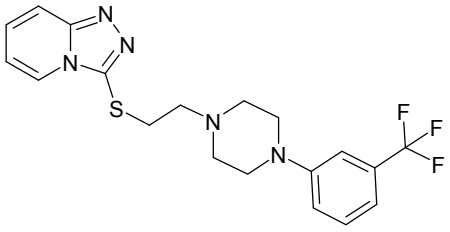

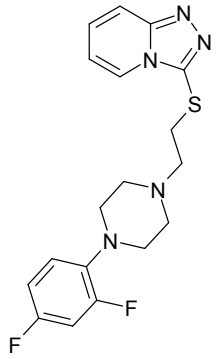

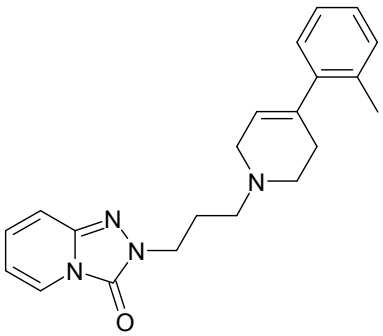

We have generated chemical space for new triazolopyridine derivatives. The designed libraries are intended to be used for different targets to treat different diseases. Some derivatives were synthesized in order to validate the chemistry. They were described by several techniques including H-NMR, C-NMR, mass-spectrometry to confirm their structural characteristics. Apart from triazolopyridine moiety our compounds contain different interesting functional groups and pharmacologically active fragments. We anticipate that these will provide interesting biological activities. Further advances of this strategy in the synthesis of small molecules and medicinal chemistry programs will be reported.

# SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF 3-(2-METHYL-4-OXO-1,4-DIHYDROQUINOLIN-3-YL)PROPANOIC ACID AND THEIR DERIVATIVES

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Antimicrobial resistance is widely considered to pose one of the greatest risks to modern medicine faced by this generation. The World Health Organization (WHO) defines antimicrobial resistance (AMR) as resistance of a microorganism to an antimicrobial medicine to which it was originally sensitive. For now the leading scientists with great concern warn the public and governments around the world about the problems that may face humanity in the near future due to increasing resistance of microorganisms. Professor Dame Sally Davies described this problem as a "ticking time bomb" and the antibiotics resistance has been characterized by him vividly and capaciously "as a big risk as terrorism".

Fluoroquinolones are successful broad-spectrum antibacterial agents, which mechanism of action is based upon of inhibition bacterial growth by blocking the enzymatic action of type II topoisomerases such as DNA gyrase and topoisomerase IV according structure activity relationship (SAR)(Fig. 1).

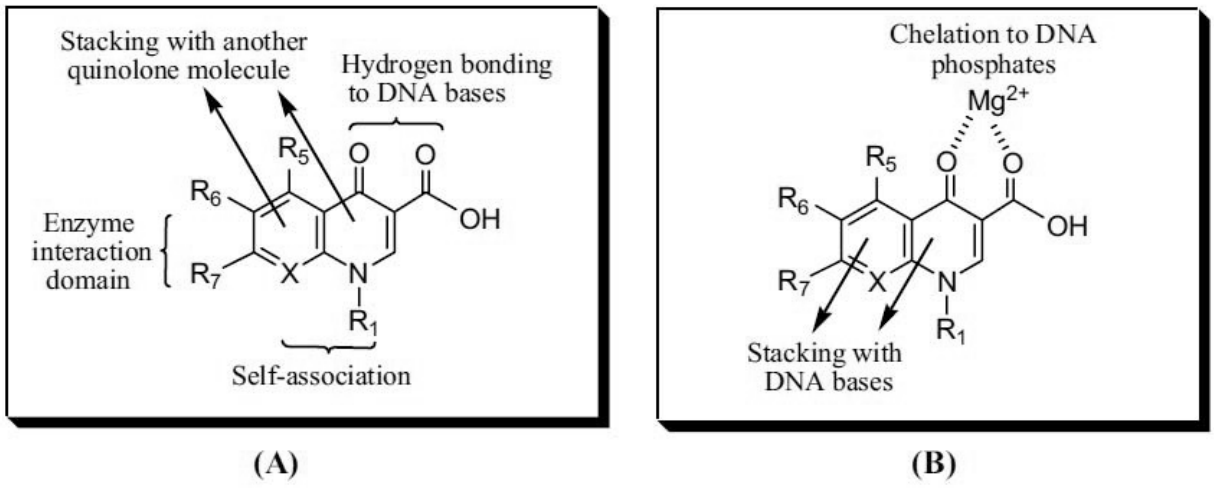



**Figure 1.** Structure activity relationship (SAR) of fluoroquinolone antibiotics.

In order to search new original antibacterial agents, the series of 12 compounds which are derivatives of 3-(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl)propanoic acid with general formula (Fig.2), has been synthesized :

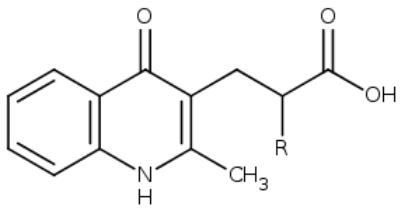
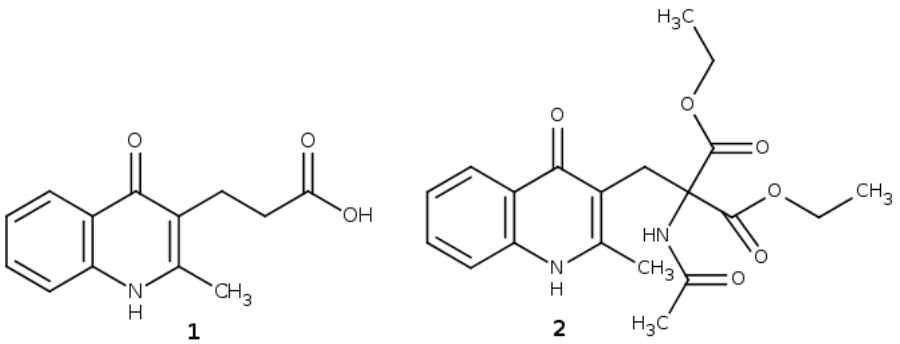



**Figure 2.** General formula of 3-(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl)propanoic acid derivatives.

The study of the antimicrobial properties of these compounds has showed that some members of this class have been exhibited a wide spectrum action. It was found, that the most active substances are 3-(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl)propanoic acid **(1)** and 1**,**3-diethyl 2-acetamido-2-[(2-methyl-4-oxo-1,4-dihydroquinolin-3-yl)methyl]propanedioate **(2)**:




Thus, carried study has shown the prospectivity and reasonability of development of this direction of throughput search of novel effective antimicrobial medicines.

# FROM THE HISTORY OF CARBOXYLIC ACIDS RESEARCH

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Carboxylic acids as a class of organic compounds have become well-known for people since ancient times.

The first mention of the practical usage of acetic acid, that was a product of the fermentation of wine, refers to the III century B.C. Greek scientist *Theophrastus* was the first to describe the effect of wine vinegar on metals: it was leading to the formation of some pigments for art purposes. Vinegar was also used to produce white lead and verdigris (green mixture of copper salts that contained copper acetate). In the VIII century Arab alchemist *Jabir Ibn Hayan* obtained concentrated acetic acid by distillation for the first time. But during the Renaissance for this purpose the sublimation of some metal acetates (was widely spread (copper (II) acetate was mainly used). Although chemists have wrongly considered that these two ways lead to the different substances. The identity of the obtained acids was proved only in the XVI century by the German alchemist *Andreas Libaviusom* and the French chemist *Pierre Auguste Ada.*

Medieval chemists continued studies in the carboxylic acids area. In XV-XVI century yatrochemists developed a method of crude dry distillation. Therefore tartaric acid from tartar, succinic acid from succinite (amber) and benzoic acid from benzoin (incense) were obtained.

In the XVII century there were already known such common trivial names for the simplest carboxylic acids: acetic acid, butyric acid, adipic acid, phthalic acid.

Formic acid was isolated for the first time in 1671. English naturalist *John Ray* obtained it by using red wood ants. This fact explains the compound name: Formica is a generic name for those insects. Then formic acid was also found in the needles, nettles, fruits, bee's corrosive secretions. So that was a period when carboxylic acids were mainly isolated from plants or other nature resources.

But in the middle of the XVIII century the most important organic acids (oxalic, citric, malic, gallic) were obtained by chemical synthesis. In 1762 *Andreas Sigismund Marggraf,* German chemist, described the differences between mineral and vegetable acids. Pharmacist and chemist *Carl Wilhelm Scheele* investigated tartaric, citric, oxalic, malic, lactic and uric acids during the period from 1776 to 1785.

XIX century was notable because of many significant achievements in the organic acids investigation. French chemist *Michel Eugène Chevreul* obtained butyric acid in 1817. *Edmond Frémy* discovered oleic and palmitic acids in 1840.

Next in 1838 the salicylic acid was found out. It was isolated from willow bark by Italian chemist *Raffaele Piria* and then synthesized as well. In 1846 the amino-acids was obtained by the reactions of the hydroxyacids.

Moreover, *Adolph Wilhelm Hermann Kolbe* synthesized typical carboxylic acid – acetic acid – using charcoal, sulfur, chlorine and water as starting materials (1845). Together with *Edward Frankland* he also obtained propionic acid by saponification of ethyl cyanide (1847). This research resulted in discovering one of the general methods of the carboxylic acids preparation.

Through this time next compounds were also synthesized for the first time: maleic acid by distillation of malic acid (*Lassen*, 1819), oxalic acid from cyanogen (*Friedrich Wohler*, 1824), benzyl acid (*N.N. Zinin,*1842,), formic acid from water and carbon monoxide (*Pierre-Eugene-Marcellin Berthelot,* 1855), isobutyric acid (*V.V. Markovnikov*, 1865). Markovnikov has also discovered that butyric and isobutyric acids have the same molecular formula ($C_4H_8O_2$), but different structural formulas; i.e., they are isomers.

The German chemist *Justus von Liebig* determined the structure of benzoic acid (1832). *Auguste Laurent*, a French chemist, investigated phthalic acid properties (1836). In 1879 *V.V. Markovnikov* and *G.A. Krestovnikov* synthesized the first carboxylic derivative of alicyclic hydrocarbons – cyclobutanedicarboxylic acid.

Also *Adolph Wilhelm Hermann Kolbe* synthesized salicylic acid in 1860. And then in 1861 he obtained formic acid by the reaction of carbon dioxide with the phenolates of alkali metals (Kolbe-Schmitt reaction is well-known nowadays for the salicylic acid preparation).

Then methods of carboxylic acids functional derivatives obtaining were developed. For example, the reaction of phosphorus pentachloride with carboxylic acids was investigated (*Auguste Andre Thomas Cahours,* 1846). *Alexander Williamson* studied the mechanism of esterification reactions, and in 1851 found out that sulfuric acid with ethanol gives ethylsulfuric acid, which then reacts with an alcohol with the ether formation. In 1881 *August Wilhelm Hofmann* discovered the rearrangement of acid amides to the primary amines.

Furthermore *Max Conrad* and *Carl-Gustav Bischof* developed common methods of synthesis based on natriummalonic ether (1880). Together with German chemist *Gutzeit M.* they discovered condensation reaction of substituted malonic esters with urea. All these methods are widely used in modern organic chemistry.

# SYNTHESIS AND PROPERTIES OF DERIVATIVES OF TIOANALOHIV OF PURINE

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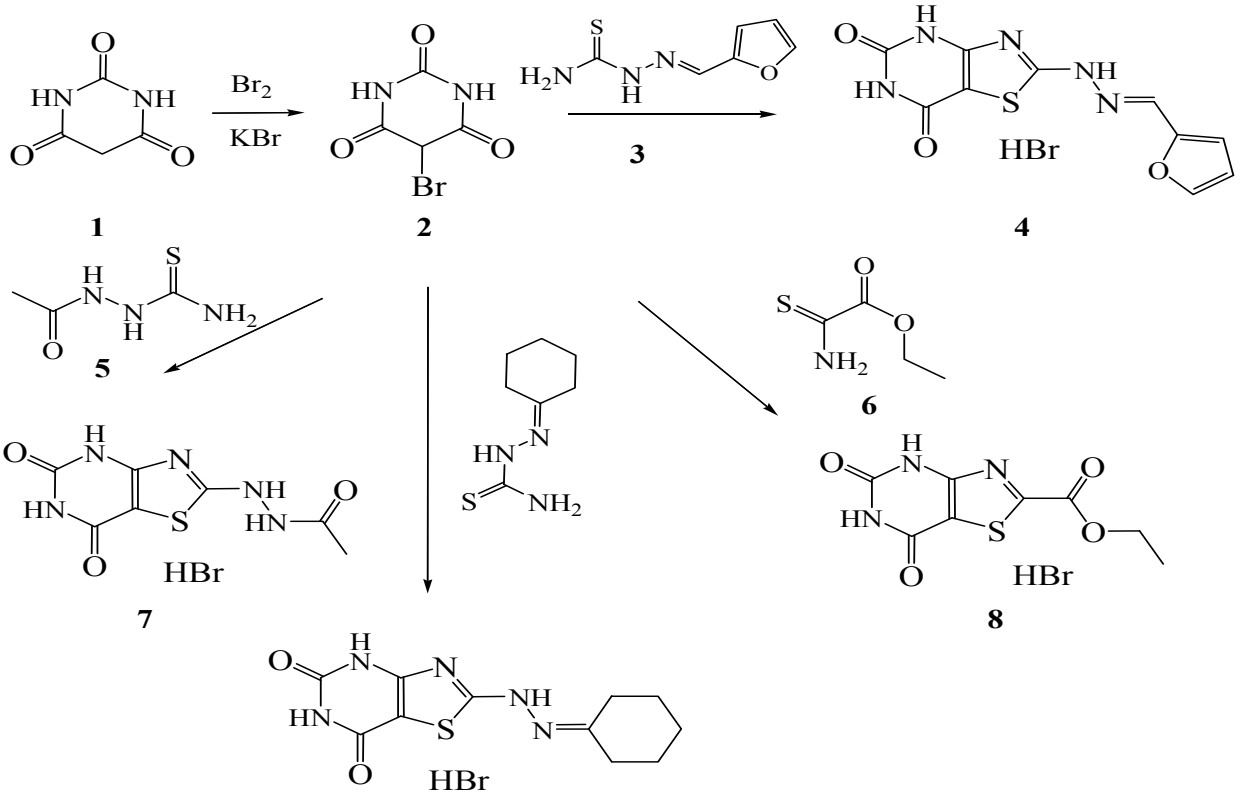
5-disubstituted derivatives of barbituric acid (or barbiturates) are widely used as medicines. Therefore, the synthesis of new derivatives of barbituric acid has not only scientific but also practical interest.

Synthesis of new derivatives of barbituric acid and research of its practically useful properties is the aim of our study.

We obtained the bromine barbiturate by Bromination of barbituric acid in aqueous solution (2), which during the interactions with thiourea form condensed compounds (4-9) by the scheme:



The composition and structure of the compounds (4-9) was confirmed by elemental analysis and ЯМР $^1$H spectroscopy method.

Modeling of pharmacological activity of the synthesized compounds we have conducted with a help of computer program PASS (Prediction of Activity spectra for Substances) by v. 1.703 version.

Found that synthesized compounds may be promising for finding of new pharmaceuticals.

# KHOTINSKIY EUGENIY SEMENOVICH AND HIS PYRROLE CHEMISTRY CONNECTED RESEARCHES

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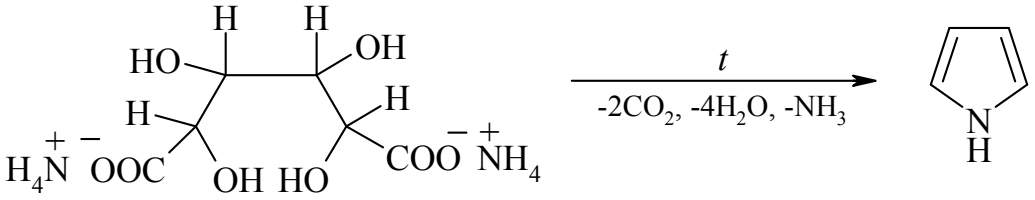
Khotinskiy Eugeniy Semenovich (1877-1959) is well-known organic chemist, the first Head of the Organic Chemistry Department of Kharkiv Pharmaceutical Institute (1925-1941) and Kharkiv State University (1929-1959). Also he was the Head of the Laboratory of Chemistry in the Organic Synthesis Research Institute.

In 1904 Khotinskiy graduated from the Faculty of Science at the University of Geneva with a Bachelor Degree of Physical and Natural Sciences. Then he performed scientific research named «Bromination and reduction of pyrroles», and received his Doctor Degree in Physical Sciences (specialization – Chemistry). After that E.S. Khotinskiy started working together with the famous chemist A. Pictet.

At that time Khotinskiy began his experimental scientific research in the pyrrole chemistry area. He studied pyrrole and its derivatives, and most of his work results later became classical. He investigated the mechanism of pyrrole formation by the distillation of the diammonium salt of mucic acid. Moreover, he developed methods of different possible pyrrole transformations: hydrogenation, halogenation, nitration. Together Pictet and Khotinskiy synthesized mix anhydrides of nitric acid and acetic acid.




ammonium salt of mucic acid — pyrrole

The results of this research work in the area of pyrrole chemistry were published in the book «Об образовании пиррола и некоторых его производных из слизевоаммонийных солей» /Евгений Семенович Хотинский – Харків: Б. и., 1914 . – 9 с. – Отд. отт. из «Трудов Общества физико-химических наук при Харьковском университете», Т. 42, 1914 г.

Pyrrole formation method, which was proposed by Khotinskiy, is still specific and classical one. It's described at all textbooks connected with heterocyclic chemistry.

# DESIGN AND SYNTHESIS OF COMBINATORIAL LIBRARIES OF [1,2,4]TRIAZOLO[4,3-*a*]PYRAZINES

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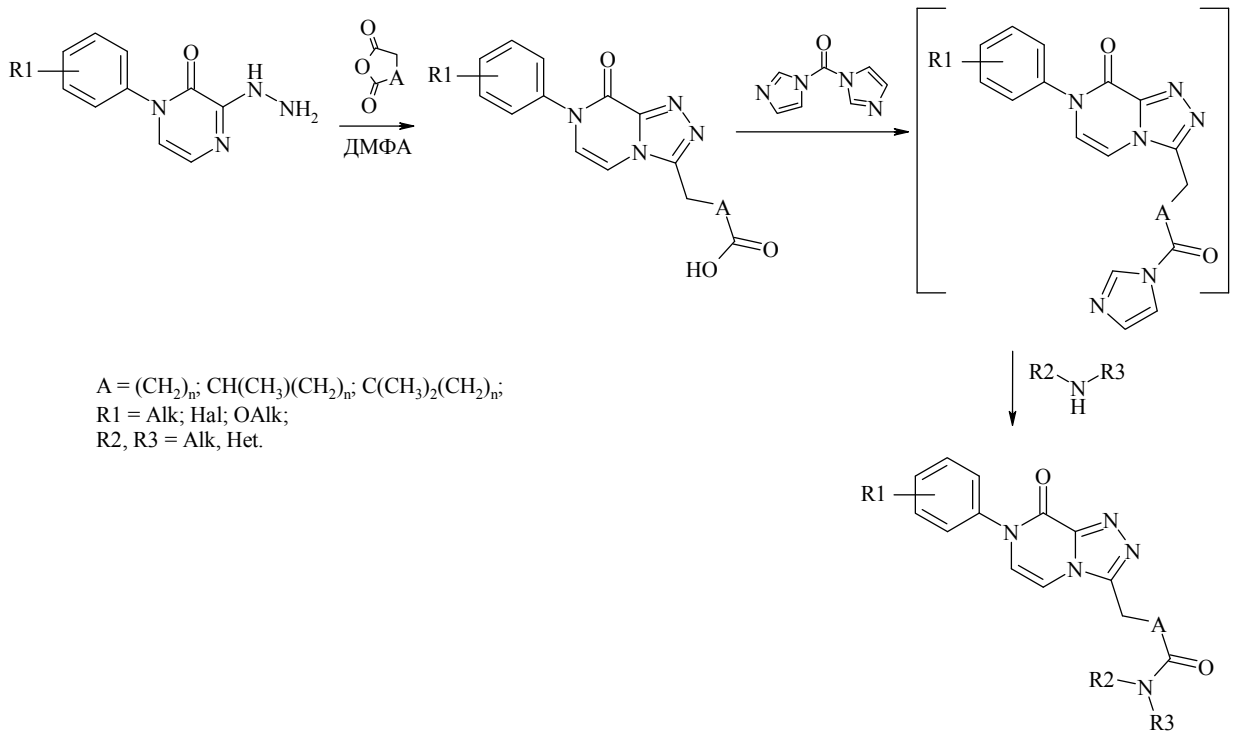
Rational design of libraries based on condensed heterocyclic systems is one of the priority areas of medical chemistry. Compounds that combine the structure of polynitrogen heterocycles and field containing conformationally mobile substituents, making them potential pharmacological rather high, are attracted the attention of scientists.

The aim of this work was the construction of combinatorial libraries based on $N^7$-aryl-ω-(8-oxo-7,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrazin-3-yl)alkyl-carboxylic acids derivatives.

Initial *building-blocks* – $N^1$-substituted 3-hydrazinopyrazin-2-ones were obtained on the basis of esters of *N*- substituted oxalamic acids. Synthesis of $N^7$-aryl-ω-(8-oxo-7,8-dihydro[1,2,4]triazolo[4,3-*a*]pyrazin-3-yl)alkylcarboxylic acids was performed by reacting of the corresponding $N^1$-substituted 3-hydrazinopyrazin-2-ones with cyclic anhydrides in the ratio 1:4 in an environment of anhydrous dimethylformamide. The systematic series of amides $N^7$-aryl-ω-(8-oxo-7,8-dihydro-[1,2,4]triazolo[4,3-*a*]pyrazin-3-yl)alkylcarboxylic acids was synthesized using carbonyldiimidazole as activator:




A = $(CH_2)_n$; $CH(CH_3)(CH_2)_n$; $C(CH_3)_2(CH_2)_n$;
R1 = Alk; Hal; OAlk;
R2, R3 = Alk, Het.

The structure of the compounds was obtained confirmed by $^1$H NMR spectroscopy and elemental analysis.

# SYNTHESIS AND ANTIMICROBIAL ACTIVITY OF SILVER NANOPARTICLES COATED BY SYNTHETIC HUMIC SUBSTANCES

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The silver nanoparticles (AgNPs) are the most effective form of silver preparations due to their ability to release silver ions and create constant ionic background. The antibacterial activity of AgNPs is result of the interaction of silver ions with the three main components of the bacterial cell: the peptidoglycan cell wall and plasma membrane, bacterial DNA and bacterial proteins, particularly enzymes.

However, it is stated that the therapeutic properties of nanomaterials essentially depend from nature of external stabilizing cover. It is known that synthetic humic substances (HSs) have also antimicrobial properties. The result of their chelating and surface-activity affects the nutrient status and cell wall integrity of the micro-organism. As a result, a synergistic effect increases therapy abilities of the metal colloids.

The aim of this work was to study the antimicrobial action of AgNPs coated by various types of synthetic HSs.

The synthetic fulvic acids were prepared by oxidative polymerization reaction of catechol or hamatoxylin with molecular oxygen in the presence of alkali at stated temperature. The synthesis of synthetic humic acids (HA) were performed by the procedure involving three steps: 1) preparation of a nitrogen-containing oligomer by condensation of urotropine with catechol; 2) oxidation of the obtained product with molecular oxygen in alkaline solution; 3) precipitation of the synthetic HA adding with stirring a concentrated HCl solution to pH = 1.5. The product was separated from the supernatant by vacuum filtration, washed with water to neutral reaction for chloride ions, and dried at 80°C.

Stable aqueous dispersions of AgNPs were prepared by chemical reduction of $Ag^+$ ions using the synthetic HSs in the presence of NaOH. The synthetic HSs are the product of oxidation reaction, characterized by a defined reduction capability that exceeds amount of natural HA. The HSs due to presences of carbonyl, carboxyl and phenols in their structure initially reduce the $Ag^+$ ions to $Ag^0$ atoms and then are adsorbed on the surface of the growing AgNPs. The chemosorbed molecules of HSs and their partially oxidized product possess a large negative charge due to ionisation of hydroxyl and carboxyl groups. The repulsive forces prevent the particles from aggregation and provide

stability of the system. The final colloids are stable and can be stored more than one year without aggregation.

The antibacterial activities of synthesized AgNPs were carried out by disc diffusion method against pathogenic bacteria. Soya bean casein digest agar plates were prepared, sterilized and solidified. After solidification bacterial cultures were swabbed on these plates. The sterile disc was dipped in AgNPs solution or synthetic HSs (5μg/ml) and placed in the agar plate and kept for incubation at 37°C for 24 hrs. The diameter of inhibition zones (in millimeters) around the different disks with synthetic HSs and AgNPs on their based against test strains are shown in Table. The results suggest that the synthetic HSs and HSs encapsulated AgNPs exhibited good antibacterial activity against both Gram-negative (Escerichia coli, Pseudomonas aeruginosa) and Gram-positive bacteria (Staphylococcus aureus). The differential antimicrobial activity of AgNPs coated by different types of synthetic HSs can be attributed to their differential sizes: the antimicrobial activity increases with decreasing size of the AgNPs.

The AgNPs also inhibited the growth of the fungus-Aspergillus niger that was seeded in the nutrient agar plate and formed a zone of inhibition around the disks saturated by solution of AgNPs.

Table 1. Antimicrobial activity different types of synthetic HSs and AgNPs on their based (mean±SD, n=3)

| S. No. | Microorganism | Diameter of the inhibition zone (mm) | | | | | |
|---|---|---|---|---|---|---|---|
| | | FAC | FAH | HA | AgNPs-FAC | AgNPs-FAH | AgNPs-HA |
| I. | Bacteria | | | | | | |
| a | Escerichia coli | 7.0±0,5 | 7.4±0.7 | 6.3±1.0 | 13.0±0.5 | 13.5±0.4 | 9.3±0.5 |
| b | Pseudomonas aeruginosa | 10.2±0.4 | 9.0±0.5 | 7.8±0.7 | 20.2±0.4 | 20.6±0.3 | 18.8±0.6 |
| c | Staphylococcus aureus | 8.8±0.4 | 8.2±0.2 | 9.5±0.5 | 22.3±0.5 | 23.1±0.6 | 20.8±0.5 |
| II. | Fungi | | | | | | |
| a | Aspergillus niger | 6.7±0.4 | 6.5±0.4 | 6.5±0.5 | 10.5±0.6 | 11.8±0.3 | 9.6±0.7 |

FAC – synthetic fulvic acid from catechol; FAH – synthetic fulvic acid from hamatoxylin; HA – synthetic humic acid

The received results indicated that AgNPs have good antibacterial and antifungal activities and promise great potential in the preparation of new drugs for biomedical applications. The advantages of HSs encapsulated by AgNPs compared with other AgNPs consisting besides ions of silver the contribution to their bactericidal properties forecast progress of the synthetic HSs.

# STUDYING OF INTERACTION (4-AMINO-5-MERCAPTO-4H-[1,2,4]TRIAZOL-3-YL)-DIPHENYLMETHANOL WITH ELECTROPHILIC REAGENTS

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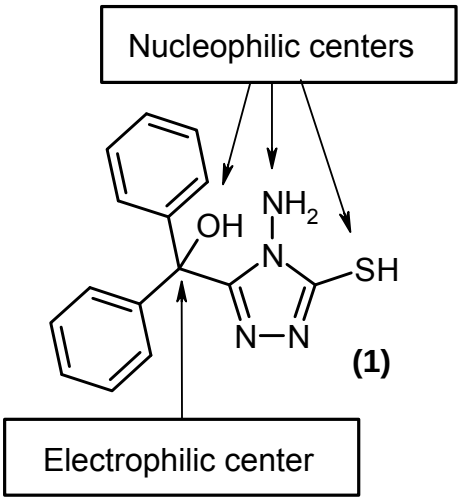
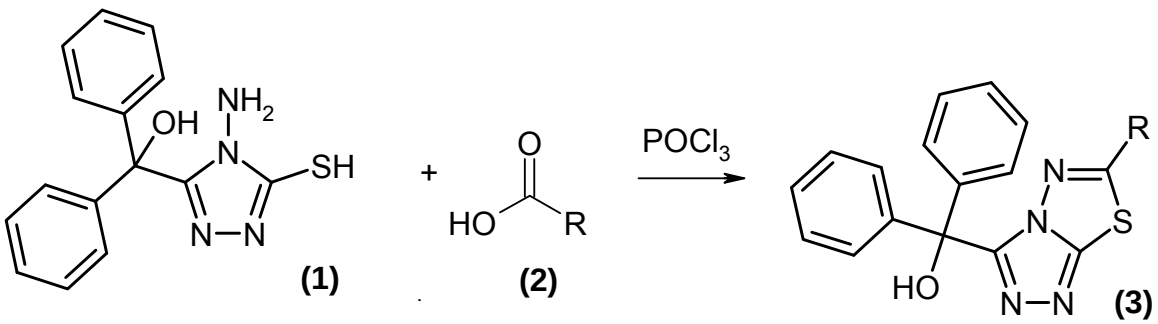



Previously, we reported the preparative pathways for (4-amino-5-mercapto-4H [1,2,4] triazol-3-yl) -diphenylmethanol. Mentioned compound contains in its structure diphenylcarbinol fragment, which also present in the structures of many medicinal substances and may be considered as pharmacophore. We noted that (4-amino-5-mercapto-4H-[1,2,4]triazol-3-yl)-diphenylmethanol contains several reaction centers, what causes high perspectives of its chemical modification aimed to formation of combinatorial libraries of substances with diphenylcarbinol fragment as pharmacophore. Thus, we decided to study the interaction of (4-amino-5-mercapto-4H[1,2,4]triazol-3-yl)-diphenylmethanol **(1)** with electrophilic reagents, namely functional derivatives of carboxylic acids. It is known that the interaction of the 4-amino-5-mercapto-4H-[1,2,4]triazole with acyl halides leads to the formation of heterocondensed 1,2,4-triazolo [3,4-b]thiadiazole. We modified this method applied to (4-amino-5-mercapto-4H[1,2,4]triazol-3-yl)-diphenylmethanol. Thus, series (6-R-[1,2,4]-triazolo[3,4-b][1,3,4]thiadiazol-3-yl)-diphenyl methanol were obtained.




The structures of all synthesized compounds were confirmed by modern instrumental methods.

# "GIANT" ORGANIC WORLD – POLYMERS

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Natural polymers are used as materials in everyday life for a long time. Such materials may replace leather, cotton, clay, nylon and cement. Prerequisites for industrial production of the chain polymers began even before the XX century. Chemistry of polymers was developed in two ways: preparation of synthetic organic polymers of low molecular weight compounds as well as the processing of natural polymers in organic synthetic polymeric materials. Polysiloxanes are elementorganic polymers having high heat resistance and elasticity, as compared with the other organic polymers. "Unique Polymers" - aromatic polyamides, polyesters, polyester - ketones and others. A feature of these polymers is the presence of aromatic rings and (or) fused aromatic structures. They possess high strength and heat resistance.

Polyethylene (ethylene polymer) - the most widely used material from all currently existing polymers. The biggest industry use of this polymer can be called the production of polyethylene films for technical and household purpose. Polyethylene has the best qualities to create the package: low density, good chemical resistance, neznachitelnoevodopogloschenie. Polyvinyl chloride (polymerization of vinyl chloride) - one of the most common plastics; it is a source for more than 3000 types of materials. Polypropylene (propylene polymer) - called the "king" of plastics. The scope of its use is expanding rapidly. Isoprene rubber (synthetic rubber). Currently known and commercially available are isoprene rubbers, butadiene, butadiene-styrene and others.

Formaldehyde resin (synthetic resins from the group phenolic resins) - cured resins are characterized by high heat -, water - and acid resistance.

It can be concluded that the polymers are "giants" of the organic world, because every day we are facing the artificial polymers in our daily lives.

# FRENCH PHARMACISTS OF XVII-XIX CENTURY AND THEIR CONTRIBUTION TO THE CHEMISTRY DEVELOPMENT

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Two or three hundred years ago chemistry as a science was deeply related to pharmacy. Thus, pharmacy was not only the place for making receipts, for drug storage and research, but it was also the field for chemist's work, the focus of new ideas and methods, the area for interested and inquired minds.

Particularly notable are the fundamental researches in inorganic and organic chemistry, which belong to the French pharmacists listed below.

***Antoine Baume*** was a French chemist, pharmacist and technician. In 1752 he became a member of the École de Pharmacie. And the same year he got an appointment as a professor of chemistry. The most important of his numerous books and papers is «*Éléments de pharmacie théorique et pratique»* (9 editions, 1762–1818). There he presented detailed information about the XVIII century chemistry in terms of the phlogiston theory. He also became a member of the Academy of Sciences in 1772.

***Bernard Courtois*** studied at the Ecole Polytechnique in Paris. He worked as a pharmacist in the military hospitals. Courtois isolated sodium and potassium compounds from the seaweed ash. And he also discovered in it iodine after adding sulfuric acid. He was actually investigating his copper vessels corrosion when he noticed that some strange purple coloured vapor was exuded as well. It was the iodine. That's the story of discovering Iodine in 1811. Most of his further works Bernard Courtois devoted to the chemistry of iodine.

***Joseph Louis Proust*** firstly worked as a manager in the hospital pharmacy, but later became a member of the Paris Academy of Sciences (1816). He was well-known for the discovering of the constant composition law in 1799, which stated that in chemical reactions substances are neither created nor destroyed. He studied copper carbonate, two tin oxides, and two iron sulfides to prove this law. Proust was also interested in studying sugars that were found out in sweet vegetables and fruits. In 1799 Proust demonstrated that sugar from grapes is identical to one found in honey. This sugar became well-known as glucose later.

***Jean-Baptiste Andre Dumas*** worked as a pharmacist assistant in a pharmacy, where a laboratory was. He is known for his works in the area of organic analysis and synthesis, as well as for determination of atomic weights (relative atomic masses) and

for measuring vapor densities. There are such compounds in organic chemistry that remain unchanged even when their hydrogens are replaced by an equivalent quantity of a halide element. Jean-Baptiste Andre Dumas supported these views and tried to prove them in his researches. For example, he successfully obtained trichloroacetic acid from acetic acid and chlorine excess, and this derivative had the same chemical properties as the acetic acid had. In 1833 Dumas developed a method for estimating the amount of nitrogen in an organic compound, which was later named 'Dumas method'. Moreover, the classification of organic compounds into homologous series was a consequence of his research of the acids generated by the oxidation of the alcohols. Together with P. Bull he suggested that alcohol and its esters are derivatives of the ethylene. Based on these statements they constructed a theory of «eterin», which is considered as the forerunner of the radical theory. In 1837 Dumas and Liebig in a joint paper defined the organic chemistry as the chemistry of complex radicals. This research was a huge blow to the dualistic theory.

***Antoine Jérôme Balard*** graduated from the School of Pharmacy in Montpellier in 1826, after that worked as a pharmacist and then became a professor of chemistry at the Royal College of Pharmacy and at the University of Montpellier. In 1826 he discovered in the seawater new component, which he recognized as a previously unknown element and named bromine. In the organic chemistry field he published papers about the decomposition of ammonium oxalate with formation of oxamic acid, about amyl alcohol and cyanides.

***Pierre-Eugene-Marcellin Berthelot*** was a chemist and a social activist, a chemistry professor at the Graduate School of Pharmaceutical in Paris (1859) and the College de France (1864), a member of the Paris Academy of Sciences (1873), corresponding member of the St. Petersburg Academy of Sciences (1876), Minister of Education (1886-1887) and Foreign Affairs. The fundamental statement for all Berthelot's chemical work was that all chemical phenomena depend on the «physical forces», which can be determined and measured. And he proved his theory by the synthetic production of numerous hydrocarbons, natural fats, sugars and other organic substances. That was the way to show that different range of organic compounds can be formed by ordinary chemical methods, that obey the same principles and rules as the same methods for inorganic substances do. He also found out that glycerin is a triatomic alcohol.

Therefore French pharmacists played a key role in the progress of different areas of organic and inorganic chemistry, and made fundamental, important and useful researches for the future chemistry development.

# ANTICANCER ACTIVITY OF THIENO[2,3-d]PYRIMIDINES

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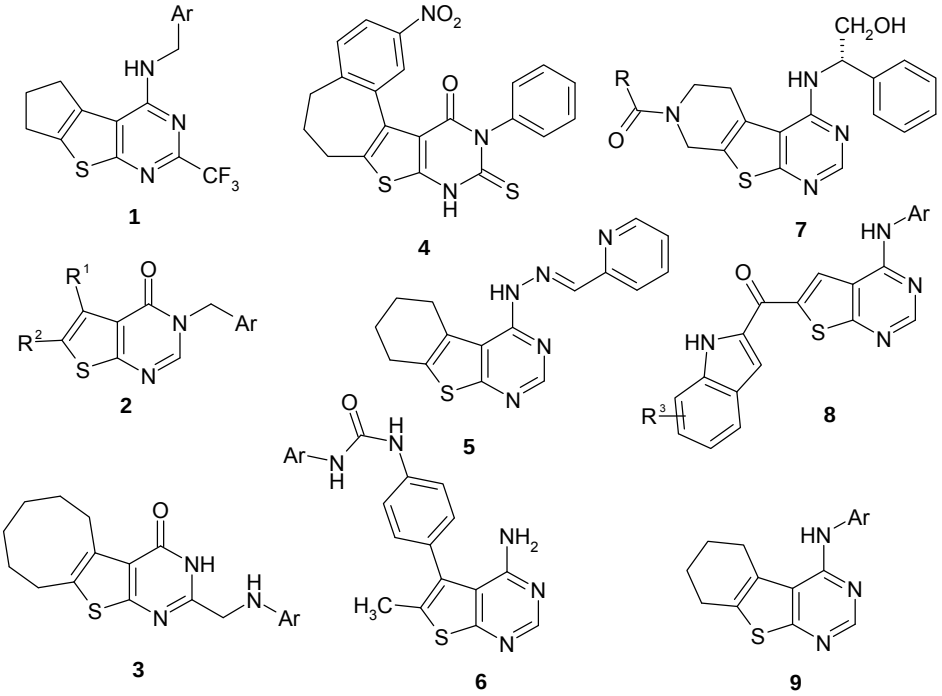
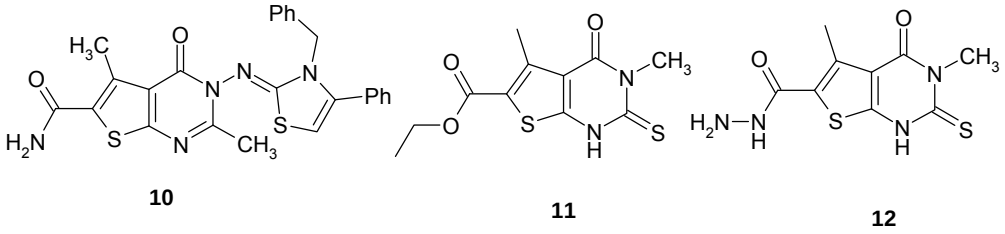
The derivatives of thieno[2,3-d]pyrimidine during the last decade were extensively studied as anticancer agents by many groups of scientists from all the world. Many of the compounds with similar structures were found to be active against the liver and breast cancer; some of them were active against adenocarcinoma **1,2**. Also thieno[2,3-d]pyrimidines were reported as the antitumor agents against colon cancer **3**, and the compounds of the wide range of anticancer activity **4,5**. Some the derivatives of thieno[2,3-d]pyrimidines are known to be tyrosine-kinase inhibitors, which may be considered as potent anticancer drugs **6-9**.



The anticancer activity study for the amides and esters of 5-methyl-4-oxo-3,4-dihydrothieno[2,3-d]pyrimidine-6-carboxylic acid, performed in last decade displayed the anticancer properties for the compounds of these series **10-12**.



Analysis of the information of about anticancer activity of thieno[2,3-d]pyrimidines showed that they might be used as medicines against this dangerous disease.

# CONSTRUCTION FOCUS LIBRARY OF 2-BENZIMIDAZOLE OXINDOL NUCLEI EXHIBITING ANTITUMOR PROPERTIES POTENTIAL

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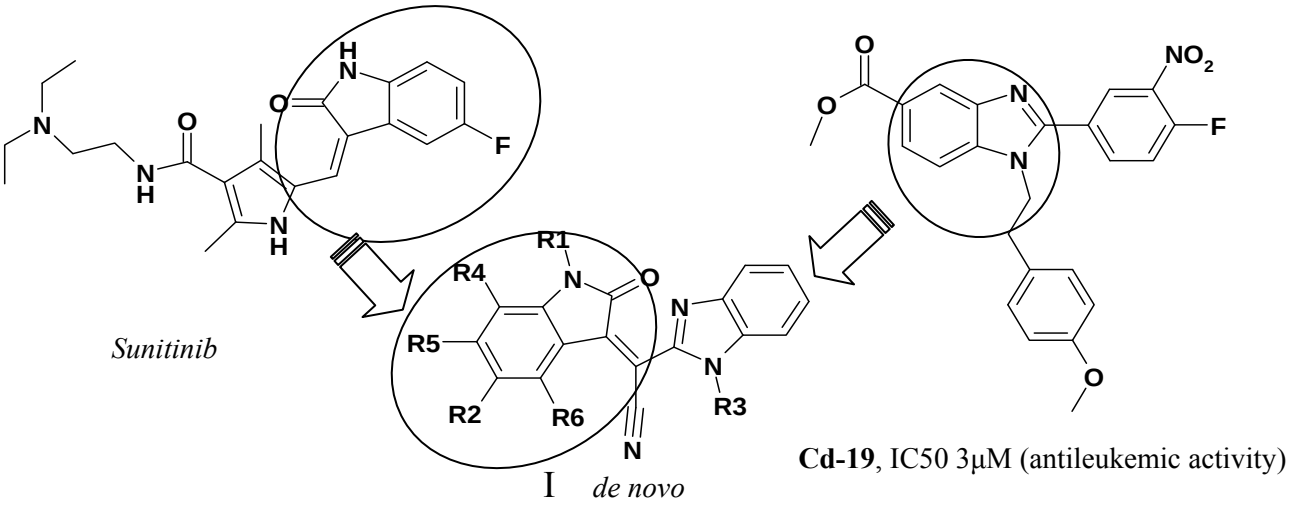
It is known that a number of diseases including autoimmune, cancer starts activating protein kinases that play a key role in the regulation of a wide variety of cellular processes, including metabolism, cell proliferation, cell differentiation, cell survival, angiogenesis and immune response. Therefore, identification of inhibitors of protein kinases that can potentially be effective as therapeutic agents against these diseases is an important task of the modern pharmaceutical science.




The greatest practical importance, such studies have to design de novo, synthesis and search for new molecules drug substances. The purpose of this paper is de novo design and the search for new drug-like molecules – potential inhibitors of kinases 2-oxindolin 3-acrylonitrile benzimidazole nuclei. To design focus library of new compounds we used Chemoinformatics methods. The initial platforms chosen synthetic 2-oxindolin metyliden fragment characteristic of already known kinase inhibitor Sunitinib, allowed for the treatment of renal carcinoma and gastrointestinal tumors. As a reference drug used as an experimental compound CD-19 high antileukemic activity. All calculations of molecular descriptors were taken with a software system Molinspiration Cheminformatics v2013.09, 2013 (University of Bratislava, Slovakia). As a result of variation over a 6-point randomization in the proposed molecular platform we were able to find the structure (I) with high forecast kinase inhibitor activity. The greatest value of the likelihood function kinase inhibitory activity was found for compounds with substituents F, OH, negative feedback caused substituents at the nitrogen atom in the 2-oxindolic nucleus.

**SYNTHESIS AND POSSIBLE PHARMACOLOGICAL ACTIVITY OF NEW DERIVATIVES OF 2-AMINOTIAZOL**

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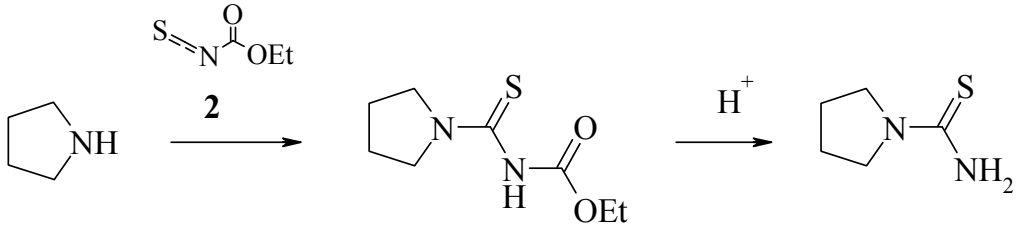
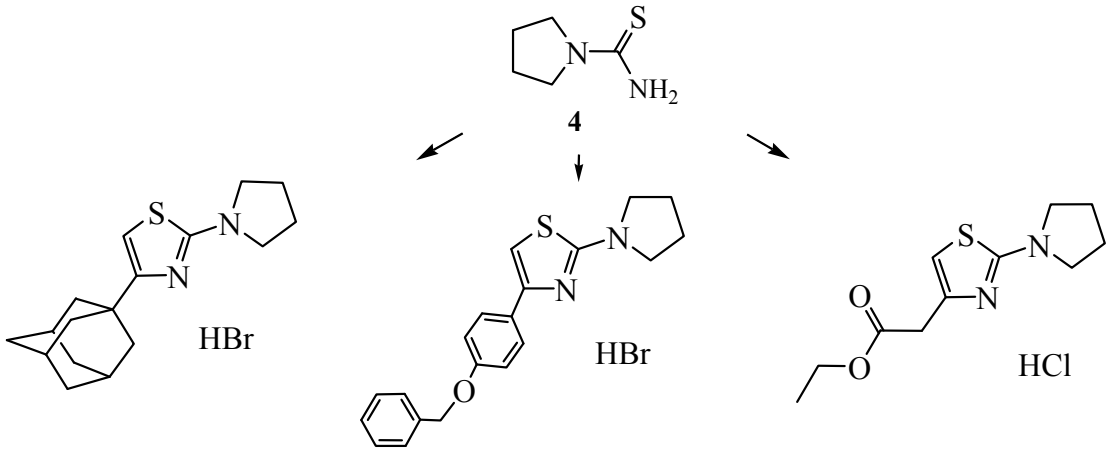
From the moment of discovery of penicillin pharmaceutical companies have developed a large number of antibacterial drugs. The problem of microbial resistance to antibiotics encourages researchers to search for new antibiotics. In order to obtain of new antibacterial preparations, we have synthesized a series of derivatives (**5, 6, 7**) based on asymmetric thioureas.

Pyrrolidine-1-karbotioamid 4 synthesized by condensation of pyrrolidine 1 with isothiocyanate 2 with subsequent hydrolysis of the ester 3. Exit of urea 4 was 73%. Key izotiotsianatoester 2 previously was synthesized from etylhlorformiat and dry potassium thiocyanate in the presence of tetramethylethylenediamine (TMEDA) as a catalyst.



**1** **3** **4**

Pyrrolidine-1-karbotioamyd 4 was condensed with substituted of b-halohenketonam in conditions of classical reaction of Ganch. The reaction occurred as follows:



5 6 7

The structure of obtained compounds was confirmed by ЯМР spectroscopy. Studied the possible pharmacological properties of the synthesized compounds. Modeling of pharmacological activity of the synthesized compounds we have conducted with a help of computer program PASS (Prediction of Activity spectra for Substances) by v. 1.703 version. It is established that the synthesized compounds can detect the activity as Antieczematic and Phosphatase inhibitor.

# SYNTHESIS OF FUNCTIONAL DERIVATIVES OF 3-AMINO-2-R-7-(R'-PHENYL)-3H-THIENO[3,2-d]PYRIMIDINE-4-ONES AIMED TO THE SEARCH BIOLOGICALLY ACTIVE SUBSTANCES

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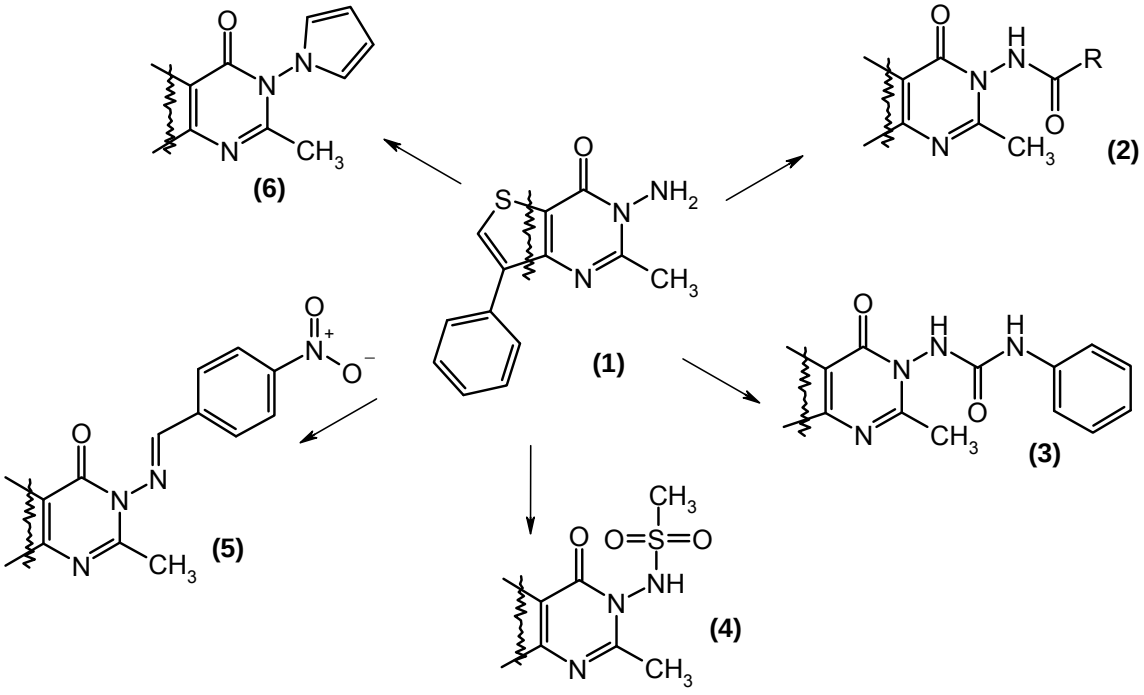
In a previous report it was shown possibility of one-pot synthesis for 3-amino-2-R-7-(R'-phenyl)-3*H*-thieno[3,2-*d*]pyrimidine-4-ones (**1**). The aim of presented work is studying of the reactivity of the amino group in structure of mentioned above compounds. It is known that such modifications lead to a significant increasing of the biological activity of corresponding derivatives. Moreover, it is known that, in some cases, modification of amino groups of bioactive substances aimed to the improving of molecule stability in acidic medium and maintaining of activity.




Chemical transformation of 3-amino-2-R-7-(R'-phenyl)-3*H*-thieno[3,2-*d*]pyrimidine-4-ones (**1**) was performed by known methods. Thus, products of acylation (**2**); non-symmetric carbamides (**3**); sulfamides (**4**); Schiff bases (**5**) and derivatives which contains pyrrole fragment (**6**) were obtained. The structures of the compounds proved by complex of physicochemical methods.

## *(S)*-PROPRANOLOL PREPARATION

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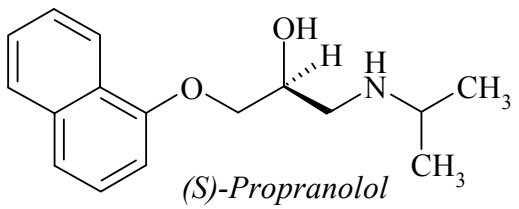
One of problems of the modern organic chemistry is synthesis of optically active compounds preserving their enantiomer individuality. Most of the new synthetic pharmaceuticals consist of two or more stereoisomers. However it is known that the pharmacological activity of racemic medications is caused by the activity of one enantiomer. This phenomenon results from the fact that only one of the enantiomers has the needed therapeutic effect, meanwhile the second antipode can cause undesirable side effects. Such distinctions are explained by the features of spatial arrangement and interaction with a receptor. The close interrelation between a configuration and pharmacological activity causes stereo-specificity of the medicinal preparations effect.

Thus Propranolol – 1-(isopropylamino)-3-(1-naphtyloxy)-2-propanol – as a non-selective $\beta$-adrenoblocker has a wide spectrum of application. It is proved that its enantiomers differ in physiological effect. (*S*)-isomer of Propranolol provides the desired effect on cardiovascular activity while (*R*)-isomer brings the side effects. That is why the replacement of racemic substance with an individual (*S*)-enantiomer is actual task for this case.



*(S)-Propranolol*

Nowadays several ways of preparation the (*S*)-propranolol are known.

- Biochemical division with the help of esterase producing microorganisms. One of examples to set is the selective hydrolysis of acetate of propranolol, which is catalyzed by pancreatic and bacterial lipases.
- Division of (*S,R*)-propranolol through formation of auxiliary diastereomer, which are received by processing of a racemic substratum dividing agent. One enantiomer can be sorted out from the formed mix via fractional crystallization.
- Also it was revealed that racemic propranolol in the form of its salts with hydrofluoric acid crystallizes as a racemic conglomerate. It allows to split the substance on enantiomer by an inclusion method.

Thus, we can obtain a chiral medicine – (*S*)-propranolol having better result in cardiovascular diseases treatment. The introduction of one-enantiomer preparations to clinical practice will allow using lower doses without any effectiveness loss, to increase safety and to decrease the risk level of side reactions within therapy.

# STUDYING OF INTERACTION OF BENZO[C][2,1]THIAZINE-4-ON 2,2-DIOXIDE WITH ARYLCARBALDEHYDES

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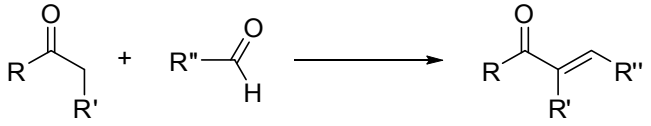
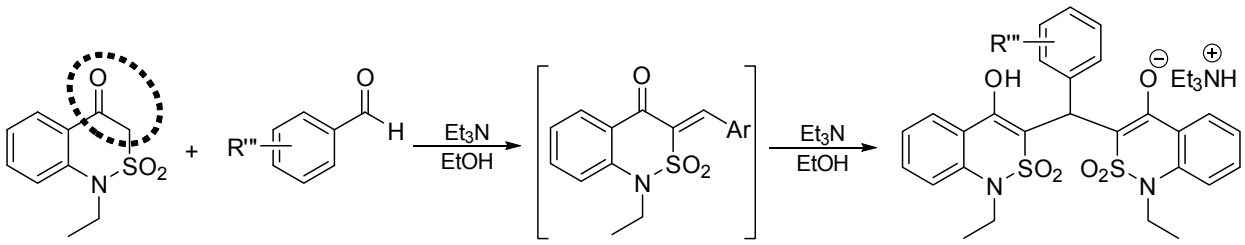
□,□-Unsaturated ketones **1** are reactive compounds and therefore they are useful reagents in synthesis of the variety of heterocyclic systems. Crotonic condensation reaction of active methylene carbonyl compounds with aldehydes is the most general and convenient method for such ketones synthesis.



**1**

Benzo[c][2,1]thiazine-4-on 2,2-dioxide **2** is an example of a carbonyl CH-acid. This fact has encouraged us to use **2** in reaction with arylcarbaldehydes **3** in order to obtain appropriate arylidenes **4**. The reaction was carried out under general conditions, namely in medium of ethanol in the presence of triethylamine as a base. But it was surprising that the triethylammonium salts **5** were the products of this reaction.

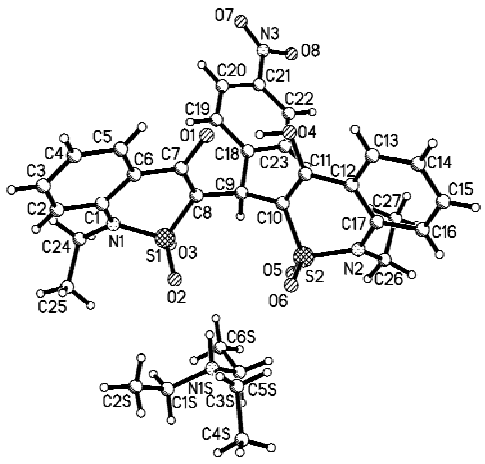


**2** **3** **4** **5**

R''' = H, 4-$NO_2$, 4-$OCH_3$, 4-Cl, 2-$OCH_3$

This result could be explained by the formation of the intermediate **4**, which subsequently reacted with the second molecule of **2** leading to synthesis of the salt **5**.

The structures of obtained compounds **5** were confirmed using the instrumental methods of analysis ($^1$H NMR, $^{13}$C NMR, IR-spectroscopy, mass-spectrometry and X-ray analysis).



# INVESTIGATION OF THE QUANTITATIVE RELATIONSHIP BETWEEN STRUCTURES – ANTITUBERCULAR ACTIVITY FLUOROHINOLONES DERIVATIVES WITH SETTLEMENT PLATFORM MOLINSPIRATION CHEMINFORMATICS

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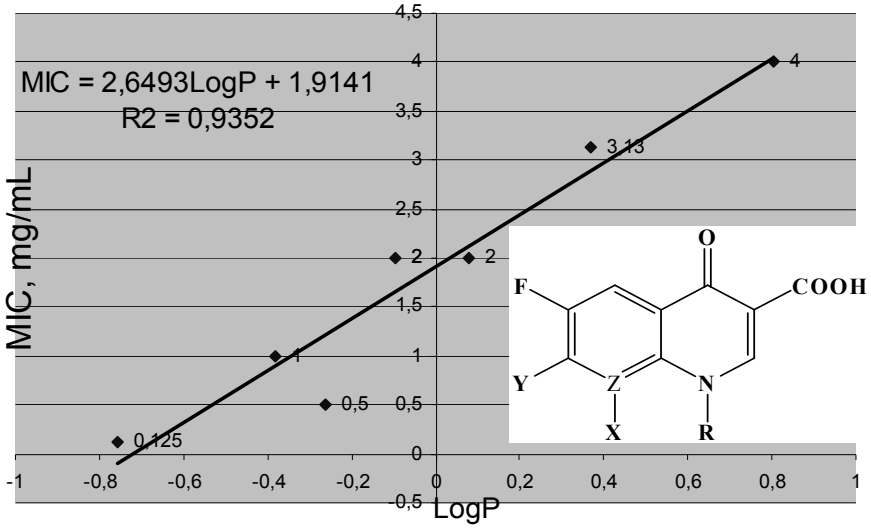
In Ukraine, the epidemic of tuberculosis (TB) has passed into the category of national problems, as has become difficult to manage as the number of TB patients has exceeded 1% of the population. Every year the number of patients increased by 40 thousand people and 10 thousand people die annually. In the World, there are approximately one third of populations infected with TB bacillus and 1.7 million people die from TB annually, and new TB patient is estimated at 8 million or more. TB has been consequently identified by the WHO as one of the three priority diseases for drug research and development. Multidrug-resistant tuberculosis (MDR-TB) and extensively drug-resistant tuberculosis (XDR-TB) make this problem become more complex. Importantly, the WHO also recommended the use of fluoroquinolones (FQ) – Levofloxacin or Moxifloxacin for the treatment of XDR-TB.




We investigated the quantitative relationship between the molecular structure of FQ and their anti-TB activity using the method of cheminformatics – settlement platform Molinspiration Cheminformatics (University of Bratislava, Slovakia). To do this, we have considered such settlement quantum chemical descriptors as octanol-water partition coefficient (LogP), topological polar surface area (TPSA), molecular volume (MV, expressed in cubic Angstroems (Å3). For the study we selected 11 FQ with known quantities the minimum inhibitory concentration (MIC, μg/mL) – Ciprofloxacin, Ofloxacin, Pefloxacin, Enoxacin, Levofloxacin, Sparfloxacin, Temafloxacin, Moxifloxacin, Grepafloxacin, Trovafloxacin, Gemifloxacin. As a result, we obtain three equations correlation of MIC values LogP, TPSA, MV. The highest level of reliability (coefficient approximation - R2) was found for the dependence of MIC & LogP (R2 = 0.9352, N = 7) for MIC&MV (R2 = 0.9148, N = 6), and the lowest for MIC&TPSA (R2 = 0.8741, N = 5). The proposed algorithm can be used to determine and describe the quantitative relationship between anti-TB activity and chemical structure in a series of fluoroquinolones in order to synthesis and search for new anti-TB drugs.

# ORGANIC FOOD COLORS: FRIENDLY AND DANGEROUS

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There are no spheres of human activity without using organic compounds. Analysis of assortment structure of food colors and their safety is capture attention.

A history of using food colors has goals a centuries. Known, that Egyptians during 400 B.C. used natural color matters for sweets and vine to improve their appearance. People of the countries of Asia and Romans added to food turmeric and saffron. But only since $19^{th}$ century thanks for increasing industrial production stand using widely to use for improving consumer quality of foods. Business necessity of using wide range at new synthetic compounds has evolved. New organic compounds obtained due to chemical and biotechnology discoveries. These natural colors lost their dominant important after discovering of first synthetic dyes: mauve (W.H. Perkin, 1856), magenta (F.-E. Verguin, 1858), indigo (A. Baeyer, 1878).

Now natural and synthetic colors are used for foods color strengthening and restoration, coloring of cakes, ice-cream and beverages.

For chemical structure natural colors divided in to:

1. aliphatic and alicyclic (carotenoids, licopines, tetraterpenes nature, polienes);
2. aromatic colors (diarylmethane dyes – curcumine; quinons – alizarine);
3. heterocyclic compounds (oxigencontaining – flavanol, luteoline; nitrogencontaining – indigo, turmeric).

All this compounds are selected from different plant and animal objects or obtained by microbiological methods. Natural colors less toxic, but there are daily intakes. Several food colors known as antibiotics, vitamins.

Synthetic colors are widely to use because of low stability of natural compounds. As natural food colors synthetic are divided in to several groups. Among organic synthetic colors are distinguished triarylmethen colors (Green S), quinolinic colors (Quineline Yellow), indigo dyes (Indigotine), azo dyes (Tartrazine, Crimson).

Preferences of synthetic organic dyes:

- very soluble in water;
- less sensitive to conditions of technological processing and storage;
- heat stability;

- brightness.

According to “E number” list was registered 80 food colors (E 100-182). Most of them are synthetic organic compounds. In Ukraine allowed about 60 food colors not only from “E number”. In addition to “E number” used metilviolent, phuxin and other. Most of food colors are xenobiotics, that’s why main requirements to food colors are non-toxic and safety. For several food colors was revealed negative influence for human body. This compounds was excluded from using.

In our country was banned E121, E123, E128. But several dangerous especially for children addition are used. Foods with such additions have special package marking and are forbidden in some countries of Europe. Among of dangerous E-colors-allergens are:

- E-102 (Tartrazine) – synthetic azo dye. Yellow food color for candies, jellies, ice cream, beverages, dairy products, purees, jams, sauces and ketchup. Side effects: allergy, especially for people who are in tolerant to salicylates, children hyperactivity;
- E-104 (Quinoline yellow) – yellow food color for baked goods, beverages, sweets, dairy, meat and fish products. Side effects: may act as a histamine liberator;
- E-110 (Sunset Yellow, FCF) – synthetic azo dye. Yellow food color for confectionery and pasta, dairy products, sauces and ketchup in the sauce and jam. Side effects: a histamine liberator, and may intensify symptoms of asthma;
- E-122 (Azorubin) – synthetic azo dye. Red food color for sausage and confectionery, desserts, drinks. Side effects: problems with kidneys implicated in hyperactivity of children;
- E-124 (Ponce 4R) – synthetic azo dye. Food color for beverages, sauces and ketchups, desserts, fish and meat products, dairy and meat products. Side effects: cancerogenic;
- E-129 (Allura Red) – synthetic azo dye, food color for snacks, sausces, preserves, soups, wine. Side effects: cancerogenic.

Health care is not only a fashion trend but emergency call of time. Therefore there is a requirement in new quality and safety food colors. The daily intake of food colors is exceeds because of often and long-term use. As result, the problem of research new food colors is actually now.

# SYNTHESIS AND PROPERTIES OF ADAMANTE DERIVATIVES

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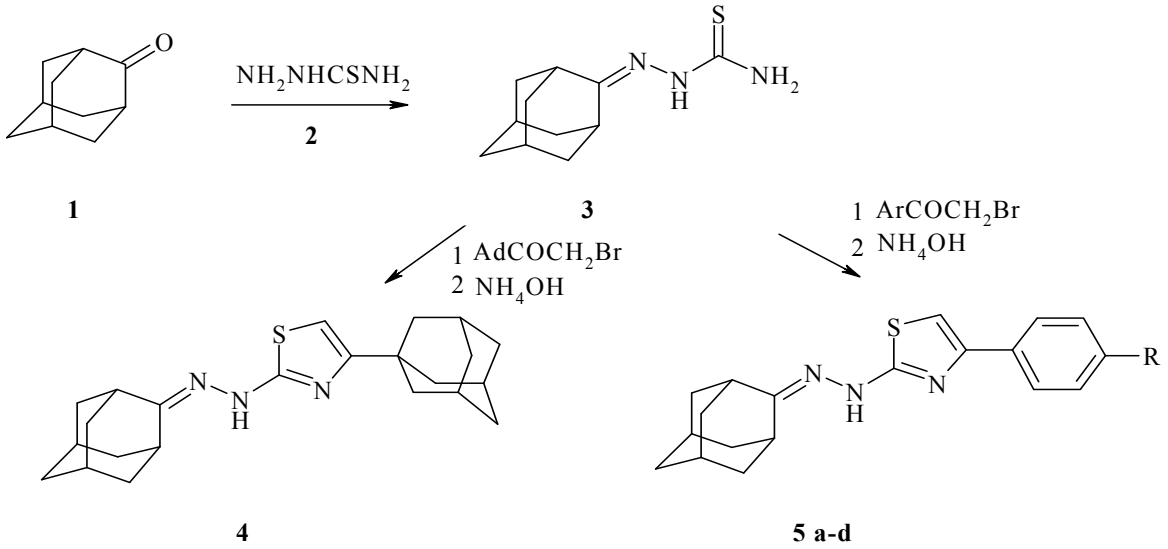
Chemistry of adamantane and its derivatives is a relatively young of organic chemistry, but its derivatives have been used as heat-resistant polymers, lubricants, jet fuels to components of artificial blood, medicines broad-spectrum, etc. Today pharmaceutical industry produces more than 20 effective medicines containing adamantane derivatives.

The purpose of our research is the synthesis of promising new adamantane derivatives from commercially available materials and possible ways of their use as pharmaceutical substrates. As the methods we used chemical synthesis and computer modeling.

With Condensation of adamantane-2 (1) with tiosemykarbazydom (2) in 89% yield was obtained tiosemykarbazon adamantane-2 (3). It is shown that condensation of the last with different α-halohenketonams under the Gancha reaction conditions leads to substituted thiazoles (4) and (5 a-d) with 52-81% yields.




where R: H (a); Cl (b); Br (c); $OCH_3$ (d).

The composition and structure of the compounds (4, 5 a–d) was confirmed by elemental analysis and ЯМР $^1H$ spectroscopy method.

Modeling of pharmacological activity of the synthesized compounds we have conducted with a help of computer program PASS (Prediction of Activity spectra for Substances) by v. 1.703 version.

Established that adamantane derivatives (4, 5 a-d) can exhibit a wide range of inhibitory action and be active as protectors of mukomembran.

Thus, synthesized compounds can be used as building-blocks to create new multifunctional pharmaceutical.

# SEARCH FOR POTENTIAL ANTICONVULSANTS AMONG THE DERIVATIVES OF 1,3,4-THIADIAZOLE

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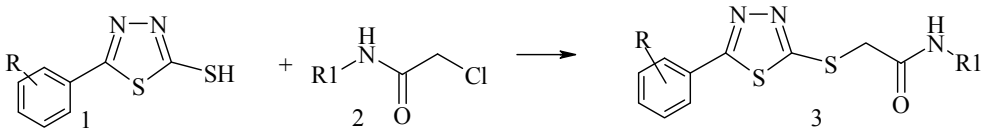
*Purpose*. The work devoted to the synthesis and researches about physical-chemical properties of the newly synthesized compounds the derivatives of 1,3,4-thiadiazoles and the study of their anticonvulsant activity. Analysis of the literature shows that among the derivatives of 1,3,4- thiadiazole there are a lot of promising compounds in terms of pharmacy, but at the same time, their biological properties have been insufficiently studied.

*Materials and Methods.* In order to search for new bioactive substances - potential anticonvulsant anilides of 5-R-phenyl-1,3,4-thiadiazole-2-yl-thioacetic acid were synthesized. The high reactivity of starting substances of 5-R-phenyl-2-mercapto-1,3,4-thiadiazoles(1) makes it possible quite easy modify their structure by alkylation, which extends the probability of finding new effective compounds in this series. Alkylation was performed by anilides of chloracetic acid (2) under the conditions of basic catalysis. Reaction was carried out in an alcohol in the presence of alkali solution. Target products have been obtained with satisfactory yields. The structure of obtained anilides of 5-R- phenyl -1,3,4-thiadiazole-2-ylthioacetic acid (3) was proved by modern physical and chemical methods of UV, IR and $^1$H NMR-spectroscopy, the purity was confirmed by the method of thinlayer chromatography. The reaction method is according to the following scheme:




The computer prognosis of biological activity spectrum of all new compound by program PASS has set that the several substances are able to show the anticonvulsant activity (activity indexes of compounds are in the range of 0.4 to 0.5) Pharmacological screening for anticonvulsant activity has been carried out.

*Results and conclusions.* New anilides of 5-R-phenyl-1,3,4-thiadiazole-2-yl-thioacetic acid were synthesized. The structure of the compounds obtained was proved by methods NMR-, UV- and IR- spectroscopy and their purity and individuality was determined by thin-layer chromatography.

The results of studying an anticonvulsive activity have shown that the compounds synthesized are antagonists against the convulsive activity of pentylentetrazol.

Performed researches have allowed to select two leading compounds for in-depth researches.

# ONE-POT SYNTHESIS OF 3-ALKYLTHIO AND 3-AMINO-SUBSTITUTED 5-AMINO-4-R-SULFONYL-*1H*-PYRAZOLES

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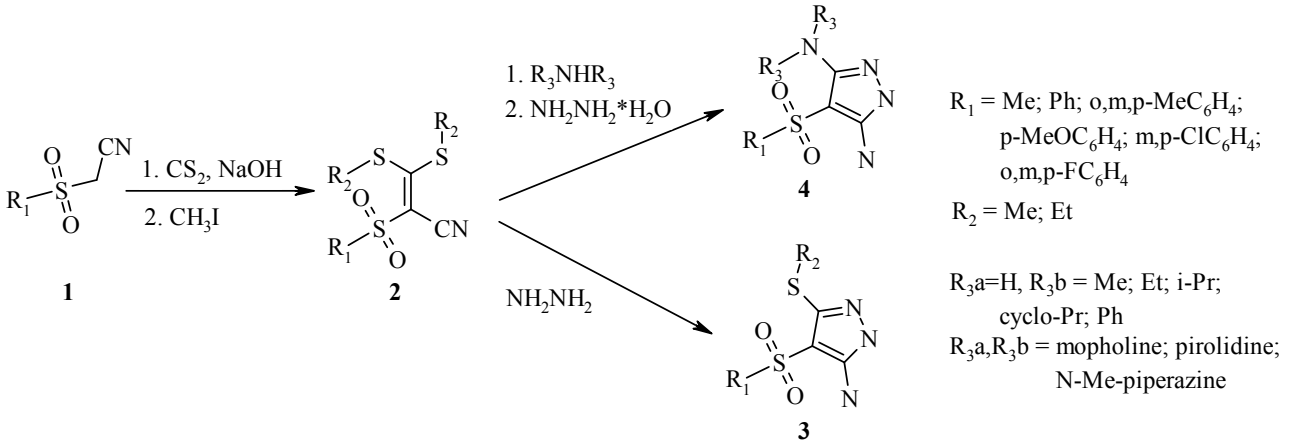
Development of the new synthetic methods and search for biological active compounds among the aminopyrozoles is obvious interested, as evidenced by the wide range of pharmacological properties of some derivatives of pyrazoles. The most known drugs for cancer treatment, as Binukleyin 2 (metanymidamin), Barasertib (AZD-1152), Tozasertib (MK-0457), are derivatives of aminopyrozole. This pharmacophore system is characterized by antimicrobial, antifungal, antiviral, antiparasitic and anti-inflammatory activity. We focused on purposeful combination of two pharmacophores in the one molecule — sulfonyl group and 3- aminopyrazole cycle.

Traditionally this reaction is conducted in three stages for the 3-*S*-derivatives and in four stages for 3-*N*-alkyl-substituted pyrazole derivatives. We have developed a one-pot method of synthesis of the corresponding aminopyrazoles **3** and **4** on the base of the methylene active cyanomethylarylsulfones **1** as starting reagents. The proposed scheme has been implemented in the laboratory version (in the Erlenmeyer flask in the mixture of dioxane : water 5:1) and scaled (ScaleLab) on 25 g batch. The resulting compounds had a high purity (> 95%) and did not require further purification.




The obtained compounds appear as promising building-blocks to build the combinatorial libraries for directional biological screening.

# ANTIMICROBIAL ACTIVITY STUDY OF 2-[6-(1H-BENZIMIDAZOL-2-YL)-5-METHYL-4-OXOTHIENO[2,3-*d*]PYRIMIDIN-3(4*H*)-YL DERIVATIVES WITH N-ARYLACETAMIDE AND (3-ARYL-1,2,4-OXADIAZOL-5-YL)METHYL SUBSTITUENTS

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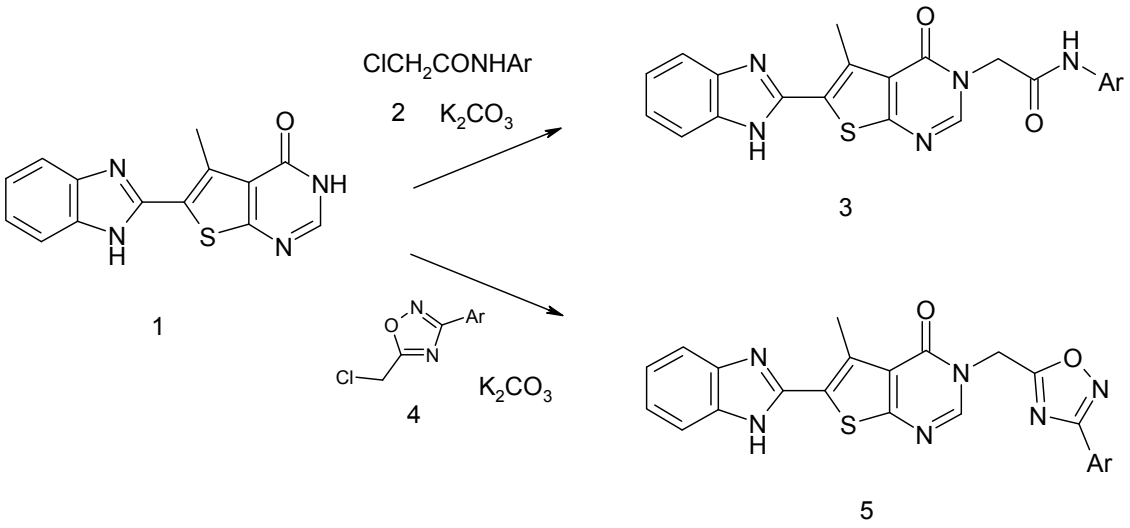
Among the derivatives of 6-hetarylthieno[2,3-*d*]pyrimidines there are compounds known as antimicrobials. Therefore, the aim of our work was to develop the methods for preparation of novel potent antimicrobials, which were the products of 6-(1*H*-benzimidazol-2-yl)-5-methylthieno[2,3-*d*]pyrimidin-4(3*H*)-one **1** alkylation with N-arylchloroacetamides **2** and 5-(chloromethyl)-3-aryl-1,2,4-oxadiazoles **4**. As the result of the mentioned alkylation reaction 2-[6-(1*H*-benzimidazol-2-yl)-5-methyl-4-oxothieno[2,3-*d*]pyrimidin-3(4*H*)-yl]-N-phenylacetamides **3** and 6-(1*H*-benzimidazol-2-yl)-5-methyl-3-[(3-phenyl-1,2,4-oxadiazol-5-yl)methyl]thieno[2,3-*d*]pyrimidin-4(3*H*)-ones **5** were obtained (scheme).

Scheme




Antimicrobial activity study was performed by the co-workers of Microorganism biochemistry and nutrient media laboratory of the Institute of microbiology and immunology n. I.I.Mechnikov NAMS of Ukraine (head PhD Tatyana P. Osolodchenko). The experiment was performed by agar-well diffusion method.

It was found that all of the compounds have moderate antimicrobial activity. Some of them inhibited the growth of *Staphylococcus aureus* ATCC 25923 and *Bacillus subtilis* ATCC 6633 bacterial strains.

# THE INTERACTION OF (±)3-DICHLOROMETHYL-1,2,2-TRIMETHYLCYCLOPENTANECARBOXYLIC ACID WITH AROMATIC ACIDS HYDRAZIDES

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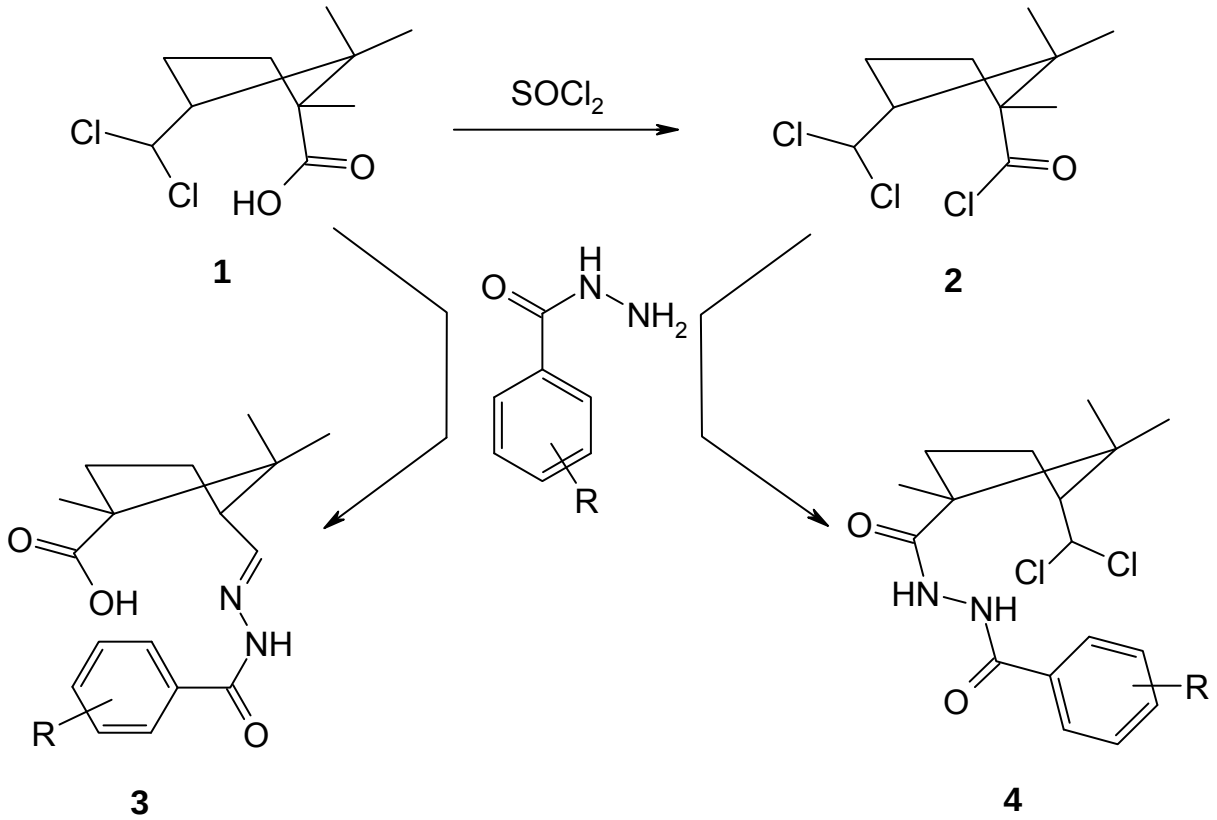
In previous studies we synthesized (±)cis-3-dichloromethyl-1,2,2-trimethyl-cyclopentanecarboxylic acid (compound 1, scheme). The aim of this work is to study the reactivity of carboxyl and  groups of acid 1 and to synthesize new substances with a potential biological activity. The interaction of acid 1 and hydrazides of aromatic acids in ethanol in the presence of potassium carbonate lead to the corresponding (E)-3-(benzoylhydrazonomethyl)-cis-1,2,2-trimethylcyclopentanecarboxylic acids 3 in high yield. R-Benzoic acid N'-(3-dichloromethyl-1,2,2-trimethylcyclo-pentanecarbonyl)hydrazides 4 were synthesized via acylation of hydrazides by the 3-dichloromethyl-1,2,2-trimethylcyclopentanecarbonyl chloride, which was obtained from acid 1(scheme).

Scheme




The purity of synthesized compounds was proved by TLC, and their structure was confirmed by methods $^{1}$NMR spectroscopy and elemental analysis.

# CHEMICAL DISPOSAL OF UNUSABLE PESTICIDES “RAMROD”

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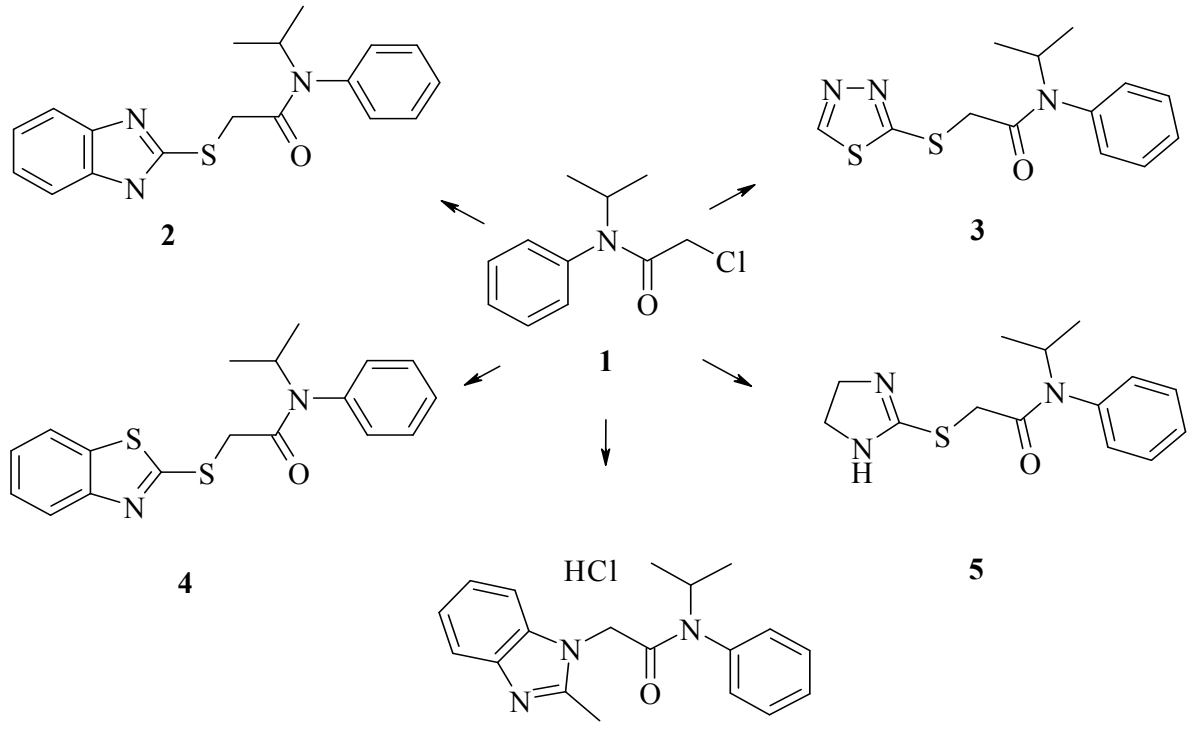
Ramrod is a systemic herbicide used for struggle with annual weeds during the cereals cultivation. The active substance of this herbicide is 2-chlor-N-izopropilatsetanilid (1). Chemical disposal of this herbicide allows you to remove a valuable raw material for new biologically active compounds.

We have shown that the condensation of active substance (1) with 2-merkaptobenzimidazol, 2-merkaptobenztiazol, and 2-merkaptotiazolin 2-merkaptotiadiazol 1,3,4 in an alkaline environment leads to formation of the corresponding tiopohidnyh (2–5), while at boiling compounds (1) with 2 metylbenzimidazol is formed corresponding hydrochloride (6):



**2** **3** **1** **4** **5** **6**

The composition and structure of the compounds (4-9) was confirmed by elemental analysis and ЯМР $^{1}$H spectroscopy method.

Modeling of pharmacological activity of the synthesized compounds we have conducted with a help of computer program PASS (Prediction of Activity spectra for Substances) by v. 1.703 version.

Found that synthesized compounds can be used as building-blocks for creation of new pharmaceuticals.

# ARYLIZATION AND HETERYLIZATION OF ETHYL ESTER 1-FURFURYL-2-OXO-4-HYDROXY-1,2,5,6,7,8-HEXA-HYDROQUINOLINE-3-CARBOXYLIC ACID

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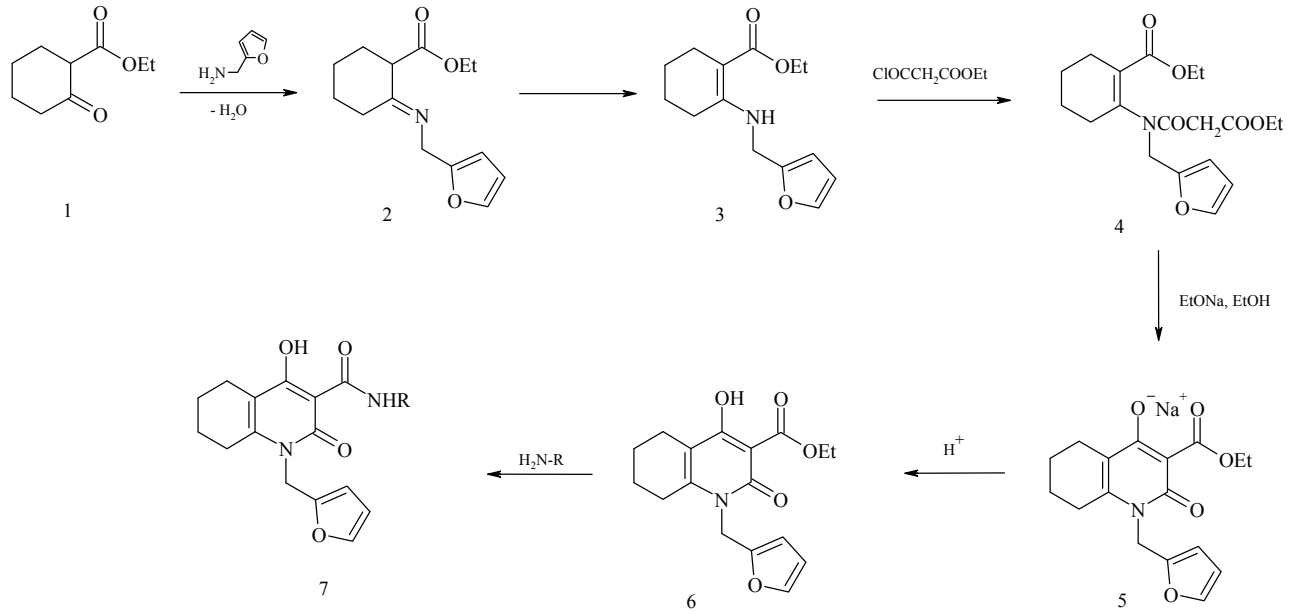
*Purpose.* As is known from the chemistry sources, furan derivatives are non-toxic or low-toxic substances that may be the basis for drugs development. So we thought it is appropriate to carry out arylization and heterylization reactions of ethyl ester 1-furfuryl-2-oxo-4-hydroxy-1,2,5,6,7,8-hexahydroquinoline-3-carboxylic acid and study the biological activity of the obtained compounds.

*Materials and methods*. For the synthesis of ethyl ester 1-furfuryl-2-oxo-4-hydroxy-1,2,5,6,7,8-hexa-hydroquinoline-3-carboxylic acid **6** starting ethyl-cyclohexanon-2-carboxylate **1** reacts with furfurylamine **2** to form Schiff bases which tautomerise to enamine **3** (scheme).




Acylation of compound **3** with ethoxymalonylchloride gives anilide **4**, which turns to quinolone **6** after treatment with sodium ethoxide in which the medium of anhydrous ethanol. In turn, the ethyl ester **6** amidating easily with amines and heterylamines, forming the corresponding amides **7** with high yields.

*Results and conclusions*. The elemental analysis and $^1$H NMR spectroscopy we used in the study of the structure of the obtained derivatives 1-furfuryl-2-oxo-4-hydroxy-1,2,5,6,7,8-hexahydroquinoline-3-carboxylic acid. The studied compounds **7** show a moderate anti-tuberculosis activity, but do not exceed reference drugs.

# DEVELOPMENT OF NOVEL QUINOLINE DERIVATIVES WITH DIURETIC ACTIVITY

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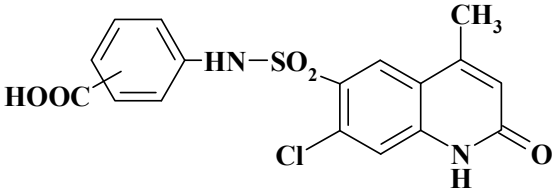
Thiazides are effective antihypertensives with long track records and low cost. The most popular agent in this class, hydrochlorothiazide, was traditionally used in doses of 50 to 100 mg per day. These doses were associated with metabolic and electrolyte complications. Therefore, low-dose therapy has been applied and demonstrated to be efficacious and to have a much lower incidence of side effects. The other way to solve thiazides disadvantages is to use thiazide-like diuretics, for example, chlorthalidone, that have been shown to provide a greater antihypertensive effect comparing with hydrochlorothiazide and, more importantly, to reduce mortality. Accordingly, thiazide-like diuretics development for edema and essential hypertension treatment is actual problem of pharmaceutical science.

The aim of this work was to search for new chemical scaffold of thiazide-like diuretics. To reach the goal, a series of new 7-chloro-4-methyl-1,2-dihydroquinoline-2-ones with sulfonamide moiety bearing different substituents has been synthesized. The procedure includes sulfochlorination of 7-chloro-4-methyl-1,2-dihydroquinoline-2-one and further amidation of corresponding 7-chloro-4-methyl-2-oxo-1,2-dihydroquinoline-6-sulfochloride with various aromatic amines.

Obtained substances (for example, I) contain basic pharmacophores of thiazide and thiazide-like drugs, in particular, essential sulfonamide group with halogen atom in *ortho*-position and amino group in *para*-position of aromatic ring.




I

Synthesized substances have been tested for their diuretic activity in rats. According to the results of the screening, derivatives with carboxylic group in the benzene ring (I) posses 37.9-71.6% of hydrochlorothiazide activity. The higher activity was found for 4-(7-chloro-4-methyl-2-oxo-1,2-dihydroquinolin-6-yl-sulfonylamino)benzoic acid (I, *para*-COOH). Thus, polar carboxylic group in *para*-position doubled diuretic activity in comparison with corresponding *ortho*- and *meta*-substituted derivatives.

## SECTION № 2

# STUDY OF MEDICINAL PLANTS AND CREATION OF HERBAL MEDICINAL PRODUCTS

# QUANTITATIVE DETERMINATION OF FATTY OILS IN ROSE HIPS

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Dog rose *(Rosa canina L.)* from the Rose family *(Rosaceae Juss.)* grows as a wild plant and it is cultivated in Ukraine as a medicinal and ornamental plant.

Rose hips *(Fructus Rosae)* contain vitamins, phenolic compounds, organic acids, fatty oil, carbohydrates, which determine their multivitamin, diuretic, choleretic, wound healing, anti-inflammatory activities.

The aim of the study was to investigate the content of fatty oil in the rose hips for further standardization of raw materials and the study of the component composition of fatty oil.

Raw materials were collected in September 2014 in the Botanical Garden of the National University of Pharmacy.

To obtain fatty oil the dog rose hips dried and crushed were extracted by chloroform and the extract was evaporated to complete removal of the solvent. The yield of fatty oil was 4.13%. At the exhaustive extracting of raw material by chloroform in the Soxhlet apparatus the yield of fatty oil was 6.7%.

The component composition of fatty oil from dog rose hips was investigated on a chromatograph Agilent Technologies 6890N with mass spectrometric detector 5973N.

As a result of the study it was established, that in fatty oil of dog rose hips there are 10 fatty acids from which prevail: linoleic (9966 mg/kg), palmitic (4395 mg/kg), stearic (606 mg/kg), palmitoleic (264 mg/kg), lauric (212 mg/kg), myristic (157 mg/kg), arachidic (136 mg/kg) and oleic (106 mg/kg); also there are phytosterols in oil: sitosterol (1906 mg/kg), stigmasterol (174 mg/kg) and campesterol (41 mg/kg); vitamin E (760 mg/kg).

With the help of TLC in fatty oil of rose hips carotenoids are identified.

Pharmacognostic study of fruits of different types of dog rose will be continued.

# THE RESEARCH OF FRUITS OF LYCIUM ORDINARY – GOJI BERRIES

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Goji berries have received the great popularity in many countries of the world and they are widely advertised. Meanwhile, it is the fruit of a shrub in the nightshade family (Solanaceae) – Lycium ordinary or box-thorn (Lycium barbarum L.) – is originally from Central China which can be found almost all over Ukraine on abandoned lots, roadsides as hedges. Edible only dried fruits of this plant, fresh ones are poisonous. According to the information resources the dried fruits are red-orange, seeded, rich in vitamins of group B, C, E, contain 21 microelement including anticancer germanium, 18 aminoacids, 8 of which the human body doesn't produce, 4 irreplaceable polysaccharides which do not exist in products of food. The experience of east medicine which practices application of berries of - goji throughout many centuries speaks about their antioxidant, rejuvenating and immunomodulatory action, about ability to normalize pressure and the content of sugar, and lower the level of cholesterol. Many types of pharmacological activity are exposed to clinical trials of foreign scientists.

Considering prospects of a new type of medicinal raw materials with an available source of raw materials and fakes, which you can find in the market and namely berries of a goji, which are replaced by the fruits of a barberry, cranberries, carrying out the anatomic studying of fruits of Lycium barbarum and establishment of anatomic signs of their structure was the purpose of our work.

Cell of epidermis from a surface from rounded to extended with unevenly reinforced covers, are covered with a thick layer of longitudinal folded cuticle which has an appearance of the longitudinal long and short straight lines and curved folds located along a fruit. Cell of pulp are rounded, thin-walled with numerous spherical red chromoplasts. The seed rind consists of the epidermis and the mechanical layer. From the surface, the cells of mechanical tissue are parenchyma, with large blades, their covers are very thickened, winding, layered. The cells are rectangular, with slightly thickened upper and radical covers on the cross section of the epidermis. The cells of the mechanical layer have significant thickenings in the shape of horseshoe.

# RESEARCH OF SAFFLOWER FATLY OIL

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Promising source of new biological active compounds is Safflower (Carthamus tinctorius L.) - an annual plant with bright yellow flowers from the family Asteraceae, or Compositae. In Ukraine, safflower appeared in the XVIII century, and since the 30s of XX century, and agro-technical study of Safflower crops in numerous regions of Ukraine were made. There are well-known safflower varieties: “Sonyachnui”, “Stepovui”, “Givchik”, “Lagidnui”. Safflower flower and fatty oil produce wide range of pharmacological effect, such as analgesic, cholagogic, anti-inflammatory, hepatoprotective.

In some countries, flowers and oil seeds Safflower is Pharmacopeia’s herbal drug and is used in folk and traditional medicine. In Ukraine there are no Pharmacopoeia requirements for quality of this herbal drug. Therefore, pharmacognostic study and development of Pharmacopoeia requirement for this new herbal drug of plant material is actual.

With the Soxlet apparatus got fatty oils and determined its content, which amounted up to 20%. Safflower oil – transparent liquid with, light yellow color, has pleasant aromatic odor, and specific taste.

Fatty acid composition of the safflower oil determined using the method of chromatography-mass spectroscopy on chromatograph Agilent Technologies 6890 with mass spectroscopic detector 5973.

To sample material in 20 ml vial, was added internal standard - tridecane, at a rate of 50 micrograms per sample, and then calculate the concentration of the internal standard, which is then used for the calculation. To sample was added 10 ml distilled water and carried out water distillation during 2 hours using a reflux cooler. To identify components was used library mass spectra NIST05 WILEY and 2007 with a total of spectra> 470000 combined with programs of identify AMDIS i NIST. The quantitative calculation was performed using the method of internal standard.

Results of compounds composition show that safflower oil is characterized by a high content of unsaturated fatty acids. In the oil extract present as unsaturated and saturated fatty acids. The dominant on quantitative content is linoleic acid (> 78%), oleic acid (> 10%), palmitic acid (> 6%).

The Safflower oil is characterizes by high linoleic acid content and it is show protects of development of dietary supplements and drugs on the basis of this medicinal plant.

# THE METHOD OF PRODUCING THE SUM OF POLYPHENOLIC COMPOUNDS FROM HERB GEUM URBANUM L.

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One of the most important task of the pharmacy is development of new pharmaceutical drugs from plant material. Search for plants that can be the additional source to the officinal species with sufficient resource base, rational and complex use of raw materials and creation on their basis new drugs - an important problem of modern pharmacy.

Special attention is deserved representative of the Ukrainian flora such as Geum urbanum L. of Rosacea, subfamily Rosoideae, which grows all over Ukraine in weedy areas, open forests, in bushes. Phytomedications from grass of this plant are used in traditional medicine from diarrhea, dysentery, fever and as a sedative due to its hemostatic, astringent and anti-inflammatory qualities. Biological activity of plant material mostly caused the content of polyphenolic compounds. G.urbanum L is non-officinalis medical plant, amount of tannins in its grass reaches 10,5%. Chemicals as carotenoids, flavonoids and phenolic acids are also present in selected plant.

Materials and methods. To study were selected sprouts of Geum urbanum L., which were collected during 2013-2014 years in the Kharkiv region during flowering. Raw materials were subjected to air-shadow drying.

Developing the method of producing the sum of polyphenolic compounds from G.urbanum L. herbs was the purpose of our study. This method involves water extraction from grass of G.urbanum L. with the ratio of raw material to extract 1:10 and the temperature 95˚C for two hours, moreover one portion of raw materials is extracted three times. Received extracts are combined, after filtration they are evaporated to 1 / 15-1 / 16 from the previous volume and air dried to dryness. Exit of the finished product is 20.1% from the air-dry matter. Obtained total complex is a non-hygroscopic amorphous powder, light green with a specific characteristic odor, soluble in the water and 50% ethanol.

Thus, the dry extract of the herb G.urbanum L. contains a set of bioactive phenolic substances, which provides a basis for further study of this type of a raw material as perspective medicinal plant.

# PHYTOCHEMICAL STUDIES, MEDICINAL USES AND PHARMACEUTICAL APPLICATIONS OF SNOWDROPS

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Snowdrop (*Galnthus* L., Greek *gála* "milk", *ánthos* "flower") – genus of perennial herbs of the family Amaryllidaceae (*Amaryllidaceae* J.St.-Hil.). Includes 18 species and 2 hybrid of natural origin. Two types of snowdrop have been used in medicine – Voronov snowdrop (*Galanthus woronowii* Losinsk.) and Galanthus nivalis (*Galanthus nivalis* L.).

Voronov snowdrop - herbaceous bulbous perennial that grows in the Caucasus from Tuapse to Batumi, has a bulb, that is 2.5 cm in diameter, and lanceolate leaves (10 - 20 cm long). Galanthus nivalis - also bulbous perennial plant, with wide area of natural habitat (Central and Southern Europe, the Balkans, the Caucasus), the diameter of the bulb is 1.2 - 1.5 cm, leaves obtuse length of 8 - 10 cm.

The main group of snowdrops biologically active substances are alkaloids ("Amaryllidaceae alkaloids"), galanthamine group, lycorine, homolycorine, tyramine, narciclasine, tazettine and haemanthamine (more than 50 compounds established structure). It was supposed by Roger Duvoisin and Andreas Plaitakis in 1983 that the magical mysterious herb “moly” that appears in Homer 's Odyssey is in fact snowdrop. An active substance of snowdrop is known as galanthamine, which, as cholinesterase inhibitor, could have function as an antidote to Circe 's poisons. Galanthamine can be very helpful in the treating of Alzheimer's disease, though it is not a cure.

Among the large variety of alkaloids galanthamine occupies a special place. Alkaloid galanthamine was first isolated in 1952 from the Voronov snowdrop, whose content in the plant is about 0.7 - 0.8%. Galanthamine is used as anticholinesterase agent (similar to the action of physostigmine), for the treatment of myopathies, myasthenia gravis, during the recovery period after suffering poliomyelitis and other disorders of the nervous system, as an antidote to muscle relaxants during surgical procedures. Recently, high efficiency was confirmed galanthamine in the treatment of Alzheimer's disease. In Bulgaria, galanthamine hydrobromide (Nivalin) made from Galanthus nivalis.

In addition to the alkaloids in the plant genus snowdrop several authors found flavonoids (quercetin and kaempferol glycosides), lectins, organic, phenolcarboxylic and fatty acids. Snowdrop lectin (GNA; *Galanthus nivalis* agglutinin) is also being

studied with regard to its potential activity against HIV (human immunodeficiency virus).

Snowdrops are widely used in traditional medicine. For the treatment of scabies, fungal infections, boils, wounds in these cases tincture of bulbs can be applied. For preparing fresh bulbs which firstly are grounded, then mixed with 40% ethanol in a ratio of 5: 100 and infused for 30 days in a cool place. The infusion is used externally: rubbed into the affected areas of skin.

A cold infusion of the fresh leaves have long been used to treat fungal infections. To make it – fresh, crushed leaves of snowdrop are mixed with cold water, infused for 12 hours.

Decoction of the whole plant - an effective tool for the treatment of pain in the joints. To make it – the dried flowers and leaves snowdrop should be boiled on the fire for 15 minutes. For an infusion: 10 g of dried flowers and leaves pour 300 ml boiling water, kept in a water bath for 20 minutes.

Decoctions and infusions of snowdrop also used in diseases of the respiratory system (asthma, pulmonary tuberculosis, bronchitis, colds, pneumonia, whooping cough), liver, gastrointestinal tract (stomach pain, diarrhea, dysentery, intestinal colic). In the treatment of fever, measles, rheumatism, infectious diseases, sciatica, gout it is taken the 15 ml of broth 3 times per day. Snowdrop used to treat inflammation of the kidneys and the bladder, for example, cystitis, pyelonephritis, enuresis, frequent and / or uncontrollable urination.

In homeopathy, it is possible to make mother tinctures based on medicinal plants of two types of snowdrop. Homeopathic medicines used snowdrop to treat fainting, headaches, heart failure, mitral insufficiency in violation of compensation, myocarditis with some degree of mitral regurgitation. Galanthus was proved by Dr. A Whiting Vancouver.

According to Materia Medica: “Faintness, sinking sensations. Sore dry throat with dull headache. Half conscious and worried feeling during sleep. Heart weak with sensation of collapse as if she must fall. Pulse very irregular, rapid and uneven, violent palpitation. Systolic murmur at apex. Therapeutically - decided benefit in cases of Mitral Regurgitation with broken down compensation. Myocarditis with some degree of mitral insufficiency.”

Dose: First potency to fifth. Potencies available in market: liquid – 4X to 30X, 3C to 30C; pills – 3X to 30X, 2C to 30C (Remedy Source).

Investigation of snowdrops is important in order to study their methods of quality control and standardization, development of normative documents on medicinal plant raw materials, products based on it.

**ELEMENTAL COMPOSITION OF SALIX CAPREA L.**

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During millenniums a man uses the different types of willow in the vital functions. Branch of willow are a rich source of connections of phenolic nature (flavonoids, tannic substances), carbohydrates, organic acids, vitamins.

Salix caprea L. (goat willow, also known as the pussy willow or great sallow) is a common species of willow native to Europe and western and central Asia. It is a deciduous shrub or small tree, reaching a height of 8–10 m. The leaves are 3-12 cm long and from 2-8 cm wide, broader than most other willows. The flowers are soft silky, and silvery 3-7-cm-long catkins are produced in early spring before the new leaves appear; the male and female catkins are on different plants (dioecious). The male catkins mature yellow at pollen release, the female catkins mature pale green.

The aim of this work was to study whether elemental composition of Salix caprea L. complies to the requirements for heavy metals content . The objects of the study were Salix caprea L. branch which were collected during 2013 - 2014 years in various parts of the Kharkiv region of Ukrainian. Earlier, we studied phenolic compounds and components of the essential oil of Salix caprea L. Study of elemental composition was carried out using atomic emission spectrophotometry on the base of DNU “STC” Institute for Single Crystals” of NAS of Ukraine. Samples were evaporated from the craters of graphite electrodes in the discharge arc AC power 16 A at 60 seconds exposure. As a source of excitation spectra IMS-28 was used. Spectra were recorded on fi lm using the spectrograph DFS-8 with 600 lines / mm diffraction grating and three-lens lighting slit. Spectral lines in the samples were registered at wavelengths from 270 to 347 nm comparing with a mixture of mineral elements standard samples using microphotometer MF-4. 15 elements in Salix caprea L. branch have been identified and quantified. Of these, 6 were macroelements (K, Na, Ca, P, Mg, Si) and 9 were microelements (Fe, Mn, Al, Pb, Sr, Ni, Mo, Cu, Zn). The specific sins of theirs content in raw material was defined. Macroelements (mg/100g) potassium (1120), calcium (895) and silicon (450) were dominant. Among microelements (mg/100g) phosphorus (195), iron (56) and aluminum (28) predominated. There were no or were beyond the device’s determinative capabilities next microelements: cobalt and lead (<0.03), cadmium (<0.01), arsenic (<0.01) and mercury (<0.01). As a result it was found that Salix caprea L. branch meets the requirements for heavy metals content.

# PHYTOTHERAPY ELDERLY PATIENTS

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A significant feature of human society at the present stage of its development was the increasing life expectancy of people and the increase of diseases mediated by age. "Age-related" diseases are usually associated with deficiency of the activity of the brain and is manifested by impaired memory, reduced mental alertness, impaired vitality and sound mind. It is noted the progression of dysfunction of the mechanisms of regulation of various organs and systems, reduced the activity of adaptive mechanisms that lead to the development of numerous pathologies. Disease of the elderly are particulary more severe than in young and middle age, their number increasing one patient, which exacerbates and accelerates the onset of old age. It is obvious that such patients need constant pharmacotherapy and constant increase in the number of accepted drugs. But it is well known that the simultaneous use of two or more drugs may lead to unusual individual reactions to the medicinal substance. In addition, elderly patients rarely perform the mode of taken medicines as prescribed by doctor. All this leads to low efficiency of drug therapy, the development side effects, the reducing compliance of patients. All of this against the backdrop of significant economic costs.

Nowadays is increasing the importance phytotherapy, which value is restoring the health of elderly patients, and not just common knowledge. Phytotherapy is attractive low risk of adverse reactions, well tolerated by patients, the wide availability, and that is very important now – low cost. Multimodal action of medicinal plants is with mediated biologically active substances, which are rich in (alkaloids, glycosides, coumarins, essential oils, vitamins, resins and others), but not always safe. Therefore, specialists pharmacy for dispensing to patients medicinal plants are required to implement pharmaceutical care, designed to pre-empt the occurrence of side reactions and increase the efficiency and safety of herbal medicine. Should take into account numerous factors determining the selection of medicinal plants, the stage of the disease and the nature of its course, the interaction between medicinal products and medicinal plants, to carry out an individual approach to the patient (age, gender, etc), adjust the dose, to explain the technology of preparation of the pharmaceutical form of medicinal plants, as well as the mode of its application. The extension of knowledge in the field of herbal medicine and its security is an important focus for the modern pharmacy specialists. This necessity is due to the increasing demand for herbal drugs.

# THICK EXTRACT OF AMBROSIA ARTEMISIIFOLIA – NEW SUBSTANCE FOR CREATION OF MEDICINES

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Medicinal plant raw material (MPRM) through rather complicated chemical composition and variety of biologically active substances it contains, is widely used in the pharmaceutical industry. Medicines, for which the active ingredient is MPRM-substances, take a certain share among the range of medicines, which industrial manufacturer of medicine proposes to the pharmaceutical market of Ukraine. Extraction of new plant substances from medicinal plant raw materials and the development of medicines based on them do not lose actuality.

Medicinal plant raw material of Ambrosia artemisiifolia (Ambrosia artemisiifolia L.) has attracted attention as the object of the study, because spectrum of theoretically known activity allows to determine modernity of its using as possible. It is known that medicinal plant raw material, which was given, contains in its structure chemical compounds such as sesquiterpene lactones, coumarins, essential oils, phenolcarbonic acids, flavonoids, triterpenoids, fatty acids and mineral elements that are responsible for its pharmacological activity.

The thick extract of Ambrosia artemisiifolia was obtained by the department of chemistry of natural compounds. To obtain a thick extract, medicinal plant raw materia of Ambrosia artemisiifolia was extracted with 40% ethanol by the method of fractional maceration exhaustively. Extraction was carried out with aqueous ethanol at a ratio of 1:30 for 5 days.

An important step was to study the chemical composition of the extract. It was revealed that the thick extract contains terpenes, phenolic compoundsin, particular flavonoids, hydroxycinnamic and phenolcarbonic acids, that opens the possibility of introducing him to the medicines. The most important characteristics of a new medicine is its efficacy and safety, and therefore the definition of acute toxicity in experiment on male rats weighing 205-240 g and female rats weighing 155-175 g by intragastric introduction was planned to carry out. It were observed for rats state for two weeks. Changes in appearance, state of the skin and mucous membranes, the dynamics of body weight, behavior were not noticed. The obtained results allow to include thick extract by the Hodge H.C., Sterner J.H. classification to practically non-toxic substances (V class toxicity, 5000 <LD50 <15,000 mg / kg). It is known from literature sources about the anti-inflammatory, wound healing, cytotoxic, disinfectant actions of Ambrosia artemisiifolia herb, so it is important to investigate the said pharmacological activity with a view to aptly using in the pharmacotherapy of diseases wich have polietiologic genesis. Information about the use of medicinal plant raw materia of Ambrosia artemisiifolia and identified components biologically active substances of thick extract make it possible to consider it as an effective substance for the development of medicines in order to correct inflammatory conditions in the dental practice.

# COMPARATIVE ANATOMICAL STUDY OF LEAVES OF MONARDA FISTULOSA AND MONARDA DIDYMA

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*Monarda didyma* – **bee balm** has bright, carmine red blossoms and is commonly known as oswego tea. *Monarda fistulosa*, commonly known as wild bergamot, has lavender or smoky pink flowers. Both spices belong to *Lamiaceae* Family. Bee balm is the natural source of the antiseptic thymol, the main active ingredient in modern commercial mouthwash formulas. Bee balm tea was used to treat mouth and throat infections caused by dental caries and gingivitis, as a carminative herb and an infusion of crushed bee balm leaves in boiling water has been used to treat headaches and fevers. The aim of our study was conducting anatomical investigation and revealing the distinguishing features of anatomical structure theirs leaves.

During anatomical studies of *Monarda fistulosa* and *Monarda didyma* their common features have been revealed. There are common diagnostic features in both species – parenchymatous cells of upper and lower epidermis with sinuous cell walls, cells are covered by many papillas. On the upper epidermis presence the multicellular simple trichomes and glandules with orange secret and surrounded by 13-15 radial-located rosette of cells. The stomas are present only beside cells of the lower epidermis.

Distinguishing features of leaf anatomical structure in *Monarda didyma* include presence 7 cells of rosette around simple hairs of lower epidermis, cells of epidermis with green content. *Monarda fistulosa* – presence in the central part of leaf plate the glandular hairs with one-celled stalk and one-celled head filled with brown secret.

The upper epidermis of *Monarda didyma* has next distinguishing features – stomatal apparatus is diacytic and anisocytic. Trichomes are 2-5 celled, 2-celled hairs has rosette around basic cell consists from 5 epidermal cells. All surface of leaf plate covered by glandules with orange secret and surrounded by 13-15 radial-located rosette of cells and glandules with the same structure, but contains the green secret. The upper epidermis of *Monarda fistulosa* characterized by presence of diacytic and anomosytic stomatal apparatus, long multicellular (up to 11 cells) and presence only one kind of glandules – with orange secret.

Morphological and anatomical characteristics of leaves of *Monarda didyma* and *Monarda fistulosa* will be used in standardization of raw materials and determination of species systematic position.

# PHYTOCHEMICAL RESEARCH OF SALIX CINEREA L.

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The genus Salix is one of the largest in the flora of the Ukraine and the largest one in the dendroflora.There are about 29 kinds of willows in Ukraine. Their bark, buds and the leaves of Salix L. which contain phenolic glycosides, flavonoids, tannin, organic acids, vitamins, terpenoids. However the Salix genus plants aren't studied enough.

Salix cinerea L., family Salicaceae is native from most of Europe, Russia and western Asia (i.e. Turkey, Azerbaijan and Kazakhstan). Common names: gray willow, common sallow, large gray willow, olive-leaf willow. It grows in moist sites, often by watersides, in regions with hot summers and cold to mild winters.

It is a deciduous shrub or small tree growing to 4–15 m high. The leaves are spirally arranged, 2–9 cm long and 1–3 cm broad (exceptionally up to 16 cm long and 5 cm broad), green above, hairy below, with a crenate margin. The flowers are produced in early spring in catkins 2–5 cm long; it is dioecious with male and female catkins on separate plants. The male catkins are silvery at first, turning yellow when the pollen is released; the female catkins are greenish-grey, maturing in early summer to release the numerous tiny seeds embedded in white cottony down which assists wind dispersal

Our goal is the research of qualitative composition and quantitative composition of flavonoids in the branch of Salix cinerea L. These branch were gathered for the research in Kharkov regions and in the Zakarpatye oblast of Ukrainian in 2013-2014. There were pointed the presence of phenolic compounds (phenolic glycosides , flavonoids, tannin) when the primary studying of the Salix cinerea L leaves was. The presence of fl avonoids was defined in the ethanol extracts with cyanidin test, ferric(III) chloride. In results of reaction show the presence of fl avonoid aglycones and glycosides. Besides the substances of flavonoids were discovered due to chromatographic method. For this method the paper "Filtrak"(FN №№ 1,4,12) and silica gel TLC plats were used. In accordance with the reference pattern rutin, quercetin, ferulic, chlorogenic, salicylic asides were identified. The method of spectrophotometry(410 nm on the spectrophotometr СФ-46) was applied for the analysis of flavonoids. The contain of flavonoids is turned out not less 2,7%. The Salix cinerea L. has the practical interest as a source for getting plant drugs of many-sided pharmacological action due to considerable quantity of phenolic compounds.

# PHENOLIC COMPOUNDS OF LAMIUM ALBUM L. HERB EXTRACT

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Lamium album L., commonly called white nettle or white dead-nettle, is a herbaceous perennial herb in the family Lamiaceae, growing in a variety of habitats from open grassland to woodland, generally on moist, fertile soils. Lamium album L. herb has been used in folk medicine of many countries for centuries as an expectorant, anti-inflammatory, antispasmodic, diuretic, hemostatic and sedative remedy.

**The aim of presented work** was to investigate the composition of phenolic compounds of Lamium album L. herb dry extract, obtained by extraction with 70% ethanol.

**Materials and methods.** The white dead-nettle herb was harvested in the flowering stage in Kharkiv region in the July of 2011.

For the analysis was prepared methanolic extract of the herb. Dividing the amount of phenolic compounds into individual components was performed by high-performance liquid chromatography (HPLC) using chromatograph Agilent 1200. For the analysis used chromatography column Supelco Discovery C18 size 250×4,6 mm, filled by octadecyl-functionalized silica grains. Chromatography mode: maximum feed rate of the mobile phase 0.7 ml/min, eluent working pressure 100-120 bar (10000-12000 kPa), column thermostat temperature 25°C, injected sample volume 5-10 ml, chromatography time 50 minutes. Elution mode – gradient, scan time – 0.6 sec, detection range – 190-400 nm, the wavelength – 320, 330 nm (for hydroxycinnamic acids) and 255 nm (for flavonoids). The identification of compounds was performed by retention time of standards and spectral characteristics.

**Obtained results.** It is established that Lamium album L. herb extract contains (in mg per 100 g of raw material) flavonolic glycosides rutin (158.0) and isoquercitrin (376.8), chlorogenic (411.0), ferulic (72.4), caffeic (28.8) and rosmarinic (49.7) acids. Total content of identified flavonoids was 534.8 mg/100 g, identified hydroxycinnamic acids – 561.9 mg/100 g.

**Conclusions.** In the white dead-nettle herb dry extract two flavonoids and four hydroxycinnamic acids were identified and quantified. These substances are biologically active and significantly contribute to the pharmacological effects of studied plant extract.

# STUDIES ON VITAMIN COMPOSITION OF SYRINGA VULGARIS BARK

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Syringa vulgaris is one the most favourite and extended ornamental bushes in our country. There are more than 31 species and more than 1500 varieties of lilac in the world. This diversity of species and varieties promote using the plant for landscaping parks and squares. At present Syringa vulgaris is cultivated in many countries of the world. However, lilac is known not only due to its unique beauty, but also because of its valuable medicinal properties. For a long time this plant was extensively used in folk medicine for many diseases treatment and prevention: rheumatoid arthritis, gout, diabetes mellitus, bronchial asthma, malaria etc. The Syringa vulgaris bark is used in officinal medicine as raw material for syringin (eleutheroside B) extraction, which serves as a marker at standardization of medical preparation, extracted from the raw material of Eleutherococcus senticosus. The purpose of the research was the determination of the qualitative composition and quantitative content of vitamins in the Syringa vulgaris bark. The object of the research was the Syringa vulgaris bark, collected in march 2013 and 2014 in Kharkiv region. The quantitative content of B vitamins was determined by fluorometer EF-3MA (vitamin $B_1$ in recast on thiamine hydrochloride, vitamin $B_2$ in recast on riboflavin, vitamin PP – in recast on nicotinic acid). The content of ascorbic acid was determined by the method of PA 38. “The brier fruits” of State Pharmacopeia of USSR XI edition.

As a result of the research the presence and quantitative content of vitamins B and ascorbic acid in the Syringa vulgaris bark were determined. The total content of vitamins made up 6,6 mg/kg, in particular $B_1$ 0.10±0.01 mg/kg, $B_2$ 0.66±0.04 mg/kg, $B_5$ ( PP ) 2.50±0.03 mg/kg, C 3.40±0.02 mg/kg. Ascorbic acid (3.40±0.02 mg/kg) prevails among the vitamins in the research object.

The vitamin content of Syringa vulgaris bark was determined. 4 vitamins in the analyzed raw material were identified and quantitatively established with the prevalence of ascorbic acid (3.40±0.02 mg/kg). So, we can make a conclusion that the lilac bark can serve as a valuable source of different vitamins in preventive and medical preparations. The results of quantitative determination of vitamins will be used in the development of the project of quality control methods on “Syringa vulgaris bark”.

# DEVELOPMENT OF COMPOSITION AND ANALYSIS OF COLLECTION FOR IMPROVEMENT OF CEREBRAL CIRCULATION OF BLOOD

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Cerebrovascular pathology was and remains among the most medical and social issues of the day in all figures of the world. Cerebrovascular diseases are one of leading reasons of morbidity, death rate and resulting in disability of population of our country. According to data of WHO, a death rate from the vascular diseases of cerebrum is 30-50% from all diseases of circulation of blood or near a 14% general death rate of population. Presently there is a tendency to the height and "rejuvenation" of cerebrovascular diseases, what is assisted unfavorable economic and ecological situation in Ukraine, often inadequate treatment of initial forms of this pathology. From data of official statistics of Ministry of Health in Ukraine, in 2002 more than 2 million persons are registered with different cerebrovascular diseases, amount of patients with this pathology from year to year grows steadily. For the last 10 years prevalence of cerebrovascular diseases increased from 3776,3 in 1992 to 6917,6 in 2002 on a 100 thousand population, so its grew in 1,8 time. It is needed to notice, that the stake of cerebral strokes in the structure of vascular diseases of brain in 2002 made just 4%, or 294 on a 100 thousand population. Cerebrovascular diseases in age 20-59, from data of epidemiology researches, in the structure of general morbidity 20%%, make from them initial displays of insufficiency of cerebral circulation of blood – 68%%, transient violations of cerebral circulation of blood is 25%%, dyscirculatory encephalopathy and strokes – 7%. With age morbidity increases a stroke in two times for every subsequent decade. Prevalence of cerebrovascular diseases among women in 2,3-2,8 time higher, than among men.

So, wide distribution, high death rate of population, because of cerebrovascular diseases rank together a prophylaxis and treatment of these illnesses with the most actual medical problems and stipulate the necessity of development of new, more accessible and more effective medicinal facilities, including phytogenous.

Analysing and generalizing these literatures about the medical plants applied for treatment of violations of cerebral circulation of blood, we offered collection of

next composition : hawthorn garden-stuffs (Grataegi fructus), periwinkle small grass (Vincae minoris herba), hop of infructescence (Lupuli strobili), uliginose grass(Gnaphalii uliginosi herba), melissa grass (Melissae herba), melilot grass (Meliloti herba). The components of collection possess spasmolytic, making better cerebral circulation of blood, hypotension, ataraxic, by an antioxidant, diuretic action.

Collection was prepared according to the requirements of State Pharmacopoeia of Ukraine, addition 2.

The next stage of our researches was a study of quality composition of bioactive substances of the offered collection. By means of quality reactions in collection for the improvement of cerebral circulation of blood were discovered free and constrained sugar , polysaccharides , coumarins , flavonoids, tannic substances of the condensed group, saponins and nitrogenated connections.

In the offered collection for the improvement of cerebral circulation of blood quantitative maintenance of bioactive substances was certain by us. So, maintenance of polysaccharidess was determined by a gravimetrical method, that was 9,52%. Determination of maintenance of coumarins was conducted by a photocolorimetric method. Their maintenance was 0,81%. A table of contents of hydroxycinnamic acids, certain a spectrophotometry method in a count on chlorogenic acid, was 1,50%. Also by a spectrophotometry method maintenance of flavonoids was certain in a count on rutin – 2,24%. Tannic substances determined a permanganometric method in a count on tanninum. Their maintenance was 9,70%. The sum of free organic acids was set by an alkalimetric method in a count on apple acid – 1,11%. A table of contents of ascorbic acid was 0,13%.

For standardization of the offered collection and development of project of methodologies of control of quality on him numerical indexes were certain by us: loss in-bulk at drying – 12,45%, ash general – 1,31%, ash insoluble in a 10% solution of hydrochloric acid, – 0,42%, extractive substances water-extractable, – 19,56%, and also morphological and anatomic diagnostic signs of this collection.

The got results testify to perspective of further study of the offered collection and will be used for development of corresponding divisions of methodologies of control of quality on collection.

# RESEARCH THE CARBONIC ACIDS OF CRATAEGUS MONOGYNA FLOWERS

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**The aim of investigation**

*C. monogyna* it is one of the pharmacopoeia species, raw material of which are fruits and flowers. Their chemical composition is studied in detail. But *C. monogyna* forming hybrids, on its base was created the sorts differ in morphological structure. Are known pyramidal form (f. stricta) – tree with pyramidal crown; weeping (f. pendula) – pubescent branches; weeping pink (f. rosea pendula) – weeping with pink flowers; bright-red (f. punicea) – with dark -red single flowers; pink (f. rosea) – petals of flowers are pink with white stripes; white terry (f. albo-plena) – with terry flowers; red terry (f. rubra-plena) – with red terry flowers; always flowering (f. semperflorens) – low shrub, flowering whole summer until autumn; (f. laciniata) – with deeply lobed leaves; white-motley (f. argentea-variegata) – with white-motley leaves; thorn less (f. inermis) – branches without thorns, flowers are simple, white.

**Materials and methods**

The objects of our study were the leaves and flowers of *C. monogyna* simple and terry forms: *C. monogyna var. monogyna*, *C. monogyna* flore rubro-plena, *C. monogyna* flore Roseo-plena. As a result of chromatographic research in a thin layer of sorbent in all the samples was identified phenolcarbonic acids and hydroxycinnamic acids, anthocyanins, flavonols and flavones, catechins. By the method of chromatography-mass spectrometry for the first time was investigated carbonic acids of flowers *C. monogyna var. monogyna.* Research conducted in chromatograph Agilent Technology HP6890 GC, mass-spectrometric detector 5973N. The exact weight of the dried material was placed into 2 ml vial and added internal standard (50 mg tridecane in hexane) and 1.0 ml 14% $BCl_3$ in methanol (agent for methylation). The mixture was kept in a tightly closed vial 8 hours at 65 ° C. At this time the acids are completely extracted from the raw material and passes them transesterification. The reaction mixture was poured and diluted with 1 ml of

distilled water. For extraction of methyl esters of acids was added 0.2 ml dichloromethane, mixture was shaken 1 hour. Putting 2 ml sample into the chromatographic column was carried out in the mode "*splitless"*, which allows to enter the sample without loss to division and significant 20-times to increase the sensitivity of chromatography method. The speed of the sample enter - 1 ml / min, the term – 0,2 min. Detector of mass-spectrometry – quadrupoles, method of ionization - electron impact, energy of ionization 70 eV, to analyze used the complete registration mode of the ion current. For division was used the capillary column HP-INNOWAX, (30 m × 250 mkm). Moving phase – helium, the gas flow rate 1 ml/min. The temperature of the heater input the sample – 250 $^0$C. The thermostat temperature is programmed from 50 to 250 $^0$C. The identification of methyl esters of acids conducted on the base of calculating the equivalent length of the aliphatic chain, using data of the library mass spectra NIST 05 and Willey 2007 in complex with identification programs AMDIS and NIST; also compared the retention time with the retention time of standard substances (Sigma). To calculate the quantitative determination of the components used equation: C = K1 * K2 * 1000 (mg / kg), where: K1 = П1 / П2 (П1 peak area of investigated substance, П2 – peak area of standard); K2 = 50 / M, (50 – mass of internal standard, introduced in the sample, mkg; M – weight of investigated sample, mg); C – content the acids in raw materials, мg/kg.

**Obtained results**

It was established that the total acids content is 2,9%. Identified 37 carbonic acids. In raw material content of fatty acids – 8309,05 mg/kg, carbonic acids – 517,54 mg/kg, hydroxycinnamic acids – 338,26 mg/kg. Among the carbonic acids are dominated (mg/kg): malic – 3104,92, formic – 3040,05, succinic – 1316,32, malonic – 1969,33 acids. The share of fatty acids among the sum of organic acids is 28,5%, phenolcarbonic – 1,77%, hydroxycinnamic – 1,16%.

**Conclusions**

In *C. monogyna* flowers were determined: fatty acids (28,5%), phenol carbonic acids (1,77%), hydroxycinnamic acids (1,16%).

# *PARMELIA PERLATA* AS A PERSPECTIVE SOURCE FOR OBTAINING NEW DRUGS

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*Parmelia prelata* is dual organisms composed of a symbiotic relationship between an alga and a fungus. The fungus, usually an ascomycete, provides the plant its shape, and the alga provides the ability to photosynthesis. This successful combination is able to produce a more elaborate and durable organism than either partner alone. *Parmelia prelata* is able to colonize inhospitable areas such as bare rock. As pioneer plants, *Parmelia prelata* break down the rock surface and, eventually form soil conditions suitable for other plants. Only a few species of parmelia tolerate air polluted with sulphur dioxide so few survive in cities. *Parmelia prelata* is variable in shape, tubular, upright and branching, or flat and leaf-like or forming an amorphous greyish crust.

*Parmelia prelata* contain different compound like anthraquinone, hypericine, bianthrone, usnic acid, evernic acid, fumarprotocetraric acid, atranorin, chloroatranorin, protocetraric acid, 4-amino-3-hydroxy-6-methoxy-2-methylcyclo-hexa-1,3-diene-1-carbaldehyde, 5-amino-2-ethoxy-4-methylcyclo-1,3-diene-1-carboxylic acid. All these compounds play a role in the treatment of many diseases, because of their effects - antioxidant, antiviral, antibacterial, anti diabetic, antihyperlipidimic, cytotoxic activity.

Different experiment are applied on parmelia specially on *Parmelia perlata,* and these experiences show positive result of the effect but till now the using of this plant isn't under any Pharmacopeia supervision.

*Parmelia prelata* thalli were taken as plant raw material for our study. The following values needed for working out the quality control procedures were determined: loss of weight during drying of plant raw material, content of total ash and ash non-soluble in 10% hydrochloric acid.

## MORPHOLOGICAL FEATURES FOLIAGES CYTISUS RUTHENICUS

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Ordinary broom (Cytisus ruthenicus) belongs to the genus broom (Cytisus L.), subfamily papilionaceous (Papilionacea), which is part of a large family of legumes (Leguminosae) and includes 30 to 70 species. Forms undergrowth in the forest-steppe and steppe zones of European Russia, in Western Siberia and the Caucasus. It can be found in the desert, and in the meadows and on rocky slopes. This is the only shrub that settles as undergrowth in dry pine forests on poor sandy soils. Light-mezokserofit. Low to 1.5m tall, deciduous shrub with straight or curved, gray branches. Shoots with silky pubescence. Growth of shoots from the first half of May and lasts until the end of August. Leaves are small, up to 2 cm, lanceolate-elliptic, on top of the spines, gray-green top, bottom, densely hairy. Flowers large, yellow, 3-5 in the axils of leaves, bloom after leafy within 25 days. Fruits - flat beans to 3 cm long, blackish or dark gray, covered with gray hairs pressed, ripen in September. Inside the bean is oval, flat, shiny, 3 mm long, yellowish or greenish seeds.

Winter-hardy, drought-resistant, undemanding. It grows well in lit areas, sandy and sandy loam soils. Propagated by seeds, root suckers.

As a medicinal herb stimulates uterine contractions, helps the body get rid of excess fluid, increasing urine formation, sometimes causes a sharp increase in blood pressure, treating congestive heart failure, with smoking can have a calming-hypnotic effect. With the purpose of treatment harvested aboveground parts of the plant, usually leaves. Cytisus ruthenicus contains alkaloids (sparteyin, cytosine) flavanoyid (genistein). Cytisus ruthenicus is a poisonous plant, so it should be used with caution, as it is contraindicated for use for children, people over 55 and people with hypertension because the plant contains a cytosine, which raises blood pressure.

The use of biologically active substances of plant origin today is important for medicine and cosmetology. So in the global pharmaceutical industry a third drug is made from medicinal plants. Medicines and cosmetics based on natural substances exhibit virtually no side effects. Their low toxicity (as biologically active substances of natural origin are easily digestible by the human body complexes and concentrations) the possibility of long-term use without significant side effects allows the use of herbal medicines for children and the elderly, especially in chronic forms

of disease. Thus, the development of drugs based on medicinal plants a promising direction of pharmaceutical science.

The aim of our work was to identify major anatomical features diagnostic leaf Cyti-sus ruthenicus usual for further identification of medicinal plants.

The object of the study was an Cytisus ruthenicus leaves collected in May and June 2014 in the Botanical Garden of the National University of Pharmacy during blooming. Cross-sections and surface specimens were manufactured from fresh, dried material and fixed with a mixture of glycerin-alcohol-water (1: 1: 1). Production and micropreparations study was carried out by conventional methods. Diagnostic microscopic signs recorded using microscope "Lomo Mikmed 1" and the camera Sony Cyber-shot (DSC-W80).

Morphological characteristics of raw materials. Leaf blade Dorzoventralnom type of structure. The cells of the upper epidermis polygonal, warehouse, have clear membrane thickening. Epidermal cells are papilliform formation. Stomata anatomotsytnoho device type. Stomata occur on both sides of the leaf blade - amfistomatychnyy type of leaf.

The lower epidermis presented polygonal cells wall-sided, clearly visible from thick shells. The cells of the lower epidermis smaller than the cells of the upper epidermis of the leaf blade. Cells with papilliform grow. Epidermal cells of the central vein prozenhimni, warehouse. The underside of the leaf blade abundantly, evenly covered with hairs. Hairs on the upper side only along the edge of the leaf blade: simple, two-cell consisting of short and long basal cell terminal, pressed to the surface of the sheet. The terminal cell with little warty cuticle. Thickened cell walls, cavity inside the hair is tremendous. The base is surrounded by a rosette hair with 6-8 epidermal cells. Hairs on the edge of the leaf blade and along veins 2-3 cell. All the hairs nestled to the surface of the leaf blade and sent to the top of the sheet. On cross-section is clearly visible all layers of the anatomical structure of the leaf. Epidermal cells are large enough. The cuticle is clearly visible. Palisadna parenchyma 1-2 row. The cells are small, are tight. Spongy parenchyma 4-5 row, the cells are loosely with large intercellular spaces. Central vein single beam. A bunch of collateral. Crystal no lining. Petiole overlooks sheet cushion. Epidermal cells almost rectangular, arranged in rows. The walls are thickened hairs, the hairs to 3 lengths cells. The bottom surface richly covered with hairs evenly.

The main morphological and anatomical features of an Cytisus ruthenicus leaves that will identify and standardization plant material. These investigations are necessary for the development of the analytical documentation.

## FATTY ACIDS OF POTENTILLA ALBA L. LIPOPHILIC EXTRACTS

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Potentilla alba L., also known as white cinquefoil, is a plant native to Central Europe where it has been used in folk medicine for centuries. Recent research shows that white cinquefoil can be successful in the treatment of hyper- and hypothyroidism, goiter and thyrotoxicosis.

**The aim of this study** was to investigate the fatty acid composition of Potentilla alba L. herb and rhizomes lipophilic extracts.

**Materials and methods**

Raw materials of white cinquefoil were harvested in Kharkiv region in 2014.

Study of qualitative and quantitative composition of fatty acids was performed with mass spectrometric detection. By adding the solution of boron trichloride in methanol to the plant material methyl esters of fatty acid were obtained. Analysis of the methyl esters were carried out using the chromatograph Agilent Technology HP6890 GC with mass spectrometric detector 5973N. The identification of methyl esters of fatty acids were carried out using the data of the mass spectra library NIST 05 and Wiley 2007. Calculation of the quantitative content of fatty acids performed by the method of the internal standard in mg/kg and percentage of their total content.

**Obtained results**

As a result, in the Potentilla alba L. herb lipophilic extract 14 fatty acids were identified, including 10 saturated (lauric, myristic, pentadecanoic, palmitic, margaric, stearic, arachidic, heneicosylic, behenic and lignoceric), 2 monounsaturated (palmitoleic and oleic) and 2 polyunsaturated (linolenic and linolenic). The lipophilic extract of Potentilla alba L. rhizomes unlike the herb one did not contain heneicosylic acid, but contained monounsaturated 7-hexadecenoiic and 10-octadecenoic acids (in minor quantities).

The total fatty acid content in the white cinquefoil herb extract amounted 16086 mg/kg, in the white cinquefoil rhizomes extract – 3438 mg/kg. Dominant fatty acids of the herb and rhizomes extracts were palmitic (8351 mg/kg and 1144 mg/kg, respectively), stearic (1853 mg/kg and 451 mg/kg), linoleic (704 mg/kg and 597 mg/kg) and linolenic (2193 mg/kg and 191 mg/kg).

**Conclusions.** In the Potentilla alba L. herb and rhizomes lipophilic extracts 16 fatty acids were identified. Dominant acids of the both extracts were palmitic, stearic, linoleic and linolenic.

## MICROSCOPICAL CHARCTERISTICS OF PARSLEY LEAF

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Despite the use of synthetic chemical agents in the treatment of various conditions, natural products still play a major role as starting material for drug discovery. According to the WHO reports, medicinal plants would be the best source for obtaining a variety of drugs. About 80% of the developed countries populations use traditional medicines, derived from medicinal plants. Therefore, the study of plants traditionally used in folk medicine may help discover new effective phytoremedies.

The aim of our research was to carry out the microscopical analysis of parsley greens collected in 2014 in Kharkiv region. Parsley or *Petroselinum crispum* is a species of *Petroselinum* in the family *Apiaceae*, native to the central Mediterranean, and widely cultivated as a herb, a spice, and a vegetable all over the world. For medicinal purposes the dry plant material is used which retains its bright green colour when dried and readily breaks up to form flakes. The taste and odour of the plant material are characteristic.

The upper epidermal cells have shown to be large with thin walls. The absence of stomata on the upper epiderm is characteristic. The underlying palisade parenchymal cells are large and loosely packed. The lower epidermis is represented by cells with then and sinuous cells. The numerous stomata are of anomocytic type. Over the large veins rounded, forward-projecting papilla occur on both epidermises. The lamina forms teeth at the margin where the epidermal cells tend to be smaller and have straighter walls; in sectional view these cells have thick cuticle. The stomata are abundant in the marginal teeth regions.

The epidermis of the petiole is represented by the large cells which are longitudinally elongated, with slightly thickened walls. From the surface view this thickening is seen as uneven pitting and beading, the cuticle is finely striated. Anomocyte stomata are occasionally found on the epiderm. Parenchyma of the petiole is composed of large cells with moderately thickened walls.

The vascular tissue contained lignified vessels, smaller and with spiral or annular thickening in the veins, and larger and reticulately thickened in the petiole.

Thus, the collected plant material according to its microscopical features has proven to be that of parsley showing the most characteristic features of *Petroselinum crispum* leaf. The study carried out was important for the authenticity determination of the plant material.

# RESERCH OF HYDROXYCINNAMIC ACIDS IN THE DRY ALCOHOLIC EXTRACT FROM MYRTILLI LEAVES

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Blueberry fruits - (Fructus Myrtilli) are widely used in the medical and pharmaceutical practice. Decoctions of blueberry fruits are used as an astringent in therapy of colitis, enterocolitis and diarrhea.

There are some of drugs which containing biologically active substances of blueberry fruits (Strix, Optics, Visio Balance, Blueberry Forte, etc.) are widespread on the pharmaceutical market of Ukraine.

Bines and leaves of blueberry are used as a hypoglycemic agent in the form of decoctions in the folk and scientific medicine. They are part of the glucose-lowering drugs- Arfazetin and Mirflazin. But there is no single novogalenic or galenic preparation based on the blueberry leaves on the Ukrainian pharmaceutical market. It would be useful to develop a standardized medicines based on this raw material.

Therefore, the aim of our study was to determine the qualitative and quantitative content of hydroxycinnamic acids in the dry alcoholic extract from the leaves of blueberry.

Previously, we have chosen the optimum extractant for extraction of phenolic compounds from blueberry and it is 50% ethanol.

For preparing the extract, 5.0 g. of dry raw materials (blueberry leaves), milled to a particle size of 2-3 mm were filled with 50 ml. of 50% ethanol and infused at room temperature overnight. The extraction was repeated twice. Extracts were combined, filtered and evaporated to a dry extract.

For determining the qualitative composition of the hydroxycinnamic acids in the extract dimensional method using paper chromatography in systems of *n*-butanol-acetic acid-water (4: 1: 2) and 5% acetic acid followed by treatment with ammonia vapor chromatograms using standard samples hydroxycinnamic acids. It was revealed at least three substances which are hydroxycinnamic acid derivatives.

Technique HPLC was used for more detailed study of the extract. The analysis was performed on the Agilent Technologies 1100 chromatograph. As a result, coffee, chlorogenic, p-coumaric acids have been identified. Five substances which are derivatives of *p*-coumaric acid could not be identified. It has also been established in the quantitative content of extract.

Also, quantification of hydroxycinnamic acid derivatives was carried out by spectrophotometry. Optical density was measured in a cuvette with a layer thickness of 10 mm. by a spectrophotometer “Specol 1500” (Switzerland). Derivatives of hydroxycinnamic acids content was determined, based on the chlorogenic acid at 327 nm. It was established that content of hydroxycinnamic compounds was 24.9% in the dry extract of the leaves of blueberry.

The data obtained will be used to standardization the dry extract of the blueberry leaves.

# DEVELOPMENT OF DRUG FEES TO THYROID MEDICATION

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According to the WHO more than 2 billion Earth's inhabitants live in iodine deficiency. According to modern concepts, the term brings together a wide range of conditions associated with iodine deficiency: from a simple increase in thyroid - endemic goiter disorders to severe mental and physical disabilities - endemic cretinism. Among endocrine disorders of thyroid disease in second place after diabetes and are urgent public health problem in many countries of the world.

Iodine deficiency and its consequences cause significant economic damage to the country. The cost of treatment is much higher than the cost of the iodine prophylaxis.

Iodine deficiency can not be eliminated once and for all. The reason for its occurrence is associated with a fatal natural iodine deficiency, leading to a deficiency of this trace element in food.

Endocrinology Research Center conducted a large-scale epidemiological studies designed to assess the iodine supply of the population. Studies have shown that the actual average consumption of iodine residents of Ukraine and Russia is 40 to 80 micrograms per day, which is 3 times less than the recommended norm.

Analyzing the range of Ukraine industrial products intended for the treatment of thyroid cancer, found that the treatment of this disease is used mostly tableted dosage form.

Studies range of drugs produced in pharmacies showed that their number slightly and make the greatest specific gravity, the liquid dosage forms. Preparations for industrial and manufacturing extemporaneous not fully meet the needs of this group of patients.

For iodine supply of the population must be a regular flow of a certain dose of trace elements in the body. The basic tool for mass prevention of iodine deficiency disorders, is the use of iodized salt and medicinal plants.

The practice of medicine with the oldest being used medicinal plants for their own purposes.

In recent decades has significantly increased the use of drugs, of which consists of active substances derived from medicinal plants. Advantages with respect to biologically active substances synthetic analogues - obvious. The main advantages are: the absence of significant side effects, they are suitable for long-term use, low toxicity.

It is necessary to take into account that today, a lot of valuable medicinal products are made only from the raw materials of medicinal plants.

Research carried out by us, at the option of medicinal plant raw materials containing iodine, allowed to establish the medicinal collection for thyroid treatment.

# DETERMINATION OF QUANTITATIVE COMPOSITION OF XANTHONES IN THE UNDERGRAUND ORGANS OF *IRIS SIBIRICA* AND *IRIS HUNGARICA*

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The representatives of the family *Iridaceae*, of the genus *Iris* – *Iris hungarica* L. and *Iris sibirica* L. – are grown not only as an ornamental plants, and have been used long in folk medicine as an analgesic, anti-inflammatory, enveloping, expectorant remedy.

There are over 250 species of irises in the world, and about 13 species – in the territory of Ukraine. They are growing in the steppes, on the slopes, there are not undemanding to the soil. Widely distributed in the Northern and Eastern Europe, Asia Minor, the Caucasus, the Mediterranean.

*Iris hungarica* is the perennial herbaceous plant 15 – 40 cm height, the stem with direct line-xiphoid or sickle curved leaves up to 45 cm long, narrowed at the ends. In the winter the leaves die off, appear after stems in the spring. The stems are thin up to 50 cm tall, the branching. Perianth is blue-violet color, back-ovoid form, has sixtyseporated limb. The orange-yellow "beards" are situated at the slightly bent outer parts. The basis of flowers are covered by swollen leathery leaves. Blooms in late of April – in beggin of May. The fruit is the cylindrical box. Fruits in July – August. The underground organs are presented by thick branched rhizome of about 2 cm in thickness with branches grows. Propagated by seeds and vegetatively.

*Iris sibirica* is the herbaceous perennial plant. The rhizome is 8 – 10 cm length and 3 cm thick, is irregularly thickened, the upper part is covered by brown remnants of leaves. It has a brown color, a faint smell. Leaves are the linear form, dense, light green color, 32 – 70 cm length and 0.5 – 1 cm wide. The leaves are much shorter than the stem, are located at the base of pneumatic cavities. It has 2 – 3 flowers on unequal pedicels with short tube of perianth, dark blue color. External share are blue with pale-blue nail. The box 2 – 3 cm long, the dull.

According to the literature it is known, that in the leaves of iris contains phenol carbonic acids, there are coffee, sinapinic, *n* – coumaric, ferulic; flavonoids – quercetin; ascorbic acid. In the underground organs of irises contain xanthones, sucrose, starch, fructans, and essential oil. The chemical composition of the rhizomes with roots has been little studied.

The particular value in the irises up xanthones, namely mangiferin with a high biological activity. It has anti-inflammatory, immunostimulating, antiviral effect.

The objects of study were rhizomes with roots of *Iris hungarica*, harvested on May, 2014, and *Iris sibirica*, harvested on September, 2012 in N. N. Gryshko National Botanical Garden of the National Academy of Sciences of Ukraine, Kiev (Ukraine).

Previously, a qualitative analysis of xanthones was conducted by paper chromatography. On chromatography paper «Filtrak FN-4" 70% alcohol – aqueous extracts of the objects was applied; then was placed in the system of solvent of I direction – *n*-butanol – acetic acid – water (4:1:2); II direction – 15% acetic acid. After passage, the chromatogram was dried and viewed in visible and UV light. Spots, that are characteristic for xanthones, had a yellow color, after tilling by ammonia vapors became yellow-orange, and after tilling by solution of 3% $FeCl_3$ – green color.

For the quantitative determination of the amount of xanthones in the re-calculation of mangiferin used previously published method (Aslanukov A.K. et al. Development, research and marketing of a new pharmaceutical products. Collection of research papers. Pyatigorsk, 2009. Vol. 64 (in Russian)). Measurements were made by Thermo Scientific Evolution 60S UV – Visible Spectrophotometer, (USA).

The results of the quantitative determination showed, that the amount of xanthones was: in the rhizomes with roots of the *Iris hungarica* – 0,85 ± 0.01%, in *Iris sibirica* – 0,10 ± 0.05% in the re-calculation of mangiferin.

Conclusions: it was found, that the quantitative content of the amount of xanthones in the underground parts of the *Iris hungarica* and *Iris sibirica* is 0.85% and 0.10% respectively. Plants of the genus *Iris* are a promising raw material for the study and selection of xanthones.

# ISOORIENIN – CONTAINING MEDICINAL PLANTS AS PROMISING SOURCES OF NEPHROPROTECTIVE PHYTOPHARMACEUTICALS

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**Objective:** To represent current scientific data on pharmacological effects and medicinal plant sources of isoorientin, considering its occurrence as an active marker of some hypoazotemic medicines; to estimate its significance at current medicinal application.

**Materials and methods:** Information search in scientific editions, medical databases, and other web-resources; analytic and generalization methods.

**Results:** Isoorientin (also known as homoorientin, luteolin-6-C-glucoside, lespecapitoside) is a flavone. The substance was first isolated from *Polygonum orientale.* A regioselective synthesis of isoorientin from the commercially available phloroacetophenone was described (Kumazawa T. *et al.,* 2000).

Within a period of from 7 to days lespecapitoside effects a lowering of the urea rate for extrarenal azotemia with a daily dosage of 0.005 to 0.01 g, administered orally, intravenously, or intramuscularly. For hyperazotemia of purely renal origin the results are favourable for sub-acute nephritis and also for chronic nephritis which has not reached the terminal stage (Cervelle C.M.H., 1975).

Bioassay-directed fractionation techniques led to isolation of isoorientin as the main and potent hypoglycaemic component of *Gentiana olivieri* in streptozotocin-induced diabetic rats as well as antihyperlipidemic (Sezik *et al.,* 2004).

The role of isoorientin in cytoprotection from oxidative damage and its free radical scavenging activity was suggested (Lu *et al.,* 2005). Isoorientin was shown to possess significant anti-nociceptive and anti-inflammatory activities in rats and mice (Esra Küpeli *et al*., 2004).

Among important medicinal plants, applied worldwide, the active principle was detected in *Crataegus monogyna, Crataegus pentagyna, Cymbopogon citratus, Fagopyrum esculentum, Hypericum perforatum, Lespedeza bicolor*, *Lespedeza capitata, Lythrum salicaria, Passiflora incarnata*, *Theobroma cacao, Viola tricolor.*

**Conclusions:** Concluding the research outcomes, isoorientin as a valuable natural compound deserves a particular attention due to various pharmacological effects, including hypoazotemic ones. Isoorientin containing plants with sufficient resources should be subjected for screening of their renal impact with a purpose to develop new herbal drugs of nephroprotective (hypoazotemic) activity.

# RESEARCH THE LIPOPHILIC COMPOUNDS FROM *CRATAEGUS PENTAGYNA* W. K. FLOWERS

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**The aim of investigation**

In Ukraine are growing 30 species of hawthorn, 4 of which are pharmacopeia and applied as antihypertensive, sedative, cardiotonic agents. It is known that for such pharmacological activity are responsible phenolic compounds (flavonoids, hydroxycinnamic acids). At the same time others classes of compounds practically have not been studied. So, the aim of this investigation is the study of lipophilic compounds of *Crataegus pentagyna* W. K. flowers.

**Materials and methods**

The object of study was flowers of *C. pentagyna* W. K., collected in bud phase.

Qualitative and quantitative analysis of fatty acids was determined by gas chromatography in gas chromatograph "Chrome - 5". Volatile compounds content conducted by used chromatography-mass-spectrometry method in gas chromatography-mass spectrograph" Hewlett - Packard ".

Content of chlorophylls and carotenoids determined in lipophilic fraction (extractant – chlorophorm). For its identification used one-dimensional and two-dimensional chromatography in thin layer of sorbent on the plates «Silufol UV-268». Solvent system was hexane-acetone (6:3). Like chromogenic reagent used the solution of phospho-molybdic acid.

**Obtained results**

In raw material identified 10 fatty acids (myristic, pentadecanoic, palmitic, stearic, palmitoleinic, heptadecinic, oleic, linoleic, linolenic, 2-oxypalmytic); chlorophylls and carotenoids; volatile substances.

Results of study are shown in Table 1, 2.

Table 1

Fatty acids composition of *C. pentagyna* W. K. flowers

| № | Retention index | Name of acid | Content, mg/kg |
|---|---|---|---|
| 1 | 2 | 3 | 4 |
| 1 | 24.241 | myristic | 172.61 |
| 2 | 26.065 | pentadecanoic | 20.79 |
| 3 | 28.357 | palmitic | 3025.83 |
| 4 | 28.697 | palmitoleinic | 38.12 |

| 1 | 2 | 3 | 4 |
|---|---|---|---|
| 5 | 29.79 | heptadecinic | 27.62 |
| 6 | 31.893 | stearic | 731.27 |
| 7 | 32.11 | oleic | 241.79 |
| 8 | 33.025 | linoleic | 2332.23 |
| 9 | 34.006 | linolenic | 1677.47 |
| 10 | 35.462 | 2-oxypalmytic | 148.80 |

As shown in Table 1, among fatty acids are dominant saturated fatty acids, unsaturated presented with oleic, linoleic, linolenic acids. Most high concentration established for palmitic, linoleic, linolenic acids.

Table 2

Volatile compounds of *C. pentagyna* C. W. flowers

| № | Retention index | Compound | Content, (%) |
|---|---|---|---|
| 1 | 4.94 | benzaldehyde | 7.7 |
| 2 | 6.65 | limonene | 1.6 |
| 3 | 7.15 | methyl ester of isoleucine | 108.6 |
| 4 | 11.47 | p-cimen-8-ol | 3.9 |
| 5 | 11.63 | α-terpineol | 11.7 |
| 6 | 13.64 | anise aldehyde | 37.5 |
| 7 | 14.91 | indol | 3.7 |
| 8 | 15.96 | methyl ester of phormylisoleucine | 6.9 |
| 9 | 16.96 | eugenol | 53.3 |
| 10 | 40.28 | squalen | 192.8 |

As shown in Table 2, in raw material was founded 10 volatile compounds: monocyclic monoterpenoids (limonene, α-terpineol), triterpenoids (squalen), aromatic compounds (benzaldehyde, eugenol, p-cimen-8-ol, anise aldehyde), amino acids derivatives (methyl ester of isoleucine, methyl ester of phormylisoleucine), nitrogen-containing substances (indol).

According to the results of fluorescence and the values of Rf 2 substances classified as chlorophylls, 3 - as carotenoids. The color of spots seen in daylight and UV- light before and after processing of chromogenic reagent.

**Conclusions**

1. In *C. pentagyna* W. K. flowers were determined 10 fatty acids and 10 volatile compounds of different chemical structure.

2. In the chloroform fraction of *C. pentagyna* W. K. flowers established the presence of chlorophylls and carotenoids.

**DISANE OF MEDICAL TREATMENT**
**FOR URTICARIA IN CHILDREN**

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One of the most common types of allergic diseases in children is urticaria. Urticaria - polietilohichnyy syndrome that is manifests blisters ( urtykaryyamy ) that are itchy and have fast dynamics. Urticaria can by allergic (with intake of allergens administered various drugs, insect bites ) and pseudo allergic

Genesis (cold , heat , solar , vibration , etc.). In 70-85% of cases urticaria in children are food products (juices , chocolate, eggs , carrots, etc.) and drugs ( analgesics , antibiotics)

However the etiology patohohenetychnoyu a common link to all types of urticaria is increased vascular permeability and microcirculation acute edema development around these vessels. In the mechanism of blisters essential belongs biologically active substances ( histamine, serotonin, bradikininu , leukotrienes , etc.). To block anti-inflammatory action of histamine blockers administered histamine H1-receptor preference II ( loratadine " Claritin ", " Loratadine ", " Laurent ", " Agist " cetirizine dihydrochloride " Allertek ", " Zodak ", " Tsetryn ") and III generation drugs ( desloratadine " Aerius ", " Eden", Levocetirizine " Tsetrylev ", " Loratek "). We investigated extemporal range of industrial and medical products in Ukraine for the treatment of allergic reactions in children are shown on the poor state of preparations in the pharmaceutical environment. We investigated extemporal range of industrial and medical products in Ukraine for the treatment of allergic reactions in children are shown on the poor state of preparations in the pharmaceutical environment.

Preparations of medicinal plants ( MPM ) , always use a popular Ukraine : from efficacy and safety in long-term treatment of chronic diseases, especially in children and in practice gerontology. Their rich chemical composition makes multivalency pharmacological actions are available and cheap.

The study of MPM, which phytotherapist and healers recommend to the practice of medicine for the treatment of urticaria in children. To develop the structure we have studied technological parameters MPM : degree of grinding proportion , combining volumetric weight and bulk , porosity and transparency.

**PHYTOCHEMICAL STUDY LYCIUM BARBARUM FRUITS**

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The goji berry, also known as the wolfberry, is a member of the Solanaceae or nightshade family of plants. It's a bright orange-red berry commonly grown in the north-central and western areas of China. It grows in remote unpolluted hills and valleys of Tibet and Mongolia, in soil so rich in nutrients that the berries are exploding with this special nutrient dense vitality. The plant also is widely cultivated. The ripe berry is easily damaged during picking, so it's common for them to be carefully dried to preserve them. Goji berries are small, up to 1,5 cm. The taste is sweet-salty, sometimes sour. The useful properties of goji berries have been used from ancient times.

Goji berries have been used in traditional Chinese medicine to manage diabetes, high blood pressure, fever, age-related eye problems and fatigue associated with living at high altitudes. Goji berries use for treatment headache, muscle pain, prostatitis. They also increase potency.

Some studies using goji berry juice found possible benefits in mental well-being and calmness, athletic performance, quality of sleep, and feelings of good health. The red colours found in goji berries, blueberries, acai berries, cranberries, strawberries, and cherries are natural anti-oxidants which may help protect the body against oxidative damage. In addition Goji berries contain complex starches called Lycium barbarum polysaccharides which may benefit the immune function. But those were preliminary studies that need to be repeated before drawing conclusions. All berries are good for you. It's not clear if goji berries are better than other types of berries, or if goji berry supplements have the same health benefits as the actual berries.

Goji berry provides two benefits are very important when you are trying to lose weight. Goji berries are loaded with vitamins and minerals to help increase energy and may help control your appetite.

The presence and quantitative analysis of organic acid, phenolcarbonic acid, carbohydrates, hydroxycinnamic acids were determined. Carbohydrates, phenolcarbonic acid are the most specific biological active substances of goji berries.

The primary researches suggest about the prospects of further study of Goji berry.

**PLANTS OF GENUS *GEUM* L. HOW SOURCES OF POLYPHENOLIC COMPOUNDS**

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Last decade there is observed growing interest of scientific and traditional medicine towards plants as a source of raw material for manufacturing medicines. One of the most spread in plants ingredients of secondary metabolism are phenolic compounds that participate in various physiological processes. Besides, high biological activity characteristic to phenols allows using them in medicine at treatment and prophylaxis of many diseases.One of the sources of phenolic compounds are plants of the genus *Geum* L. (avens) that belongs to the family *Rosaceae* subfamily *Rosoideae.* Seven species are spread through NIS countries territory. We have investigated the chemical content of 3 species: *G. aleppicum* Jacq. (aleppic avens), *G.rivale* L. (water avens), *G. urbanum* L. (common avens) spread over the whole territory of Ukraine and used widely in folk medicine as astringent, haemostiptic, anti-inflammatory, antiseptic, analgetic, restorative remedies. It is known that plants of the genus *Geum* contain hydroxycinnamic acids, coumarins, flavonoids, tannins, amino- and fatty acids. The aim of our study was to investigate phenolic content of 3 species of the genus *Geum* of Ukrainian flora and to establish pharmacological activity of substances obtained. As a raw material there were used samples of herb and rhizomes of named avens species collected in 2012-2013 at the territory of Kharkov and Kharkov region. For investigation of phenolic content of the raw material there were used qualitative reactions, UV-spectrophotometry, paper and thin layer chromatography (on “Silufol” plates) in the systems of ethylacetate-formic acid-water (10:2:3), 15% acetic acid; chromogenic revealing reagents were: ammonium vapor, 2% ethanol solution of NaOH, 2% ethanol solution of AlCl3. Based on the results of qualitative reactions, UV-fluorescence, Rf data of substances as well as the data of direct and differential spectrophotometry in the herb and rhizomes of avens species studied there were identified 5 flavonoid compounds. In the herb and in the rhizomes it is identified 3. coumarins and 6. phenocarbonic acids. Determination of antibacterial activity of different fractions of biologically active compounds of the genus *Geum* was carried out at the base of I.I. Mechnikov Kharkov research institute of microbiology and immunology. Particularly, phenolic compounds complex of ethanol fraction expressed pronounced antimicrobial activity against: *Staphylococcus aureus*, *Esherichia coli*, *Proteus vulgaris*, *Proteus aeruginosa*, *Candida albicans* . Thus, the results obtained proved expediency of further investigation of the genus *Geum* plants as promising medicinal plants.

# CHEMICAL COMPOSITION RESEARCH OF THE SALVIA OFFICINALIS LEAVES DRY EXTRACT GETTING AFTER ESSENTIAL OIL PRODUCTION

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There are 38 drugs based on salvia leaves biologically active substances on the pharmaceutical market of Ukraine. In the main these drugs involve Salvia officinalis leaves, essential oil and tincture. The pharmaceutical industry use terpene nature substances. This raw material is rich on the other classes of biologically active substances, phenolic in particular. Tons of liquid extractions became waste after distillation in manufacture of salvia essential oil every year, although they contain numbers of biologically active substances, phenolic compounds in particular.

The aim of research was to study the chemical composition of the dry extract, which remains after Salvia officinalis essential oils production.

For receiving the dry extract 0,1 kg Salvia officinalis leaves were placed in a flask with slide, added 3,0 l of water and conducted distillation to obtain essential oil according to The State Pharmacopoeia of Ukraine during 2 hours. The extraction which was received was boiled down at the 85 - 95C under vacuum in circulating vacuum device at depression 680-700 mm., dilute to volume of the water rest of 0,5 liter. The getting extract is dense dark brown liquid. It was left for 4-5 days in the refrigerator. The water concentrate which was received was dried in the spray-type dryer with a temperature of heat carrier 160 C and 80 - 90 C at the exit until the dry extract was obtained. The dry extract of Salvia officinalis leaves after production of essential oil was analyzed then.

Research of qualitative composition was carried out using conventional methods of paper chromatography and thin layer chromatography. As a result of the preliminary qualitative research of biologically active substances in the Salvia officinalis extracts were discovered monosaccharides (glucose, galactose, rhamnose and arabinose), amino acids (arginine, tyrosine, aspartic and glutamic acids), flavonoids (myricetin-3-O-arabinoside, quercetin-3-O-arabinoside, quercetin and kaempferol), hydroxycinnamic acid derivatives (chlorogenic, caffeic and protokatehinic acid), coumarins (umbeliferon and skopaletin) and tannins (galo- and elagotanins) were found.

For determining the quantitative content of biologically active substances in the extract spectrophotometry was used. Derivatives of hydroxycinnamic acid in terms of chlorogenic acid was measured at a wavelength of 327 nm; flavonoids in terms of rutin after reaction with aluminum chloride - at 417 nm; sum of polyphenolic substances in terms of gallic acid - at wavelength 270 nm. As a result, extract consists of hydroxycinnamic acids (5.12%), flavonoids (9.33%), the amount of phenolic compounds is 33.55%.

The data obtained will be used for standardization of the Salvia officinalis leaves dry extract.

# COMPARATIVE PHARMACOGNOSTICAL STUDIES OF SPECIES IN GENUS VERONICA

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The aim of the research is the morphological and anatomical analysis and chemosystemetic of common Veronica group in Ukraine, species identification, perspective, medical, standardization of raw materials.

Materials and methods. The samples of grass Veronica officinalis (V. officinalis) and Veronica chamaedrys (V. chamaedrys). Description of morphological features, anatomical and histochemical determination were carried out due to the appropriate methods.

The obtained results. Due to the APG-classification, genus Veronica is assigned to the Plantaginaceae family. Earlier, it included the family Scrophularia (Scrophulariaceae). The problem of kind systematization arises because of large number of features, the lack of clear boundaries with neighboring families, the proximity of certain groups of species and their release into independent genera. When the differences among species genus Veronica investigates, then we investigate various phytochemical characteristics, analyzes of morphological and anatomical structures as additional features for streamlining and standardization kind of possible medicinal plant. Flora of genus Veronica is represented with 47 species in Ukraine. Widespread spring and summer honey herbs are Veronica officinalis (V. officinalis) and Veronica chamaedrys (V. chamaedrys). They are included in the Pharmacopoeia of some countries of Western Europe. Grass contains glycosides aukubin and veronicin, flavonoids, phenolcarbonic acids, iridoid, saponins, essential oil, tannins and bitter substances, vitamin C and so on. Medication is used as an expectorant and has anti-inflammatory, hemostatic, fungicidal effect, stimulate cardiac function, is used for treatmant of bladder, kidney, stomach, adrenal glands and skin. The external distinguishing features include: V. officinalis - stems uniformly rough-pubescent lanuginous; leaves obovate or elliptic, rough, crenate; thick brush placed in the bosom of one of opposite leaves; pedicels shorter bracts and calyx has narrow lanceolate shape; stigmas is complete. Veronica chamaedrys - stems with two opposite rows of hairs; Leaves are rounded-ovate, blunt, crenate and serate; bloom without many flowers. The stems and leaves are slightly different in types of quantitative and qualitative anatomical features. The structure stems are fasciculated. Common features are mesomorphic anatomical structure of leaves: a thin plate, medium size epidermal cells with moderately thick and thin outer side of walls, dorsoventral moderately layered, loose mesophillous with an average rate of palisade, wide palisade cells that accumulate phenolic compounds.

Conclusions. The results can be used for further correction of cladograms, dendrograms and for standardization of medical raw materials.

# QUANTUM-CHEMICAL INVESTIGATION OF THE MECHANISM OF EUGENOL AND ISOEUGENOL EPOXIDATION BY PERACETIC ACID

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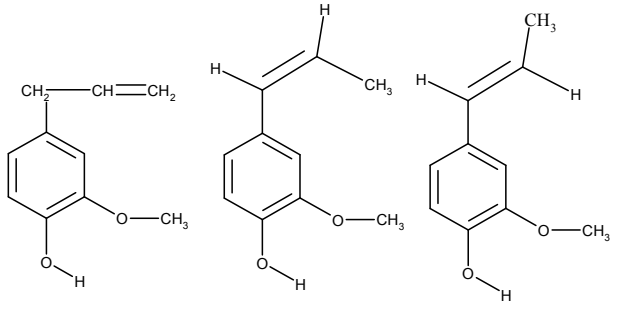
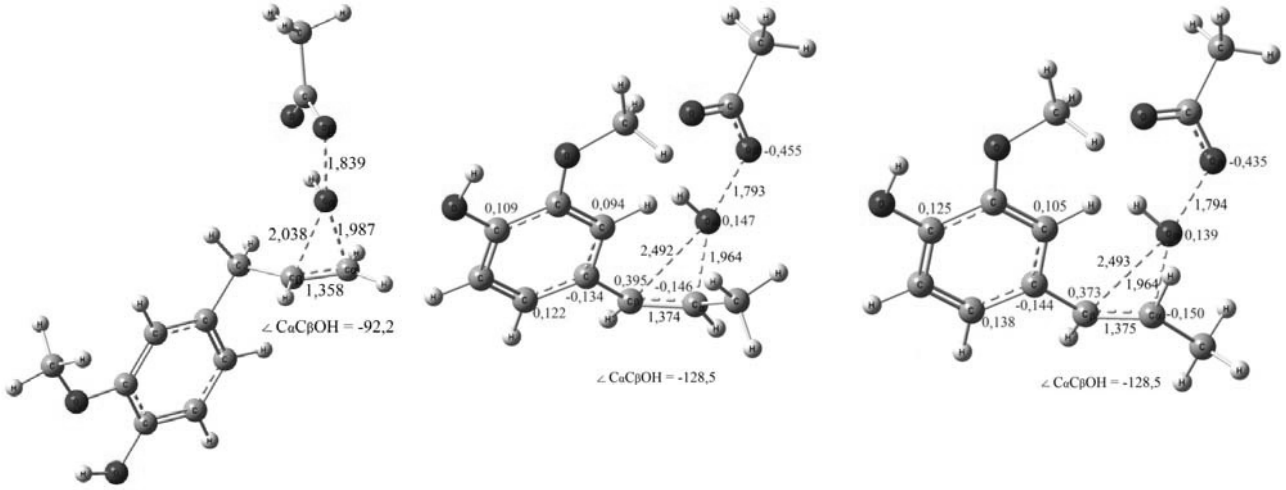
It is well-known that terpenoids such as eugenol and isoeugenol posses a broad spectrum of biological activity. Thus, the most valuable component of clove oil is eugenol own. This compound is responsible for a specific flavor, which associated with number of medicinal properties. Clove oil inherent analgesic, spasmolytic, antimicrobial, diaphoretic and diuretic action. Eugenol is used for the production of perfume compositions, such as fragrances for tobacco, as well as for isoeugenol synthesis. It is part of painkillers, antiseptic and biocidal agents. Ether clove oil as eugenol itself, has anti-inflammatory effect and used in dentistry, with pulpitis, caries, paradontosis, lesions of the oral mucosa. Eugenol's isomer (isoeugenol) also found in ether oils. Clove oil contains mostly *cis*-isoeugenol, while basil and coluria oils contain *trans*-isomer. We have performed quantum chemical study of the reaction mechanism for epoxidation of three isomers – eugenol (**1**) and *cis*- and *trans*-isoeugenols (**2a, 2b**) by peracetic acid (also known as peroxyacetic acid, or PAA). Density functional theory has been used for calculations at UBH&HLYP/6-31G (d) level. This method allows to correctly describe the structure of diradicals and cost-effective enough for investigation of complex organic compounds and reactions. It has been shown experimentally that rate constant for epoxidation of isoeugenol by PAA is in 5 times higher if compare to its isomer – eugenol.




1 2a 2b

As could be seen from Table 1, the values of activation barriers for epoxidation of *cis* and *trans* forms of isoeugenol is in about 20 kJ/mol lower if compare to eugenol epoxidation, which is consistent with experimental data. The transition state for eugenol epoxidation characterizes rather synchronous process where C-O bond lengths of forming epoxide cycle have close values. It is important to note that this structure has a closed electron shell, thus, in contrast to other olefins epoxidation

reactions, not showing biradical character of transition state. According to calculations, the activation barriers for epoxidation of *cis* and *trans* forms of isoeugenol have similar values, indicating a negligible effect of its structure on reactivity. Values of geometrical parameters and spin density on the corresponding atoms for transition states (**TS2a, TS2b**) are also closet to each other. As shown in Fig. 1, transition states (**TS2a, TS2b**) are close to the planar nature (see $C_\alpha C_\beta OH$ angles), and asymmetric with a significant advantage in the formation of $C_\alpha$-$O_\alpha$ bond over $C_\beta$-$O_\alpha$. Analysis of the wave function of the transition states (**TS2a, TS2b**) shows their biradical nature. The largest spin density localized on $C_\beta$ and $O_\beta$ atoms. Partial delocalization of spin density at the *ortho*- and *para*- carbon atoms observed due to conjugation of olefin fragment with benzene ring.




**TS1** **TS2a** **TS2b**

Figure 1. Structure, selected geometrical parameters (printed in black, Å, deg.) and values of spin density on atoms (printed in blue) of (**TS1, TS2a, TS2b)**

Table 1 – Values of activation parameters for eugenol (**1**) and isoeugenols (**2a, 2b**) epoxidation by PAA, calculated at UBH&HLYP/6-31G(d) level of theory

| Compound | $\Delta H_{act.}$, kJ/mol | $\Delta G_{акт.}$, kJ/mol |
|---|---|---|
| **1** | 122.39 | 137.37 |
| **2a** | 101.43 | 117.18 |
| **2b** | 101.29 | 112.40 |

Thus, the obtained results reveal in the following concluded: the ratio of activation energy for interaction of eugenol and isoeugenols with peroxyacetic acid shows higher reactivity of isoeugenols. The results are in line with experimental data confirming the correctness of UBH&HLYP/6-31G (d) approach which could be also used for investigation of the regio-chemical particularities of epoxidation of alkenes containing two or more double C=C bonds, such as terpenoids.

*Research has been conducted under supervision of Prof. S.I. *Okovity*[1] and Prof. M.Ye. *Blazheyevskiy*[2]

# PROSPECTS OF STUDYING OF PLANTS OF THE GENUS GLADIOLUS

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Plants of the genus Gladíolus of Iridaceae family are perennial herbs, with corms. The stalks are straight, single, approximately 50-150 cm tall. Gladíolus with purple flowers grows in damp soil, in bushes (G. imbricatus L.), on marshy meadows (G. paluster Gaud.), in the Crimea, in the Caucasus (G. communis L. и G. segetum Gawl.), on the humidified slopes and rocks, grassy places, at falls, in mountains in the Cape region of South Africa (G. cardinalis, G. blandus, G. angustus L., G. alatus L., G. ceresianus), in the mountains of Turkey and Iran (G. anatolicus Van Thub.). G. palustris Gaudin and G. imbricatus L. etc. grows in Ukraine.

Vitamin C is richly contained by Gladíolus, it has an anti-oxidizing role. Vitamin C has an important role in the synthesis of collagen in the tissues and bones, also being anti-inflammatory, anti-bacterial, anesthetizing and very useful to the immune system.

Preparations of a gladiolus are applied at diseases of kidneys, an allergy, scrofula, against a toothache and gastric diseases, quicken process of release of milk for women and at impotence for men, to children with inguinal hernia. At a result, G. quartinianus was known as cancer deterrent remedy. It includes flavonoids, phenols, tannins, sterola, triterpena.

Chemical composition of gladioluses is studied insufficiently. It is known that leaves contain ascorbic acid (from 546 mg% and more (according to some information to 1700 mg)), starch, saponins, a glycoside of an isoflavones irigenin, fatty oil, sugar, essential oil.

Unstudied chemical composition and a broad resource base of a species and varieties of gladiolus, makes plants of this genus are promising for pharmacognostical studies. We have collected corms in two varieties of gladiolus: variety “Zephyr” (pink), garden selection, variety "Leda" (galanter (hybrid gladiolus and acidentaly) (light Magenta) and one natural type of gladiolus (orange) from Madagascar prepared in autumn, 2014 in N. N. Gryshko National Botanical Garden of the National Academy of Sciences of Ukraine, Kiev (Ukraine). The raw material is dried to air-dry for chemical analysis. At this stage, phytochemical analysis of BAS in corms of gladiolus conducts known qualitative reactions to identify and chromatography on paper.

# PHYTOCHEMICAL RESEARCH OF VERONICA TEUCRIUM L.

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Approximately 70 species of genus *Veronica* L. of family *Plantaginaceae* grow on territory of Ukraine, which are grouped into 8 sections. The most common species is perennial plant *V. teucrium* L., that has a large area of distribution.

The herbal drug is herb (stems, leaves and flowers), that are harvested in the flowering stage. The recent herb has the bitter taste and a faint smell, which are disappeared during drying. Occasionally, are used roots, that are harvested after dying off the aerial part. The herbal drug are dried in the shade and in well-ventilated premises or in the dryer.

A herb used in folk medicine (as infusion) long ago and have shown an anti-inflammatory, expectorant, analgesic, anticonvulsant, anti-bacterial (against Gram+), fungicidal, and haemostatic activity. The recent herb had used topically for chronic purulent skin diseases and as wound healing remedy.

According to the experimental data, the aqueous extracts from herb of *V. teucrium* L. have shown iron-binding, antioxidant, reducing and prebiotic activity.

*V. teucrium* L. herb contains carbohydrates, steroids, iridoids, steroid saponins, cardenolides, phenolcarboxylic acids, tannins (up to 4%), coumarins, flavonoids, choline, vitamine C.

The aim of our study was the identified and quantified study of flavonoids.

Materials and methods.

The objects of the study were herb, leaves and flowers of *V. teucrium* L., that have been harvested in the flowering stage in Kharkiv region, Ukraine, in 2013.

Extract from *V. teucrium* L. obtained by ethanol 70% have used for paper chromatography (PC) on «Filtrak» (FN-12), the solvent system: ethylacetate – formic acid – water (10:2:3) (I direction) and 15% acetic acid (II direction). The process of chromatography was performed using single division at the temperature 20-22ºC. Detection was performed in filtrated UV-light (354 nm). The detection was conducted by ammonia vapor, 10% spirituous solution of sodium hydroxide, 5% solution of iron (III) chloride after drying chromatogram. The compounds were identified by features fluorescence in UV-light and coloration with chromogenic reagents, and by the value of $R_f$.

For quantified study of flavonoids 20 ml of 70º ethanol was added to the exact sample of crushed herbal drug (m=1.050 g, d=2 mm) in 50 ml flask. The flask was attached to a reflux condenser and heated in a water bath for 30 min. After cooling the extract was filtered through cotton in a volumetric flask, then a cotton was added into a flask for extraction. The extraction was repeated twice, 10 ml of 70º ethanol was added in third time, and then an extraction was filtered into a volumetric flask. After cooling the volume of solution was adjusted to 50 ml mark using 70º ethanol. In volumetric 10 ml flask was added 1.0 ml of the obtained solution, the volume adjusted up to the mark using solution 70º ethanol and had registered UV-spectrum of an obtained solution, and the reference solution was 70 º ethanol.

For the differential absorption spectrophotometry 2.5 ml of obtained solution was transferred into 25 ml volumetric flask, was added 1 ml of 2% solution $AlCl_3$ in ethanol 96º, and the solution volume was adjusted up to the mark with 5% solution of acetic acid in ethanol. After 40 min had registered a differential UV-spectrum of an obtained solution on the spectrophotometer SPh-46 ($\lambda$=412 nm, *l*=10 mm). As the reference solution was used solution prepared in aforementioned conditions, without the addition of $AlCl_3$.

Specific absorption coefficient of the complex hyperoside with $AlCl_3$ at $\lambda$ = 415±5 nm is equal to 291.09, was used for calculations.

The obtained results.

In the result of the chromatographic study of *V. teucrium* L. herb had been found 8 phenolic compounds in leaves and 12 – in flowers. According to the results a value of $R_f$ and features coloration of spots before and after reaction with chromogenic reagents in daylight, and fluorescence in UV-light in leaves had been found 4 compounds belonging to flavonoids, and 6 – in flowers.

By spectrophotometry method flavonoids of *V. teucrium* L. herb had been quantified. The total content of flavonoids in herb was 0.59±0.03 % (m=5, P=0.95), in recalculation on hyperoside.

Conclusions.

In *V. teucrium* L. leaves had been found 8 phenolic compounds, 12 – in flowers, including flavonoids: 4 in leaves and 6 in flowers

The quantitative content of flavonoids in *V. teucrium* L. herb was 0.59±0.03 % (m=5, P=0.95), in recalculation on hyperoside.

# PRELIMINARY PHYTOCHEMICAL STUDY OF CARROT ROOTS

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The carrot (*Daucus sativus* (Hoffm.) Roehl. = *Daucus carota* subsp. *sativus* (Hoffm.) Schubl. et G. Martens) belongs to the *Apiaceae* family. It is a biennial herbaceous plant. During the first year of vegetation carrot develops a rosette of leaves and, depending on the variety, a fusiform, long, elliptic, conical or cylindrical taproot of orange, red-orange, or rarely yellow, colour. Leaves are bi- or tetrapinnate, basal on long petioles, upper – sessile. Leaf segments are linear-lanceolate, lanceolate or spatulate. At the second year of vegetation the plant develops an erect stem branched on top with alternate leaves of the same form as the basal ones. Inflorescence is a compound umbel with 13-25 rays. The fruits are ribbed thorny schizocarps.

The chemical composition of carrot roots is not studied well enough, which is connected with the large number of varieties cultivated in Ukraine. Thus the aim of our research was the preliminary phytochemical study of carrot roots for the presence of polysaccharides and saponins.

The object of the research were the carrot roots collected in 2012-2014 in Rivne region. The plant material was air-dried under the shade.

The presence of polysaccharides was determined using the conventional qualitative tests. Polysaccharides were identified in the carrot roots water extract where 96% ethanol was added. Formation of the light-brown sediment confirmed the presence of polysaccharides in the plant material studied.

The presence of saponins was determined in the carrot roots 50% ethanol extract which was filtered after cooling and then evaporated on the water bath. The water extract obtained was used for the foam test and reactions with 10% lead acetate solution and barium hydroxide. The formation of foam and sediments with the abovementioned reagents allowed to identify saponins in the carrot roots.

Therefore, the conventional chemical tests allowed confirming the presence of polysaccharides (with 96% ethanol) and saponins (foam test, reactions with lead acetate and barium hydroxide) in the carrot roots.

The qualitative tests carried out have shown the abundant chemical composition of the plant material studied. This confirms the prospects and necessity of the further profound phytochemical study of carrot roots for the main classes of biologically active compounds.

# ANATOMICAL RESEARCH OF LEAVES AND SHOOTS OF PLATYCODON GRANDIFLORUS

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Platycodon grandiflorus is a species of herbaceous flowering perennial plant of the family Campanulaceae, popular and promising plant in Chinese medicine, belong to perspective sources of medicinal plant raw material for obtaining medicines with the anthelmintic, anti-inflammatory, expectorant, astringent, analgesic actions. Platycodon grandiflorus characterized by such an important feature of the presence of biologically active substances – triterpenoids, flavonoids, anthocyanins, phytosterols, carbohydrates etc. According to the aim of present work, anatomical investigation of leaves and shoots has been carried out. In the process of our investigation the diagnostic features of vegetative organs have been determined.

During of the study of the anatomical structure of leaves was found that cells of the epidermis the upper side is slightly sinuous, thin-walled, tightly closed. The stomatal apparatus is of anomocytic and tetrocytic types. Occasionally, along the veins encountered multicellular hairs consisting of 5 cells. It was found that the main cells of the lower epidermis there are small, polygonal, with stomas of anomocytic and tetrocytic types. Along the veins the epidermal cells is elongated, wall-sided, polygonal. There is a large number of simple unicellular hairs of different lengths, located along the veins. Two layers of columnar parenchyma and five layers of spongy parenchyma represent leaf mesophile. A cross section of the shoot has round shape. The stem is covered with epidermis presented by small, elongated, polygonal cells are often found convex papillae with thickened walls. Under the epidermis situated 3-layer angular collenchyma. Bark parenchyma consists of 10-12 layers of large thin-walled cells without intercellular spaces. Under it is pawned pericyclic ring of sclerenchyma that consist of 5-6 layers. Next is situated a narrow ring of phloem consists of 7 layers of cells. The cambium is composed of colorless, thin-walled cells in several layers. In the xylem there are visible single row medullary rays. The central position in the stem takes a well-developed parenchyma presented rounded cells without intercellular spaces.

Conclusions. Anatomical study of leaves and shoots of Platycodon grandiflorus has been conducted for the first time. The results of our investigation can be used in developing analytic and regulatory records intended for incorporation of the additional sources of medicinal herbal raw materials in the practical fields.

# PHYTOCHEMICAL OF STUDY OF ERIGERON ANNUELLE

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In spite of the fact that medications of synthetic origin are occupied by considerable positions in the assortment of pharmacy networks, interest to phytoterapy continues to grow. Therefore search of new unexplored plants is always remains an actual task for researchers.

Such raw material is Erigeron annuelle (Annual Fleabane L. (Pers.) from Aster family (Asteraceae). This plant in a wild type meets in South America, on territory of Ukraine it is brought as weed.

In Ukraine Erigeron annuelle it is possible to meet in Western Ukraine and in the Kharkiv area as well. In literary sources practically absent information about chemical composition of this plant, that appeared base for its subsequent research.

The object of our researches was the herb of Erigeron annuelle collected at flowering time in summer in 2014 in the Kharkiv area.

After previous phytochemical researches were found out the following classes biologically active compounds: amino acids, organic and hydroxycinnamic acids, coumarins, flavonoids, tannins compounds, saponins, alkaloids, free and compound sugars and others derivatives.

By extraction of raw material by solution of hexane in the Soxhlet apparattus, got lipophilic fraction, by a chromatography method in the layer of sorbent found out the presence of carotinoids, chlorophylls, and tocopherolls.

By the HPLC was defined quality and quantitative content of fat acids. An amount of fat acids was 16 among which the unsaturated fat acids prevail in quantitative content.

By atomic-emission spectrophotometry investigation quality and quantitative composition of macro- and microelements, were defermined. It was established the presence of is elements presence was as a result set 15 elements. In the herb of Erigeron annuelle outside possibility determination by a method atomic-emission spectrophotometrys cobalt (<0,03), cadmium (<0,01), arsen (<0,01), mercury (<0,01), lead (<0,03), nickel (<0,03) and molybdenum (<0,03).

These researches defined as base for subsequent research of plant of sort of Erigeron annuelle of Annual Fleabane (L.) of monogynopaedium of Aster family (Asteraceae), which is a perspective source for a receiption on his basis of new medications.

Determined by HPLC quantitative content of organic acids in the herb Erigeron annuelle Among the dominant prevail following acids: oxalic - 174.65 mg / kg, syrengic- 184.62 mg / kg, vanillic - 213.01 mg / kg, malonic - 499.65 mg / kg, succinic - 539.20 mg / kg, citric - 1248.57 mg / kg, levulinic - 1682.13 mg / kg, malic- 1830.85 mg / kg.

Determined by HPLC content of volatile components in the flowers and herb Erigeron annuelle The flowers contains 70 components, herb - 62 components.

# THE CHOICE OF OPTIMAL EXTRACTANT FOR OBTAINING EXTRACT FROM BORAGE'S ROOT

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Borage (Borago officinalis L.) of Boraginaceae L. family is grown up in many countries of the world as decorative, melliferous, vegetable and medicinal plant. In folk medicine the herb, flowers and fruits which use for treatment of cardiovascular, gastrointestinal diseases, diseases of the upper airways, kidneys and an urinary excretive system, rheumatism, malignant tumors, a depression are applied. Previously we carried out the phytochemical studying of the rosette leaves, herb and fruits. Studying of borage's roots was the following stage of our work.

The aim of our study is to define the optimal extractant for obtaining extract from borage's root.

Materials and methods. The roots of the borage were prepared during mass fruiting (June, 2012) in Kharkov region. Extractant was being chosen among traditional solvents: refined water, water-ethanol mixture with such concentration of ethanol: 10%, 20%, 30%, 40%, 50%, 60%, 70%, 80%, and also 96%. Ratio raw material – extractant was 1:50. Extraction was carried out on the boiling water bath for 2 hours. The content of the oxidized phenols phenols sum and the yield of extractive substances were chosen as assessment criteria. For determination of the sum of the oxidized phenols USSR SF technique, edition XI was used. The content of extractive substances was determined according to the technique given in SF of Ukraine, edition I.

The received results. As a result of the conducted researches it is established that the content of the oxidized phenols sum was higher at extraction by water-ethanol mixtures (concentration of ethanol 30%, 40% and 50%) and made 3,30%, 3,31% and 3,38% accordingly. The yield of extractive substances was the greatest in the extracts received by water – ethanol mixtures 30% and 40% (33,29% and 28,06% accordingly). The ratio of the quantitative content of the oxidized phenols sum and extractive substances doesn't correlate accurately with a type of an extractant.

Conclusions. Thus, we established that from the point of view of the yield of extractive substances and the oxidized phenols sum, an optimal extractant for receiving substance made of a borage's root is water-alcohol mixture with concentration of ethanol 30%. The obtained data will be used for carrying out further researches.

# MICROSCOPIC CHARACTERISTIC THE HERB OF CENTAURIUM PULCHELLUM

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We have found by analysis of scientific literature, that Centaury normal or umbrella (Centaurium erythraea Rafn. or umbellatum Gilib.) describes in European pharmacopoeia (Ph. Eur.) 8.4, but in State Pharmacopoeia XI has the description of Centaurium pulchellum (Centaurium pulchellum (Sw) Druce), besides this species. State Pharmacopoeia XI contains the general description two types of raw materials, but their differences are wasn't describe.

The aim of our research was in finding of diagnostic anatomic signs of Centaurium pulchellum during microscopic investigations. Herb of Centaurium pulchellum, procured in July-August of 2014, was the object of researching.

We have used samples, treated by solution of chloral hydrate and we have done microscopic research of this staff according to requirements of Ph. Eur. 8.4 for finding the anatomic structure of stems, leaves and flowers of Centaurium pulchellum.

Stems. Parts of stems haven't ear-like outgrowths or have short or more extended ones, where angular collenchyma are situated (this sign is described in Ph. Eur. 8.4.). Cover tissue of stem is epidermis, created by large cells, covered by plicate cuticle. Under the epidermis chlorenchyma and several layers of parenchyma are situated. Sometimes groups of fibres can be finding by using the reaction with aniline sulphate (yellow coloration observed). Conducting elements of xylem have the same diameter. Vessels are narrow, porous, spiral. In the underbody of stem a core is gap-filling, and in overhead – considerably destroyed. Leaves. Leaf of centaury is isolateral. There are fragments of columned chlorenchyma that consists of the shallow rounded cells and cells-idioblusts with large druse in powder materials. Epidermal cells are winding, covered by a plicate cuticle. Stomas are large and numeral. Type of stomatal apparatus is anisocytic. Flower. The tube of calyx of flower is presented by tetragonal epidermal cells, with the thick-walled shells, pierced by pores. Small stomas of anomocytic type can be found in sepals' epidermis. Epidermis of corolla limb consists of extended, narrowed cells, which often have significantly winding shells. Yellow pollen grains are three-cornered-rounded or elliptic, about 30 mcm in a diameter. Seeds accumulate fat oil (reaction with Sudan 3 was used).

Thus, establishment of anatomic signs of herb of Centaurium pulchellum was did with the aim of standardization of homeraw materials.

# THE STUDY OF INFLUENCE OF BLACK CHOKEBERRY LEAVES EXTRACTS ON THE DEVELOPMENT OF THE PAW OEDEMA, INDUCED BY CARRAGEENIN IN RATS

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Introduction. The growing prevalence of gout and the shortage of antigout agents makes it necessary to develop new herbal drugs with proven efficacy and safety. Fruits of black chokeberry (Aronia melanocarpa (Michaux.) Elliot) are widely used in atherosclerosis, arterial hypertension, blood coagulation disorders etc. The leaves of chokeberry are considered a perspective raw material because of the high content of phenolic compounds (catechins, flavonols, phenolcarboxylic acids and others). It has been shown in our previous experiments that water and ethanol extracts from chokeberry leaves counteract hyperuricemia in the experiment; ethanol extract also shows favourable renal effects in hyperuricemia and in intact animals. According to the data available in literature, chokeberry leaves extracts eliminate the disturbances of the peroxidation balance. To complete the pharmacological spectrum of these extracts, it is rational to investigate their influence on the inflammation process that is an important link in gout pathogenesis.

Objects. Water and 50% ethanol extracts of the chokeberry leaves were obtained by pharmacopoeial techniques.

The model of the paw oedema induced by carrageenin in rats was used with the measurement of oedema and inhibition percentage calculation. All studies were in accordance with the bioethics requirements. The extracts were administered at the dose 500 mg/kg, which was determined as the effective one in the previous experiments concerning uric acid metabolism. Diclofenac sodium as a classical COX inhibitor, recommended for experimental research, was chosen as the reference drug.

Results. It was established that water extract of chokeberry leaves tends to reduce the paw oedema at the periods of inflammatory process not associated with prostaglandins mediatory role. Ethanol extract does not influence on the oedema development, while diclofenac sodium renders a significant anti-exudative effect, and its dynamics is in accordance with the known data about mechanism of action.

Conclusion. The results do not confirm the significant anti-inflammatory properties of aronia leaves extracts. The tendency to oedema reduction against the background of water extract may be increased with the dose change. The absence of the significant influence on prostaglandins system may indirectly indicate the absence of the significant ulcerogenic action (similar to classical NSAIDs).

# DEFINITION OF HYPOCLYCEMIC EFFECT IN ANTIDIABETIC PLANTS GATHERING ON RATS WITH NORMAL GLUCOSE HOMEOSTASIS

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Diabetes is global medical and social problem with epidemiological distribution. So promising area of pharmacology is search for new antidiabetic agents.

The purpose of this study was to determine the effective dose of antidiabetic plants gathering for hypoglycemic effect in animals with normal glycemic status.

The level of glucose in blood samples obtained by tail vein of the animals was determined after 1, 2 and 3 hours after introduction of plants gathering using the glucose oxidase method with the test sets "Glucose-D" company "Filisit-Diagnosis" (Ukraine).

For determination hypoglycemic action of plants gathering decoction was introduced intragastric in doses of 3, 6 and 9 ml/kg to female rats with a weighing 250-300 g with normal glycemic during 3 days. The control animals received the water. The results of research showed that blood glucose levels after 1, 2, 3 hour when administered antidiabetic plants gathering at a dose of 3 ml/kg weight of animals were 3.3±0.1 mmol/l, 3.3±0.1 mmol/l , 3.9±0.13 mmol/l, respectively; introduced at 6 ml/kg – after 1 hour was 3.04±0.07 mmol/l, after 2 hour was 3.4±0.1 mmol/l, after 3 hour was 3.3±0.2 mmol/l. The dose of 9 ml/kg caused such blood glucose levels: after 1 hour – 3.3±0.1 mmol/l, after 2 hour – 3.4±0.09 mmol/l, after 3 hour – 3.26±0.16 mmol/l.

Therefore, the study showed that the antidiabetic plants gathering has not hypoglycemic effects because the blood glucose level under the influence of remedy is not change during all term of research and did not differ from the values of the negative control. Nevertheless, the absence of hypoglycemic action under conditions of normal glucose homeostasis is a positive fact, because possible to predict the soft hypoglycemic effect in diabetic patients , which will reduce the dose of synthetic hypoglycemic medicines with a combination of plants gathering and avoid the development of undue hypoglycemic reactions (hypoglycemic coma, etc.).

# MICROELEMENT COMPOSITION OF SLENDER JON'S WORT (*HYPERICUM ELEGANS STEPH.)*

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Medicinal plants are source natural of mineral compounds. Medicinal plants are a natural source of mineral compounds. These compounds are essential for metabolic processes in the human body as part of the specific organic compounds (enzymes, hormones, vitamins, etc.) and often determine their chemical and biological activity. The main advantage of the element of the complex of medicinal plants is a harmonious union and complete assimilation by the human body.

The purpose of this study was to investigate the microelement composition of herb Slender Jon's wort *(Hypericum elegans Steph.)*.

The object of our study was to St. John's wort herb collected in different years in the territory of the Kharkov region. Qualitative and quantitative composition of the mineral compounds in the plant was determined by atomic emission spectroscopy of the analyst, which is based on the complete evaporation of the substance in the discharge arc of variable-current (excitation source - PVS-28) and the detection of radiation-spektogra vom DFS-8. Certified standards materials were prepared on the basis of coal powder os.ch. Administration of 7-4 dose volumes of standard solutions of metals. Both methods identify the elements, regardless of the form in which they are present in the samples.

The sample herb St. John's wort contains of about 18 elements, such as iron, zinc, copper, cobalt, manganese, molybdenum, chromium, and arsenic. In the largest amount of iron in the feed accumulate also in considerable quantities contains manganese, chromium, aluminum, copper and silicon. The quantitative content of toxic elements does not exceed the permissible limits.

Iron, chromium, manganese, copper, zinc, molybdenum are essential. Iron deficiency leads to hypochromic anemia, zinc - lead to underdevelopment of the nervous and reproductive systems, deeply connected with the problems of immune deficiency, copper - to a violation of the elasticity of the connective tissue. Equally important is the lack of cobalt, which plays an essential role in the homeostasis of hematopoietic and nervous system, manganese - an integral part of enzyme systems, participates in oxidation-reduction processes, affect the metabolism of proteins.

The data obtained elemental composition can be used to create remedies from herbs St. John's wort with new pharmacological actions.

# MODERN TECHNOLOGY OF DEVELOPMENT TINCTURES AND HERBAL COLLECTIONS FROM NATIVE MEDICINAL PLANTS, WHICH HAVE A HEALING EFFECT

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The purpose of our research is to develop new dosage forms - create the collection, is used for the preparation of infusions and decoctions, the development of the tinctures from domestic vegetable raw materials honeysuckle family Caprifoliacea and actinide family Actinidiaceae suitable for use in medical practice.

Species and varieties of honeysuckle growing in Kazakhstan were studied. A result of study is noted that honeysuckle Ili and honeysuckle Altai - have anti-inflammatory, astringent, diuretic, antispasmodic and hypotensive action. Fresh honeysuckle fruits is used as a tonic and regenerating agents. Leaves of both species have antibacterial activity. All aboveground part (leaves, bark, stems, buds), reformed in powder can be combined with many medicinal agents, which makes it possible to combine and create new effective dosage forms.

The another studied medicinal plant is Actinidia, family Actinidiaceae (Actinidiaceae), which is currently poorly understood. Not created and not standardized dosage forms prepared from raw materials of the family Actinidiaceae (Actinidiaceae), so we studied some properties of the domestic vegetable raw materials - Actinidia, which also can be used in pharmaceutical, food and decorative purposes. This bush vines with deciduous leaves. Actinidia - valuable fruit plants with tasty, tender, fragrant fruit. We undertook a study of winter-hardy and early appearance of fruit varieties of Actinidia - Actinidia kolomikta (Actinidia kolomikta) and polygamous Actinidia (Actinidia polygama), which has successfully growing in our region. For therapeutic purposes are used flowers, leaves, fruits and bark Actinidia. The fruits of the plant contain large amounts of vitamin C (more than lemon, blackcurrant or orange), carotene and other vitamins, minerals, starch, pigments, organic acids, fiber, sugar, pectin and tannins. The high medical value to the fruit of Actinidia is determined of glycosides and volatile, stimulating and regulating cardiac function. Actinidia can apply as a general tonic and antiscorbutic, as well as colds and respiratory diseases.

Therefore, knowing the properties of these plants are the subject of our first development was the medicinal collection i.e. dosage form is a mixture of several

kinds of dried and ground medicinal plants, sometimes the addition of essential oils. As a raw materials were used fruits, leaves of honeysuckle, Actinidia, blackcurrant. This mixture consist of a large amount of biologically active compounds possessing anti-inflammatory and tonic action body. Depending on the application, to the some collection was added essential oils, mainly coniferous.

Using the studied materials were developed tinctures on the basis of S.D. Asfendiyarov KazNMU laboratory. The prepared tinctures are simple, derived from one type of stuff honeysuckle and actinides and complex, consisting of a mixture of extracts from several plants, in particular the raw material used Honeysuckle (Ili, edible) and actinides (kolomikta, polygamous).

For the preparation of infusions were used methods: the maceration and its some varieties, percolation, dissolution thick and dry extracts. The best way was the last, the dissolution of thick extracts. Maceration was performed as follows: chopped raw material of honeysuckle and actinidia with a prescribed amount of extractant loaded in maceration tank and infused at a temperature of 20° C, stirring occasionally for 7 days. After infusion extract was decanted and the residue was squeezed, wrung extract was washed with a small amount of the extractant, again squeezed, wrung extract was added to the initial fusion, after which the combined extract was adjusted to the required volume extractant. The process was very long, there were losses. Second method: percolation is performed by straining extractant through the plant material to extract soluble substances in the extractant. The process is conducted in percolators. It was also very inconvenient method. Another more suitable method was: dissolving dense extracts in 70% ethyl alcohol. The samples were carried out on 40, 70, 90, 95% ethyl alcohol, the best was 70% ethyl alcohol, which has been used by us for the preparation of tincture. For obtaining thick extract has been used method of producing CO2 extraction, which is currently the most efficient extraction with a sufficiently large preservation of biologically active compounds, as shown by our study. In the manufacture of infusions together with technologists prepared new formulations in the ratio of 1: 5, from thick materials honeysuckle extract and Actinidia 70% ethyl alcohol, and then standardized the formulations.

In the Republic of Kazakhstan grows a wide variety of medicinal herbs. The object of our study were native plants honeysuckle and actinides, using them we developed a number of new dosage forms - drug collection and tinctures. It should be noted that new data on the chemical nature of the biologically active compounds in combination with modern instrumental methods of analysis, enables a new way to draw attention to the problem of galenic production, especially tinctures, coupled with the failure of extraction processes.

# COMPARATIVE STUDY OF PLANTS GENERATION OF ARCTIUM LEAVES

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The Arctium generation numbers twelve species but there are only tree species in Ukraine. This is Arctium lappa, Arctium tomentosum and Arctium minor. Arctium lappa is the most widespread species in Ukraine. The plants of these species are very similar by morphological features, that's why raw materials of Arctium tomentosum and Arctium minor are often produced by the name of Arctium lappa leaves. Therefore, studying qualitative composition and quantitative content of some groups of biological active substances was actual in different species of Arctium leaves.

The aim of the work is comparative studying of Arctium lappa, Arctium tomentosum and Arctium minor leaves.

Research techniques. The leaves of plants Arctium species were prepared in the area of Vinnitsa in May-June 2014. We used test-tube reactions and chromatography on the paper and thin layer of sorbent for preliminary research of qualitative composition of the raw material. The quantitative content of organic acids, ascorbic acid and sum of oxidative phenols, hydroxycinnamic acids and phlavonoids was studied by titration method and spectrophotometry.

Results. Arctium lappa, Arctium tomentosum and Arctium minor leaves contained sugars (positive reaction with the Feling's reagent), free and fixed amino acids (positive reaction with 0.2% spirit solution ningidrin before and after hydrolysis). We identified apple, lemon, oxalic and chlorogenic acids, kempherol and astragalin. The quantitative content of some groups of biological active substances in different species of Arctium leaves distinguished insignificantly and made at least 0.75% of sum organic acids, 21mg% of ascorbinic acid, 5% of sum oxidative phenols, 1.5% of sum hydroxycinnamic acids and 1.5% of phlavonoids.

Conclusions. As the result of studying of Arctium lappa, Arctium tomentosum and Arctium minor leaves sugars, amino acids, organic acids, phenolic acids and phlavonoids in raw materials were detected. Besides, the quantitative content of organic acids, ascorbic acid and sum of oxidative phenols, hydroxycinnamic acids and phlavonoids were determined. The obtained data shows that the Arctium lappa, Arctium tomentosum and Arctium minor leaves have similar qualitative composition and quantitative content and they may be used for saving medicinal plant raw material "Leaves Arctium" which may widen saving base of raw material.

# FATTY ACIDS OF LAMIUM ALBUM L. HERB EXTRACT

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White dead-nettle (Lanium album L.) is a herbaceous perennial herb of the family Lamiaceae. White dead-nettle herb has been used in folk medicine of many countries for a long time as an expectorant, anti-inflammatory, antispasmodic, diuretic, hemostatic and sedative remedy.

**The aim of this study** was to investigate the fatty acid composition of Lamium album L. herb dry extract, obtained by extraction with 70% ethanol.

**Materials and methods.**

The herb of Lamium album L. was harvested in the flowering stage in Kharkiv region in the July of 2011.

Study of qualitative and quantitative composition of fatty acids was performed with mass spectrometric detection. By adding the solution of boron trichloride in methanol to the plant material methyl esters of fatty acid were obtained. Analysis of the methyl esters were carried out using the chromatograph Agilent Technology HP6890 GC with mass spectrometric detector 5973N. Identification of methyl esters of fatty acids were carried out using the data of the mass spectra library NIST 05 and Wiley 2007 with a total of more than 470000 spectra in conjunction with programs for identification AMDIS and NIST. Calculation of the quantitative content of fatty acids were performed by the method of the internal standard in mg/kg and percentage of their total content.

**Obtained results.** As a result, in the white nettle herb dry extract 15 fatty acids were identified, including 10 saturated (caproic, myristic, palmitic, margaric, stearic, arachidic, heneicosylic, behenic, lignoceric and cerotic), three monounsaturated (palmitoleic, oleic, eicos-11-enic) and two polyunsaturated (linolenic and linolenic).

The total fatty acid content in the Lamium album L. herb dry extract amounted 14621.92 mg/kg, including: saturated – 6537.97 mg/kg (44.71% of the total fatty acids content), monounsaturated – 1958.83 mg/kg (13.40%), polyunsaturated – 6125.12 mg/kg (41.89%). Dominant fatty acids are palmitic (4442.01mg/kg), linolenic (3425,11 mg/kg), linoleic (2700,01mg/kg) and oleic (1367,59 mg/kg).

**Conclusions.** In the white nettle herb dry extract 15 fatty acids were identified by chromatography-mass spectrometry method. Investigation of the fatty acid composition of Lamium album L. herb of Ukrainian flora was carried out for the first time.

# POLYUNSATURATE FATTY ACIDS AS A SOURCE OF LONGEVITY

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Essential polyunsaturated fatty acids omega-3 and omega-6 are necessary to maintain the health of all body systems, but they are not synthesized by the human body. Sources are the products of animal and vegetable origin.

The aim of this work was to study plant sources of polyunsaturated fatty acids (PUFA) and their application in various diseases due to the unstable economy and rising prices on seafood.

A detailed study of the scientific literature on the topic and analysis of medicinal plants containing polyunsaturated fatty acids methodological basis was

The preservation of health and life is impossible without omega-3 and omega-6 PUFA. Linum usitatissimum, Júglans régia, Heliánthus ánnuus are the sources of obtainig PUFA.

Flax seeds and Flaxseed oil are the main supplier of omega-3 from plant products.

Flaxseed oil promotes activation of fibrinolysis and reduce the clotting properties of blood, in this connection, it is recommended for use in patients with cardiovascular disease, thrombophlebitis and varicose veins.

The presence of this oil omega-3 prevents the formation of atherosclerotic plaques, thins the blood and, as a consequence, it is a good preventive remedy for varicose veins.

Use of Linum usitatissimum, you can activate a complex metabolism and for a short time to solve the problem of overweight.

The PUFA deficiency is one cause of most mental illnesses and disorders. Eating flax seed improves the condition in schizophrenia, depression, alcoholism, drug abuse (especially when the syndrome), the number of violations of conduct.

Peanut butter enhances peristalsis, helps with kidney disease; lowers cholesterol. Whole nuts are consumed with depression, insomnia and multiple sclerosis.

Polyunsaturated fatty acids are true “medicine” for vessels, they are an indispensable element for human life.

# COMPARATIVE STUDY OF ARTEMISIA TAURICA AND ARTEMISIA BALCHANORUM ESSENTIAL OILS COMPONENTS

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Genus Artemisia L. (wormwood) is represented in the Ukrainian flora by about 30 species of herbaceous and suffrutescent plants. Many members of the genus are studied insufficiently, so it is appropriate to study of biologically active substances (BAS) and physiological activity of wormwoods. A. taurica Willd. grows in the Crimea, the Caucasus and Asia Minor and used in folk medicine as anthelmintic, antibacterial, antiprotozoal remedy and topically against warts and corns. A. balchanorum Krasch., whose natural habitat is located in Turkmenistan, is cultivated in the Crimea for the needs of perfume and cosmetics industries. Both of these species belong to the subgenus Seriphidium and are phylogenetically related.

**The aim of this study** was to investigate the essential oils (EO) composition of A. taurica and A. balchanorum herbs, harvested in the budding phase in the Crimea in August of 2011.

**Materials and methods.** EO were obtained by microhydro-distillation method in vials. Study of the composition of the obtained EO was performed by gas chromatography-mass spectrometry (GC-MS) method using Agilent Technology 6890N chromatograph with 5973N mass spectrometric detector under the following conditions: capillary chromatographic column INNOWAX: internal diameter of 0.25 mm and 30 m long; the speed of the carrier gas (helium): 1,2 ml/min; the temperature of the injection heater: 250°C, programmable thermostat temperature from 50 to 250°C at a rate of 4°C/min. In order to identify the components the libraries of mass spectra NIST05 and WILEY 2007 were used. For quantitative calculations the method of internal standard (tridecane at 50 mg/1 mL) was used.

**Obtained results.** Quantitative yield of A. taurica EO was 0.12%, A. balchanorum – 0.78%. In A. taurica oil a high contents of α- and β-thujones (the total content of over 80% of EO), 1,8-cineole, terpinen-4-ol, camphor and sabinol were revealed. Dominate components of A. balchanorum EO along with α- and β-thujones were sesquitherpenoids vulgarone B and calarene.

**Conclusions.** A comparative study of A. taurica and A. balchanorum herbs EO was carried out. It is established that oils are similar in composition, but EO of A. balchanorum is characterized by a lower content of toxic α- and β-thujones and a larger share of sesquiterpenoids.

# RESEARCH OF PHENOLIC COMPOUNDS OF DRY EXTRACT MADE FROM WASTES OF SALVIA OFFICINALIS LEAVES OBTAINED AFTER INITIAL ETHYL ACETATE EXTRACTION

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Nowadays a wide range of different herbal medicines is represented on the pharmaceutical market. The greatest part of their production requires a large quantity of medicinal plants. In addition manufacturing technology of these medicines doesn't include the allocation of the maximum number of biologically active compounds (BAC), so the inefficient use of medicinal herbs becomes evident. That's why complex processing of medicinal plants is considered as the main direction to solve this relevant problem.

There are 38 medicines that contain biologically active compounds extracted from Salvia officinalis species at the Ukrainian pharmaceutical market. They include the essential oil and the tincture.

For example, our pharmaceutical industry has previously produced medicine «Salvin». «Salvin» was notable due to its important anti-inflammatory and antimicrobial properties. But acetone was needed for its production technology. And nowadays acetone belongs to the precursors.

According to the previous researches ethyl acetate can substitute acetone in order to obtain new medicine from the leaves of Salvia officinalis similar to «Salvin». But there is still the significant number of phenolic BAC in wastes that remains after the ethyl acetate extraction. That's why further studying of its chemical composition is reasonable in order to create new medicines by using the complex processing method.

To obtain the dry extract wastes of Salvia officinalis leaves, which remain after previous ethyl acetate extraction, were poured with purified water (1:5 ratio). The mixture was heated in a water heater and then infused during one day. The extraction was performed twice. At the next stage the extract was purified by settling, and then it was filtered and evaporated in the vacuum spray machine. In such way12-15% yield was achieved.

To establish the qualitative composition of the obtained dry extract qualitative reactions, paper (HRP) and thin-layer chromatography (TLC) were used as generally accepted research methods.

In order to determine hydroxycinnamic acids the ethyl acetate fraction of the investigated extract was used. It was chromatographed on paper with standard hydroxycinnamic acids samples in the following systems: I – n-butanol-acetic acid-water (4:1:2) and II – 15% acetic acid. The resulted chromatogram was then treated with ammonia vapor and diazoreagent.

Flavonoid compounds was discovered by HRP and TLC methods with standard flavonoid samples in the following organic solvents: n-butanol-acetic acid-water (4:1:2); chloroform-acetic acid-water (13:6:2); chloroform-methanol (9: 1). The presence of this compounds group was determined by their fluorescence in UV light before and after next chromatogram treatment: ammonia vapor, 1% aluminum chloride alcoholic solution.

Therefore amino acids, sugars, hydroxycinnamic acids, flavonoids and tannins were discovered in the resulted extract. Caffeic, ferulic and chlorogenic acids were identified among hydroxycinnamic acids. And apigenin as well as luteolin 7-O-glucoside were found out among flavonoids.

Quantitative determination of hydroxycinnamic acid derivatives, flavonoids, polyphenolic compounds was performed using spectrophotometric method. Optical density was measured in cuvette with a 10 mm layer thickness at spectrophotometer Specol 1500 (Switzerland) at the appropriate wavelength. The amount of hydroxycinnamic acids derivatives was determined at 327 nm (calculated as chlorogenic acid). The flavonoids amount (calculated as routine) was confirmed at a 417 nm wavelength after a complex with aluminum chloride formation. Also the amount of phenolic compounds (calculated as gallic acid) was found out at 270 nm wavelength.

All experiments were repeated at least five times for statistical significance.

As a result, it was discovered that the dry extract from the Salvia officinalis leaves obtained by the complex processing contains such amounts of BAC: hydroxycinnamic acids – 5.5%, flavonoids – 6.61%, phenolic compounds – 32.49%.

Thus, our research demonstrated significant prospects of the complex processing of Salvia officinalis leaves in order to obtain new anti-inflammatory and antimicrobial herbal medicines similar to «Salvin». Such complex processing not only helps to solve the problem of medicinal herbs misuse, but also considerably improves the production technology of the herbal medicines.

The experimentally discovered data will be the basement for further standardization of Salvia officinalis dry extract obtained using the complex processing.

# QUALITATIVE COMPOSITION AND QUANTITATIVE CONTENT OF MACRO- AND MICROELEMENTS IN PLANT RAW MATERIALS OF PLANTS OF HEMEROCALLIS L. GENUS

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**The aim of research.** Investigation and analysis of macro- and microelements of plant raw materials of two prospective species of Hemerocallis L. genus and determination of the content of total ash were the aim of the research. Biological effects of the preparations of plant origin are realizing over the chemical constituents of plant raw material at the base of which they are made; macro- and microelements have some significance in the development of such effects. Some plants are able to accumulate certain elements, because of that investigation of elementary composition of plant raw material is necessary in it's phytochemical analyzing. Modified roots, flowers and leaves of daylilies are used in Oriental systems of folk medicine for the treatment of skin diseases, liver's and pancreas' diseases, as sedative and anti-inflammatory remedies. In Ukraine the plant raw materials of daylilies are studied insufficiently and the potential value of such herbal materials is not employed in medicine.

**Materials and methods.** The object of research is the study of content of macro- and microelements in modified roots, flowers and leaves of orange daylily (Hemerocallis fulva L.) and hybrid daylily (Hemerocallis hybrida var. "Stella de Oro") and determination of total ash content in such objects. Dry raw materials were ground, dried to the constant weight; the sample was prepared by mineralization and acidic hydrolysis. Determination of the content of macro- and microelements was carried out with atomic absorption spectrophotometry based on absorption of resonance radiation by free atoms of chemical elements by passing the beam of light through a layer of atomic fume.

**Results.** Qualitative composition and quantitative content of macro- and microelements and total ash content have been investigated in modified roots, flowers and leaves of orange daylily (Hemerocallis fulva L.) (ODMR, ODF, ODL respectively) and hybrid daylily (Hemerocallis hybrida var. "Stella de Oro") (HDMR, HDF, HDL respectively). Five macroelements (sodium, potassium, calcium, magnesium, phosphor) and seven microelements (iron, cooper, zinc, manganese, nickel, cadmium, selenium) have been identified and their quantitative content has

been determined. Total ash content has been determined. Results are displayed in the following table.

**Table.**

Total ash content, qualitative composition and quantitative content of macro- and microelements in the investigated plant raw materials

| Elements | Plant raw materials | | | | | |
|---|---|---|---|---|---|---|
| | ODMR | HDMR | ODF | HDF | ODL | HDL |
| Total ash content,% | | | | | | |
| Ash | 3,6 | 9,1 | 5,5 | 5,6 | 7,0 | 8,5 |
| Macroelements content, mg/kg | | | | | | |
| Na | 481 | 815 | 672 | 1523 | 1523 | 1582 |
| K | 2007 | 1757 | 7862 | 10513 | 6462 | 15597 |
| Ca | 941 | 913 | 1426 | 1493 | 6815 | 5982 |
| Mg | 713 | 633 | 2017 | 2304 | 3767 | 4274 |
| P | 2335 | 2291 | 2791 | 3969 | 2546 | 88 |
| Microelements content, mg/kg | | | | | | |
| Fe | 41 | 36 | 39 | 44 | 63 | 20,6 |
| Cu | 15,8 | 3,8 | 11,2 | 21,7 | 15,6 | 6,5 |
| Zn | 6,7 | 5,7 | 13,4 | 11,5 | 3,2 | 24 |
| Mn | 6 | 5,3 | 15 | 16 | 17 | 24 |
| Ni | 0,38 | 0,25 | – | – | – | – |
| Cd | 0,062 | 0,054 | 0,17 | 0,072 | 0,17 | 0,14 |
| Se | 2,26 | 4,05 | 1,94 | 1,21 | 1,94 | 4,05 |

Ash content does not exceed permissible limits for the relevant types of plant raw materials. High content of potassium, sodium, magnesium, phosphor and calcium should be noted. The content of potassium is significantly higher than sodium in all samples of raw materials. Leaves of both daylilies species are characterized by the high content of calcium and iron, flowers – by the high content of zinc. Hybrid daylily modified roots contain a considerable amount of selenium possessing significant antioxidant properties and it's regular intake is necessary. A small nickel content has been found in underground organs of both species of daylilies.

**Conclusions.** Macro- and microelement content of modified roots, flowers and leaves of orange daylily (Hemerocallis fulva L.) and hybrid daylily (Hemerocallis hybrida var. "Stella de Oro") have been investigated for the first time. The presence and qualitative content of the twelve elements have been determined, five macro- and seven microelements among them. Among macroelements potassium predominates in all types of raw materials; also considerable content of phosphorus has been determined; among microelements relatively high content of iron has been determined. The obtained results indicate the expediency of investigation of plants of Hemerocallis L. genus as perspective medicinal plants.

## SECTION № 3

# THE STANDARDIZATION OF MEDICINES. PHARMACEUTICAL AND CHEMICAL-TOXICOLOGICAL ANALYSIS

# THE STUDY OF LINEARITY OF SPECTROPHOTOMETRIC QUANTITATIVE DETERMINATION BY SPECIFIC ABSORBANCE OF RIBOFLAVIN

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The chemical structure of riboflavin (6,7-dimethyl-9-(D-1-rybityl)-izoalloksazyn) allows to quantitatively determine the substance by the following methods: spectrophotometry, photocolorimetry, fluorymetry, alkalimetry.

Today new methods of quality control for riboflavin methods have been developing: HPLC, electrophoretic extraction, voltammetric. In pharmacopoeial analysis for quantitative determination of riboflavin in substance European Pharmacopoeia, The State Pharmacopoeia of Ukraine (SPhU), the British Pharmacopoeia proposes absorption spectrophotometry method according to the specific absorbance. According to the SPhU, quantitative determination of riboflavin in substance is produced by the spectrophotometry method according to the specific absorbance in a buffer solution at a wavelength of 444 nm. Riboflavin content is calculated using the specific absorption, which is equal to 328.

The aim of our work is to study the linearity parameters of method of quantitative determination of riboflavin by the spectrophotometry method by specific absorbance in order to standardize procedures for analysis by the specific absorbance.

The study of linearity was performed at 9 points. The values used for calculations ($C_{nom}$ and $A_{nom}$) are calculated by the formulas: $C_{nom} = [m_{nom} \cdot (100 - LOD)] \cdot Dil \cdot (Cont_{nom} / 100)$, $A_{nom} = A_{1cm}^{1\%} \cdot C_{nom}$.

Due to the fact that the concentrations and analytical signals are advisable to give in normalized coordinates, the following values were calculated: $X_i(\%)=100 \cdot C_i/C_{nom}$, $Y_i(\%)=100 \cdot A_i/A_{nom}$, $Z_i(\%)=100 \cdot Y_i/X_i$.

The plot of linear dependence of $Y_i$ from $X_i$ ($Y = b \cdot X + a$) was built, it is shown in Figure.

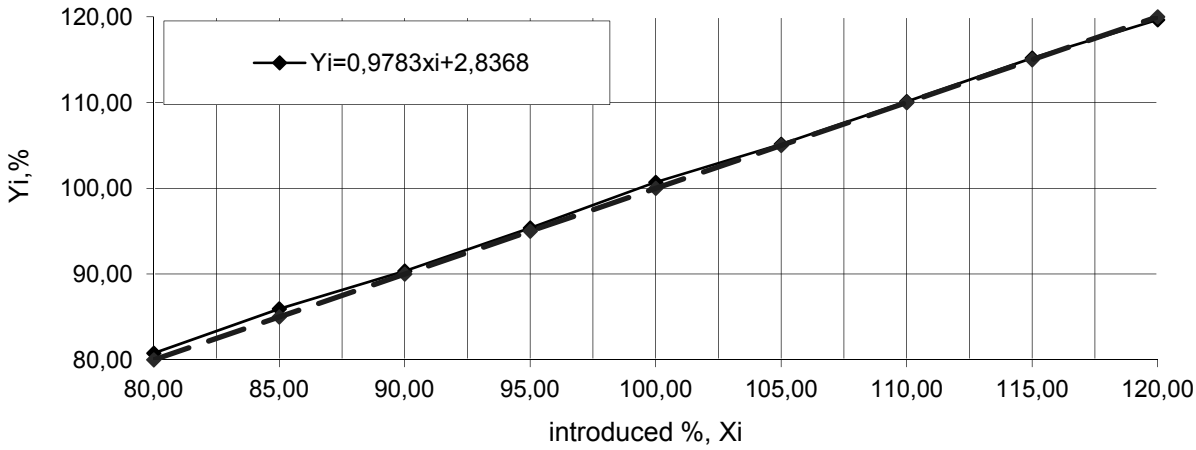


Fig. The plot of dependence of the absorbance on the concentration of riboflavin in normalized coordinates.

The calculation of parameters of linear dependence was performed by the least square method. The calculated statistical values *b, $s_b$, a, $s_a$, $RSD_0$* and *r* - are shown in Table.

| Value | Significance | Criteria (for tolerances 97-103%, the number of points 9) | Conclusion |
|---|---|---|---|
| *b* | 0.9783 | - | - |
| $s_b$ | 0.0057 | - | - |
| *a* | 2.8368 | statistical insignificance $a \le t(95\%, g-2)\cdot s_a = 1.89\cdot s_a$. =1.89·0.5774=1.09% | not corresponds |
| | | practical insignificance $\left\|a_{\delta A}\right\| \le \max \delta_A = 0.71\cdot \max \Delta_{As}$. =0.71·3=2.13% | not corresponds |
| | | max *a* = 4.39% | corresponds |
| $s_a$ | 0.5774 | - | - |
| $RSD_0$ | 0.2218 | $RSD_o \le 1.12$ | corresponds |
| *r* | 1.0000 | min $R^2_c$=0.99331 | corresponds |

The table shows that the requirements for the parameters of linear dependence are performed. The free member of the linear dependence *a* slight exceeded the criterion of practical uncertainty, so it can be neglected, considering that the general requirements of acceptability are executed ( $2.84\% \le 4.39\% = \max a.$ ).

# DEVELOPMENT OF THE NON-AQUEOUS ALKALIMETRIC METHOD OF THE QUANTIFICATION OF METHYL 1-ALLYL-4-HYDROXY-2,2-DIOXO-1H-2Λ$^6$,1-BENZOTHIAZINE-3-CARBOXYLATE

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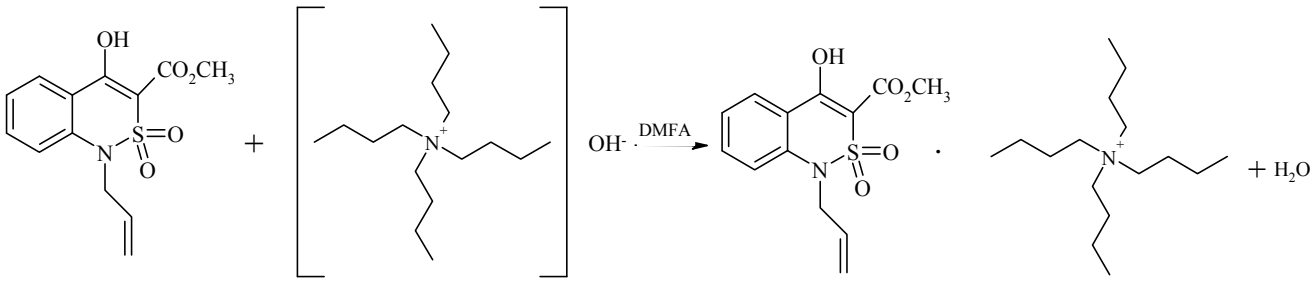
Pains of various origin and pain syndromes occur so often as it is difficult to find a person among the world population that does not know this feeling. Hence it is not surprising that pain-killers are among the most popular and often used drugs. The drug arsenal of this pharmacological group that is available in modern medicine is exceedingly wide. However, even under such conditions the appropriate pain relief is not always successful. That is why to create new high-performance and low-toxic medicines that have analgesic activity range of 1-R-4-hydroxy-2,2-dioxo-1*H*-2λ$^6$,1-benzothiazine-3-carboxylates was synthesized. The highest analgesic activity among the obtained substances methyl 1-allyl-4-hydroxy-2,2-dioxo-1*H*-2λ$^6$,1-benzothiazine-3-carboxylate revealed, the analgesic effect of which (+71.1%) exceeded that of all the reference compounds (piroxicam, diclofenac and ketorolac) used in the experiment. Therefore one of the important tasks of our study was to develop a method for the quantitative determination of the most active compound. Based on the chemical properties of the obtained compound we have chosen the method of non-aqueous alkalimetric titration.




Titration was carried out in a non-aqueous solvent medium of dimethylformamide (DMFA), universal organic solvent. As a titrant tetrabutylammonium hydroxide in 2-propanol was used, the endpoint is determined potentiometrically.

The results were subjected to quantitative determination of the statistical processing. The sample can be called reliable if options included in it are not burdened blunder.

# COMPOUNDING PREPARATION SYRUPS AND THEIR STANDARDISATION

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Compounding pharmacists around the world are faced with the demand for a novel pediatric preparation. The manufactured market of medicines in Ukraine for pediatric patients is smaller than market for adults. Most of the medicines for treatment of children have not been clinically studied in the pediatric population. In this case, extemporaneously prepared medicines with new effective active ingredients can help to meet the unique needs of the pediatric patient. Infants and children prefer sweet tastes and do not want to take the bitter preparations. Extemporaneously prepared syrups are promising dosage forms for use in pediatrics.

Syrups are thick, clear liquid, containing one or more active substances dissolved in water, usually sugars or sweeteners. Syrups are used for dissolving, suspending or emulsifying of the active pharmaceutical ingredients, appropriate medicinal forms formation, for easy use and dosage to give a pleasant taste and aroma. Usually, sucrose, glucose, fructose, aspartame, saccharin etc. are used for preparation of syrups bases. For preparation of complex syrups bases other agents are used as dextrose, sorbitol, mannitol, xylose.

There are no official flavored/sweetened vehicles for compounding preparations in the State Pharmacopoeia of Ukraine, but list of them are given in USP/NF. For example: sorbitol solution is a water solution containing D-sorbitol; suspension structured vehicle contains potassium sorbate, xanthan gum, anhydrous citric acid, sucrose, and purified water; sugar-free suspension structured vehicle contains xanthan gum, saccharin sodium, potassium sorbate, citric acid, sorbitol, mannitol, glycerin, and purified water; simple syrup contains sucrose and purified water and others. The main questions for compounding pharmacies are standardization and proving of stability of vehicles which prepared for stock and after preparation of the dosage form. Presumably all of these vehicles are generally self-preserving as long as the sugars concentration is maintained at a sufficiently high level. But in spite of this, pharmacists need with documented stability studies to prove the terms and conditions of storage for the possibility of syrups stock preparation and further use when compounding. The evaluation should include appearance, clarity for solutions, color, odor, assay, degradation products, pH, viscosity, preservative content, and microbial limits.

**QUANTITATIVE DETERMINATION OF CAROTENOIDS IN THE $CO_2$-EXTRACT OF PLANTAGO MAJOR**

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One of the main priorities for the development of the pharmaceutical industry of the Kazakhstan Republic is the development and introduction of original domestic substances from medicinal plants and drugs based on them.

Promising targets of modern herbal medicine are reperesentatives of the genus Plantago L. family Plantaginaceae Juss. Preparations of Plantago major leaves have anti-inflammatory, antimicrobial, antioxidant and hypolipidemic activity. Currently, the most studied biologically active substances of Plantago major are from the group of polysaccharides. In this regard, it was of interest to identify and study the lipophilic fraction BAS of plantain leaves.

We obtained a $CO_2$ - extract of Plantago major, for which standardization is a prerequisite to study the complex of biologically active substances contained in it.

By TLC in the solvent system hexane: acetone (8: 2) it was found that solution of $CO_2$ - plantain extract in hexane in the chromatogram is characterized by the presence of at least three yellow spots, one of which corresponds to a spot of standard β-carotene. Therefore, we carried out a further quantitative content analysis of the amount of carotenoids in this extract. Determination was conducted for $CO_2$- extract solution in hexane waybread spectrophotometrically at 450 nm. As a compensation solution was used hexane. Content of total carotenoids calculated in two ways - by the standard, which is used as β-carotene, and external standard method - solution of potassium dichromate.

As a result of studies, it was found that the total content of carotenoids in $CO_2$-Plantago major extract is not less than 0.70%. The results of this work will be used futher in the development of formulations based on $CO_2$ extract.

# DEVELOPMENT OF PHOTOCOLORIMETRIC METHOD OF SULPHACETAMIDE SODIUM QUANTIFICATION

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The research related to the development of efficient and cost-effective methods of analysis of medicinal substances is carried out at the Department of Pharmaceutical Chemistry of National University of Pharmacy. This work is devoted to quantification of sodium sulphacetamide which is a representative of group of sulphonamides of antimicrobial action and is widely used nowadays as an antimicrobial agent for the treatment of eye diseases. The sodium sulfacetamide eye drops of industrial preparation contain sodium thiosulphate as an excipient.

For the assay of sulphacetamide sodium the method of nitritometry is used most often in spite of the fact that this method has certain disadvantages such as the needed reduced temperature, the low speed of titration, and the complicated determination of the end-point. The presence of excipients may prevent the proper quantification of the main substance.

The target of our investigation was to develop a new practical method for the quantification of sodium sulphacetamide that can be used both for the assay of this substance and medicinal forms containing it.

We suggested the method of photocolorimetric determination of sodium sulphacetamide based on the measurement of absorbance of the coloured complex obtained as a result of interaction of sodium sulfacetamide with sodium nitroprusside alkaline solution and hydrogen peroxide solution. The obtained complex has a green coloration and absorbs in the range 590-700 nm.

The determinations were carried out by the method of standard using the photocolorimeter with the orange color filter.

The validation studies of the suggested method were carried out. They showed good precision and accuracy of its results, which makes it suitable for the quality control of medicines.

The possibility of quantitative determination of sodium sulphacetamide in eye drops was checked. It was shown that the presence of the excipient does not affect the results of determination of the active ingredient.

The method of photocolorimetric determination of sodium sulfacetamide based on the reaction with sodium nitroprusside alkaline solution can be recommended for the quantitative analysis of sodium sulfacetamide in the substance and in eye drops.

# DEVELOPMENT AND VALIDATION OF THE METHODS OF CAPTOPRIL SPECTROPHOTOMETRIC DETERMINATION IN BLOOD BY THE REACTION WITH THE ELLMAN REAGENT

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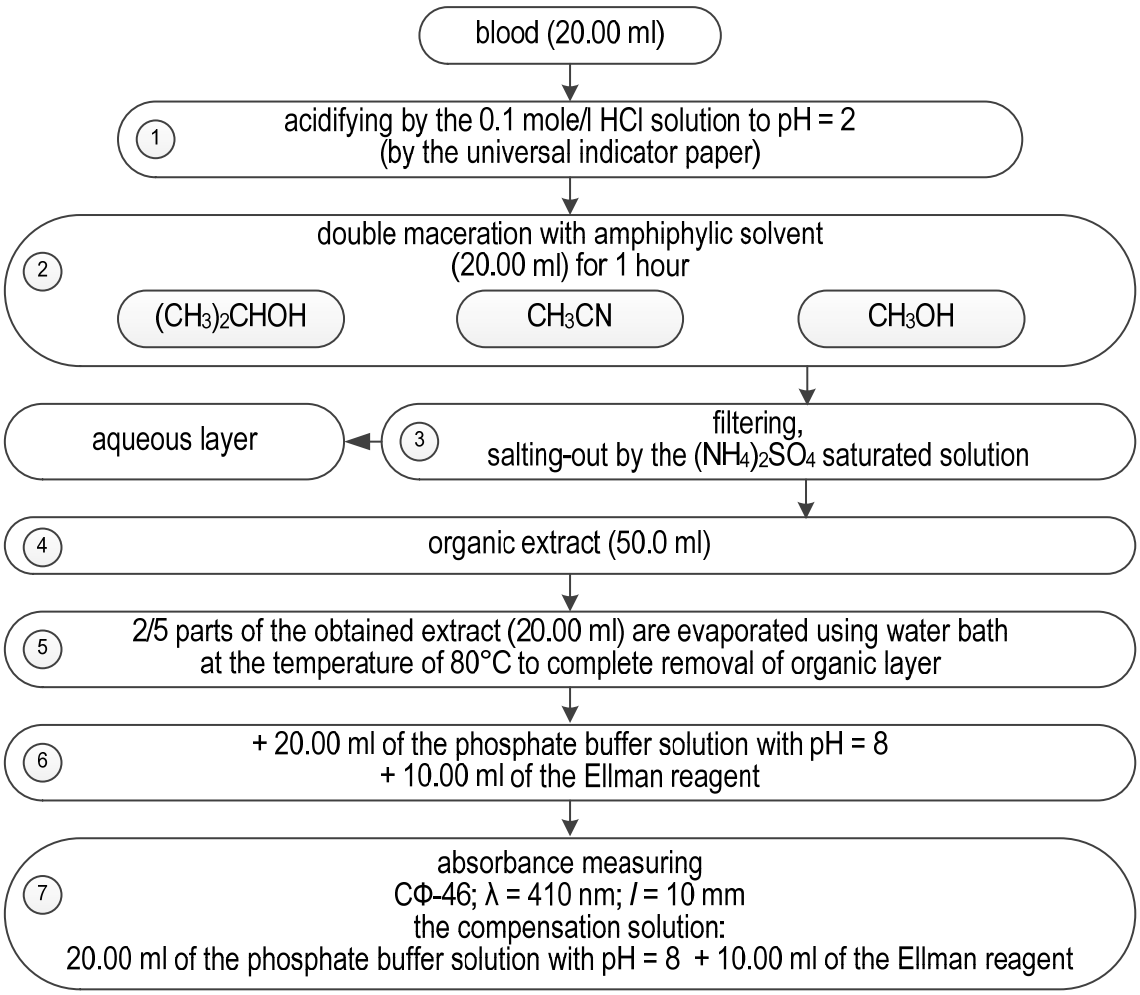
The purpose of our paper is developing the set of methods of captopril quantitative determination in blood using different procedures of sample preparation based on spectrophotometric method by the reaction with the Ellman reagent, carrying out validation of the offered methods and choosing the optimal procedure of sample preparation provided effective captopril isolation from blood and low content of co-extracted substances in the obtained extracts at the minimum value of the method uncertainty.

The design of experiment on development of methods is presented on the scheme.




For captopril determination the spectrophotometric method based on the photometric reaction with the Ellman reagent at pH = 8 has been developed by us.

In the present paper it has been suggested to carry out captopril isolation from

blood by its maceration with amphiphylic solvents and subsequent separation of organic layer under the conditions of aqueous phase saturation by electrolyte for increasing the efficiency. Such amphiphylic solvents as methanol, isopropanol and acetonitrile were used in the experiment; ammonium sulphate was applied as electrolyte for saturation of aqueous phase; isolation was carried out in the acid medium (pH = 2).

Thus, the development of the set of methods of captopril determination in blood using the method of spectrophotometry by the reaction with the Ellman reagent has been become the result of this stage of investigations; the methods differ by the procedures of sample preparation.

For choosing the optimal methods of captopril determination in blood we carried out their validation by such parameters as specificity, recovery, linearity, accuracy, repeatability and intermediate precision.

The methods validation was carried out at the first stage using model solutions – the results of validation allow to point to the conclusion about acceptable linearity, accuracy and repeatability of the method of captopril quantitative determination by the method of spectrophotometry by the reaction with the Ellman reagent.

The results of specificity study show that carrying out captopril isolation from blood using amphiphylic solvents provides low contribution of biological matrix components into the absorbance of the sample to be analysed. It is possible to point to the conclusion about high efficiency of captopril isolation from blood – not less than 90% – by the results of recovery study. The method with acetonitrile application is characterized by the best extraction efficiency.

The values of reproducibility for recovery and blank-samples absorbance satisfy the acceptability criteria for all variants of the methods. The absorbance values obtained for the blank-solutions are the evidence of the correct choice of sample preparation procedure for all considered cases.

On the whole, all examined methods are characterized by the acceptable parameters of linearity, accuracy and precision, and the obtained data are the evidence of application possibility of the developed methods for captopril spectrophotometric determination in blood by the reaction with the Ellman reagent.

Thus, we have developed the set of spectrophotometric methods of captopril quantitative determination in blood by the reaction with the Ellman reagent using amphiphylic solvents (isopropanol, acetonitrile, methanol) for analyte isolation from matrix under the conditions of aqueous phase saturation by ammonium sulphate. Acetonitrile application in the acid medium (pH = 2) is optimal – contribution of matrix components into the absorbance of the sample to be analysed does not exceed 10%, extraction efficiency is ~97%.

# CEPHALEXIN SULFOXIDE OSCILLOPOLAROGRAPHIC QUANTITATIVE DETERMINATION USING POTASSIUM HYDROGENPEROXOMONOSULFATE

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Cephalexin monohydrate is a derivate of amynodesacetoxycephalosporane acid, belongs to β-lactamic antibiotics of the I generation with a wide range of pharmacological activity. Cephalexin has a great Gram-negative and Gram-positive antimicrobial properties. It is produced in gelatin capsules and in the form of suspension. The aim of this work research is the development of a simple, rapid, and costeffective method for the determination of cephalexin in neat substances and powders by the preliminary oxidation of cephalexin in weakly acidic media to respective S-oxide, followed by its quantification by oscillographic polarography.

We used a cephalexin substance meeting the requirements of GFU with the concentration of the titular material 100.9% The oxidant was Oxone®, i.e., a triple potassium salt of Caro's acid, $2KHSO_5 \cdot KHSO_4 \cdot K_2SO_4$ (Acros Organics). Its active ingredient was the potassium hydrogen salt of peroxomonosulfuric acid, $KHSO_5$. The choice of the reagent was determined by its rather high oxidative capacity, $E^0 = 1.84$ V, easy availlability, and satisfactory solubility in water, and also by sufficiently high stability in use and storage.

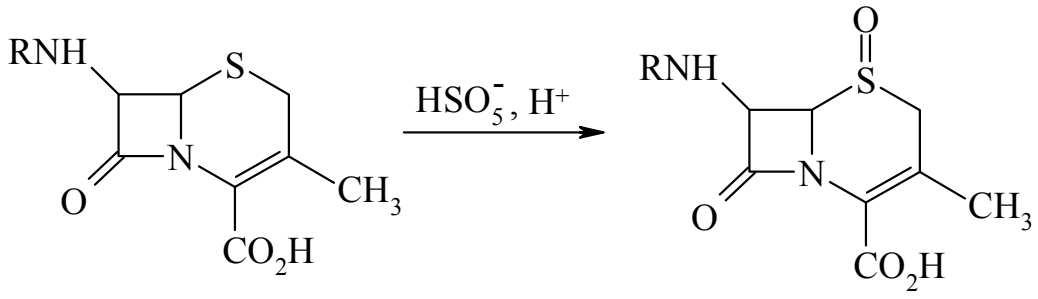
Working solutions of cephalexin and potassium peroxomonosulfate were prepared by diluting stock solutions with twice-distilled water.

Polarograms were recorded in a 0.03 M supporting acetate buffer solution with pH 4.0. To prepare it, 20.4 g of $CH_3COONa \cdot 3H_2O$ of chemically pure grade were dissolved in 50 mL of twice-distilled water, and pH 4.0 was set using 0.1 M HCl; the mixture was diluted to 500 mL with twice-distilled water and stirred carefully

The calibration plot was obtained. The relation of current I, μA, at –0.800 V to the concentration of cephalexin c, M, was approximated by the equation $I = (1.55 \pm 0.1) \cdot 10^4 c + (0.04 \pm 0.01)$, $r = 0.996$. The plot is linear in the range $(1–10) \cdot 10^{–5}$ M. This made possible the further determination by a refference method.

Cephalexin S-oxide in the reaction under study forms through an electrophilic attack of the β-oxygen atom in the peroxide group of the peroxoacid to sulfur within 1 min, i.e., the time of observation. The scheme of cephalexin oxidation by potassium peroxomonosulfate to give the respective S-oxide is presented below.

As was found, the redox reaction proceeds commpletely and stoichiometrically, 1 mol of $KHSO_5$ is consumed per 1 mol of the substance. Three peaks were recorded in the cathodic branch of the voltammograms of solutions: at –0.485 V (average sharp), at –0.800 V (average smooth), and –1.120 V (small smooth, Fig. 1). Considerable changes in peak height at –0.800 V was observed with changes in cephalexin concentration. It was chosen for analytical purposes.




Scheme. Cephalexin oxidation using potassium hydrogenperoxomosulfate

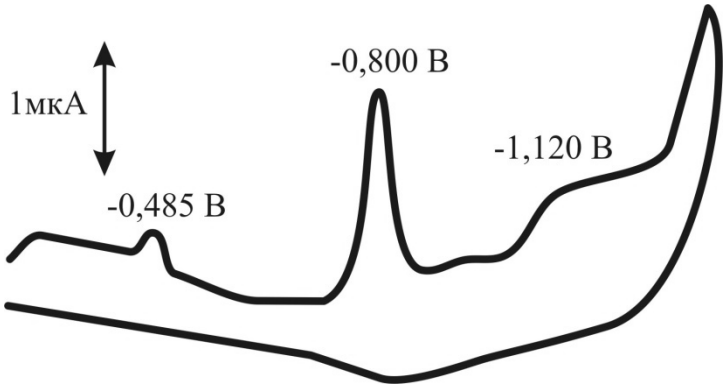



Fig. 1. An oscillographic polarogram of cephalexin S-oxide prepared by the reaction of cephalexin with potasssium peroxomonosulfate.

The data of determining cephalexin in the neat substance are given in the table.

Table. Results of cephalexin quantitative determination in the form of its S-oxide using potassium hydrogenperoxomonosulfate as analytical reagent

| Added, neat substance, g | Cephalexin found, $C_{16}H_{17}N_3O_4S$ | | Metrological characteristics ($P = 0.95$; $n = 5$) |
|---|---|---|---|
| | g | % | |
| 0.3654 ($100.9^{+2.0}_{-3.0}$ %)* | 0.3551 | 102.22 | $\overline{X}$ = 0.3428 (98.70%)* |
| | 0.3474 | 100.00 | S = $\pm 1.07 \cdot 10^{-2}$ |
| | 0.3358 | 96.66 | $S_{\overline{x}} = \pm 4.79 \cdot 10^{-3}$ |
| | 0.3474 | 100.00 | $\Delta\overline{X} = \pm 1.33 \cdot 10^{-2}$ |
| | 0.3281 | 94.44 | RSD = 3.12% |
| | | | ε = ±3.88 %; δ = –0.46% |

As is shown, in the determination of 5 $10^{-5}$ M cephalexin in the substance, RSD was 3% at the accuracy errors δ = -0.46 %.

# NIFEDIPINE CHEMILUMINESCENCE QUANTITATIVE DETERMINATION IN PHARMACEUTICAL PREPARATIONS

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Nifedipine (***N***) (3,5-pyridinedicarboxylic acid, 1,4-dihydro-2,6-dimethyl-4-(2-nitrophenyl)-dimethyl ester) is the main representative of antagonists of dihydropyridine calcium channel blocker.

The intensive literature survey revealed the ***N*** can be quantitatively determined using ceriometric method, HPLC, voltammetric, polarography and UV-spectrophotometric methods. The analytical system $H_2L$ - ***N*** - $H_2O_2$ was proposed for quantitative determination of ***N*** using chemiluminescence (*ChL*) method in pure substance and pharmaceutical preparations, where ***N*** is the activator of *ChL*. The *ChL* occurrence was studied in discrete mode, measurements were performed by photoelectric method. The maximal value of ($I_{ChL}$) *ChL* intensity was chosen as analytical response.

The Nifedipine pure substance, that meets the BPh requirements, and pharmaceutical preparations that contain Nifedipine: tablets “Phenihydin-Zdorovye” produced by OOO “Zdorovye” Pharmaceutical Company, Ukraine, 10 mg of active substance and “Nifedipine” tablets produced by „Actavis”, Bulgaria were used. All standard solutions were prepared using Hillenbrand method. The intensity of chemiluminescence was measured in conditional units (c.u.) on the device with photoelectric multiplier FEU-84-A, using measurement of low currents IMT-0.5 and quick-acting (time constant 0.1 s) automatic potentiometer.

The performed experiments revealed that the following mixing order when $H_2O_2$ solution is the last is optimal for *ChL* activation in the system $H_2L$ - ***N*** - $H_2O_2$. Optimal reagents concentrations are: $c(NaOH)$ = 0.03 mol $L^{-1}$, $c(H_2O_2)$ = 0.3 %, $c(H_2L) = 1 \cdot 10^{-4}$ mol $L^{-1}$. The $I_{ChL}$ (c.u.) against ***N*** (mol $L^{-1}$) concentration linear dependence was observed in the concentration range $(1\text{-}10) \cdot 10^{-8}$ mol $L^{-1}$. Calibration graph equation is $I_{ChL} = 2.96 \cdot 10^8 c + 0.61$ ($r$ = 0.998). ***N*** quantitative determination in pharmaceutical preparations was performed by the method of standards using linear parts of mentioned before $I_{ChL}$ concentration dependence.

So, the selective procedures of quantitative determination of Nifedipine in pure substance and tablets were developed by the chemiluminescence method of luminol reaction activation effect. While ***N*** $5.575 \cdot 10^{-5}$ mol $L^{-1}$ determination in model solutions of pure substance by the activation method *RSD* = 3.9% ($n$ = 5, $P$ = 0.95), *LOQ* = 2 ng $mL^{-1}$.

# SOME QUESTIONS OF STANDARDIZATION OF ANTIMICROBIAL ACTIVITY OF EXTRACTS FROM PLANTS

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At the moment, there are still many blind spots in the field of standardization of herbal remedies, including those having antimicrobial activity. In normative documents of Ukraine, Europe, the United States, there is no assessment and evaluation criteria for antimicrobial activity testing of commercially available remedies, both synthetic and herbal ones, which certainly is a significant gap in standardization of antimicrobials.

The purpose of the research is to check antimicrobial activity of some natural and synthetic materials, and make the conclusion about the possibility of their use as a standard for testing of antimicrobial activity of herbal remedies.

Materials and methods. Substances of different groups have been selected for study purposes: flavonoids, tannins, alkaloids, triterpenes, anthraquinones, naphthoquinones, simple phenols, and xanthones. Antimicrobial activity of drugs has been determined by the diffusion method of "wells" with diameter of microorganism growth delay zone. In order to evaluate antimicrobial activity of the formulations, the following six test strains of microorganisms have been used: *Staphylococcus aureus ATCC 25923*, *Escherichia coli ATCC 25922*, *Pseudomonas aeruginosa ATCC 27853*, *Proteus vulgaris ATCC 4636*, *Bacillus subtilis ATCC 6633*, and *Candida albicans ATCC 885/653.*

Results and discussion. Below there are the comparison results of antimicrobial activity of substances in order of descending. The following alcohol-aqueous solutions demonstrated medium-range antimicrobial activity: fluorescein 0.1% wt.; quinine 1.0% wt.; tannin 0.5% wt.; Alizarin 0.1% wt.; menadioni natrii bisulfis 1.0% vol.; and Vinpocetine 0.5% vol. The following alcohol-aqueous solutions showed

weak activity: glycyram 0.5% wt.; platyphyllin 0.2% vol.; gallic acid 0.5% wt.; Atropine 0.5% wt.; and papaverine 0.5% wt. The following alcohol-aqueous solutions demonstrated low activity: scopolamine 0.5% wt.; routine 0.5% wt.; baicalin 0.1% wt.; baicalein 0.5% wt.; quercetin 0.1% wt.; and escin 0.1% vol.

As it can be seen, the most active of the alcohol-aqueous solutions studied are fluorescein (a representative of synthetic xanthones) and alizarin (a representative of synthetic anthraquinones) at a concentration of 0.1 % wt., followed by the solutions of tannin (a tannin representative) and vinpocetine (alkaloid) at a concentration of 0.5% wt., then the solutions of quinine (alkaloid) and menadioni natrii bisulfis (a representative of synthetic naphthoquinones) at a concentration of 1.0%wt., solutions of platyphyllin (alkaloid), glycyram (triterpene saponins), gallic acid (simple phenol), atropine, and papaverine (alkaloids) are promising, if the concentration of solutions of these substances is not less than 1.0% wt.

These data show that plant extracts, in which concentration of these substances is equal to or larger than those indicated above, will have middle-range antimicrobial activity, which may be indicative of their antimicrobial potential.

In general, solutions with a concentration of the substance to be 1.0 % wt., but not less than 0.1 % wt, may be selected as a standard for antimicrobial activity.

Data of our research can be used not only for standardization of extracts by the diffusion method of "wells", but also, in the long term, by combining thin-layer chromatography and microbiological diffusion method in serial - bioautographic method of analysis. This will identify the specific substance exhibiting antimicrobial activity in the extract and standardize it exactly according to it.

However, realization of this method requires a lot of research to identify optimal parameters of the process of analysis conducting, both as for chromatographic conditions and microbiological conditions.

Conclusions. Antimicrobial activity of several classes of compounds has been investigated. The most active antimicrobial agents have been selected. The prospects of combination of chromatographic and microbiological methods of analysis in the analysis of integrated drugs from plants have been demonstrated.

# TETRACYCLINE HYDROCHLORIDE AND METAL SALTS INTERACTION RESEARCH

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Antibiotic tetracycline is well known in a pharmacotherapy as an organic ligand, which can form chelate complexes with metal ions. But it can be assumed, that the process of forming complexes can be different and depends on a ratio of antibiotic and metal salts or an antibiotic`s concentration.

Considering mentioned above, the purpose of the research was to study tetracycline hydrochloride and $MgSO_4$, $CaCl_2$, $FeSO_4$, $FeCl_3$, $Al_2(SO_4)_3$ salts interactions in different proportions. The research was carried out using absorbance spectrophotometry methods in the UV part of the spectrum, where the absorbance of tetracycline hydrochloride and its metal salts complexes were measured in proportions 1:1, 1:2, 1:3, 1:4, 1:5. The solution of tetracycline hydrochloride in concentration 0,2M was used as a standard solution. All experiments were conducted in the purified *water medium.*

Comparing the parameters of spectra we can assess following positions: the character of spectra was not changed; absorbance intensity was changed for all samples except magnesia sulfate, in all their ratios. In complexes tetracycline hydrochloride with aluminum sulfate the shift of absorbance maximums for all concentrations was observed, compared with the pure solution of substance. The direct proportion between increasing of the tetracycline hydrochloride and metal salts ratio and absorbance intensity difference was observed.

In terms of the results obtained in experimental conditions, we may conjecture that the complexes with tetracycline hydrochloride and metal salts are forming since the 1:1 ratio and their stability might be decreasing according to the decreasing proportion.

As a conclusion we can assume that the interaction of tetracycline hydrochloride can be stronger with some salts and weaker with another. We can`t still exactly say where is the lower and where is the upper limit and how it interconnected with the strength of these complexes. And in what limits the interaction between the tetracycline hydrochloride and metal ions can affect the pharmacokinetics and bioavailability of the medication. Therefore our study will carried out using another methodics.

# DEVELOPMENT AND VALIDATION OF TANDEM UV-SPECTROPHOTOMETRIC/EXTRACTION-PHOTOMETRIC PROCEDURE OF ZOPICLONE QUANTITATIVE DETERMINATION

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Realization procedure of toxicological examinations requires to give the results of analyte content determination in the sample obtained with the help of at least two methods of analysis, which are based on different principles. Therefore elaboration of so-called tandem procedures allowed to carry out substance determination in the same sample simultaneously by means of two methods of analysis is actual.

The purpose of our paper is development and validation of tandem UV-spectrophotometric/extraction-photometric procedure of zopiclone quantitative determination.

The extraction-photometric procedure of zopiclone quantitative determination using acid dye methyl orange was described before – methyl orange in the acid medium formed ionic associates with zopiclone, which were extracted by chloroform. Under these conditions the chloroform layer becomes yellow – for increasing colour intensity and method sensitivity the obtained ionic associates are decomposed by adding sulphuric acid solution in absolute ethanol to their chloroform solutions and intensive pink colour related to liberating free methyl orange appears. The amount of methyl orange is equivalent to the amount of zopiclone in ionic associates under these conditions.

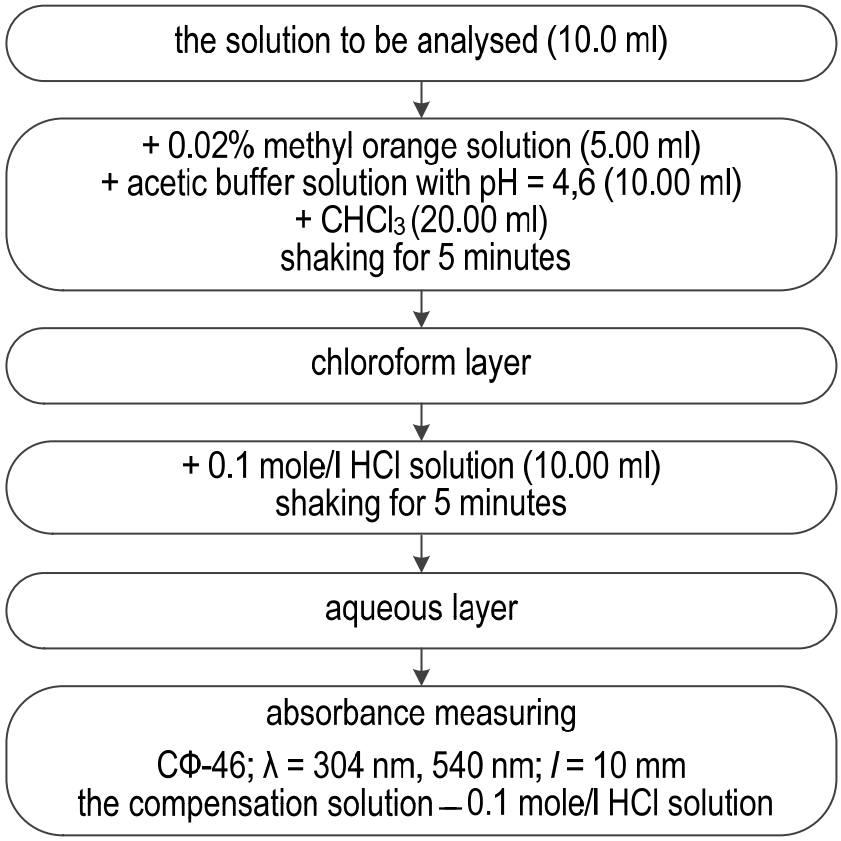
On the first stage of our researches we have modified the described procedure in the way of increasing the volumes of solutions in such a manner that it is possible to measure them with greater exactness that must considerably decrease the total uncertainty of the procedure of analysis.

On the second stage we have carried out validation of the modified procedure in the variant of the method of calibration curve using model solutions with the purpose of confirmation of its applicability for quantitative determination of zopiclone in biological liquids – the offered modified procedure is characterized by satisfactory accuracy and unsatisfactory linearity and precision for all variants of range of the methods application.

From our point of view, unsatisfactory linearity and precision of the procedure are connected, firstly, with application of photoelectrocolorimeter for absorbance measuring, and, secondly, with preparation of the solutions with application of

volatile solvent – chloroform.

With the purpose of leveling the specified defects we have developed tandem UV-spectrophotometric/extraction-photometric procedure according to the presented scheme.




I. e. it is suggested by us to carry out decomposition of ionic associates and reextraction of methyl orange and zopiclone in 0.1 mole/l hydrochloric acid solution simultaneously and to measure the absorbance of methyl orange and zopiclone in the obtained aqueous solution by spectrophotometer.

We have carried out validation of the offered tandem procedure in the variant of the method of calibration curve using model solutions. The obtained data specify that the offered tandem procedure of zopiclone quantitative determination is characterized by satisfactory linearity, accuracy and precision for all variants of range of the methods application and for both variants of the used wave length that makes it suitable for development of procedures of zopiclone quantitative determination in biological liquids.

It is necessary to point that the offered procedure allows to determine simultaneously zopiclone both by its own absorbance in UV-range of spectrum and by absorbance of methyl orange in visible range of spectrum that provides additional reliability of analysis and satisfies the requirements to researches realization in chemical and toxicological analysis – determination should be carried out with the help of at least two methods of analysis, which are based on different principles.

# ASSESSMENT OF THE POSSIBILITY OF DEVELOPING A NEW METHOD FOR QUANTITATIVE DETERMINATION OF PREDNISOLONE IN OINTMENT

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Quality control of soft dosage forms containing prednisolone is not only very important, but difficult task, because of many components in the ointments complicating pharmaceutical analysis. Current methods of analysis for prednisolone and other corticosteroids are less sensitive and need additional reagents (photocolorimetric methods) or need valuable equipment (HPLC using different detectors and solvents). The development of simpler methods is still relevant.

The aim of the study is assessment of the possibility of developing and validation a new simpler method for quantitative spectrophotometric determination of prednisolone by the standard method in the «Prednicarb-Darnitsa» ointment.

There was used such analytical equipment during the experiment: Mettler Toledo AB 204 analytical balance, Thermo Scientific Evolution 60S spectrophotometer, water heater, reagents and measuring glassware (class A) according to the State Pharmacopoeia of Ukraine (SPhU).

To an accurately weighted ointment, 0.025 g prednisolone equivalent, add 15-20 ml of 96% alcohol R and heated it on a water heater to the dissolution of the base, then cooled it in ice. The resulting mixture is filtered through paper filter previously soaked in ethanol. Repeat twice more, starting with “add 15-20 ml of 96% alcohol R”. Extraction of prednisolone is carried to the 50.0 ml volumetric flask and diluted with 96% alcohol to volume. 2.0 ml of this solution is carried to the 50.0 ml volumetric flask and diluted with 96% alcohol to volume. Determine the absorbance of the solution at the wavelength of maximum absorbance at about 243.5 nm against dehydrated alcohol. The standard solution is prepared in parallel according to the SphU.

Three dilutions for the standard substance of prednisolone and six dilutions for prednisolone of the ointment with a concentration of 0.002% were prepared for method's assessment. Measurement of the optical density of obtained model solutions was conducted three times with removing of the cell. The absorption spectrum of the extraction has the same properties as the standard spectrum. This indicates a lack of influence of the excipients.

According to results, quantitative content of prednisolone in the ointment was 97.40% of the nominal (0.5 g per 100 g of the ointment), that is practically identical with the data specified in the certificate of quality (98%) and fully complies with acceptable values.

Therefore, based on the fact that the character of the spectrum of the ointment extraction corresponds to the spectrum of the standard solution, the data of the quantitative determination statistically do not differ from the declared and the method is simpler than presently known, further validation of the method is sufficiently relevant and possible task.

# QUALITATIVE ANALYSIS OF MEDICINES CO-TRIMOXAZOLE

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In addition of the research of the department of analytical chemistry a qualitative analysis of the drug "Co-trimoxazole", tablets (400mg / 80mg) № 20 in blisters was carried out. Active ingredients: 1 tablet contains sulfamethoxazole – 400.0 mg trimethoprim - 80.0 mg. Co-trimoxazole – is a combined antibacterial drag chemical therapeutic agent with wide spectrum of bactericidal action, conditioned by blocking of biosynthesis of pholats in microbial cells: sulfamethoxazole violates synthezes of degidropholy acid, trimethoprim prevents its turning in tetragidropholy.

The drug has been adopted in the treatment of respiratory infections; urinary tract; digestive tract; surgical infections and other infectious diseases.

During the experiment parameters confirming the authenticity of the substances Sulfamethoxazole and Trimethoprim were studied. Legacy IR absorption spectra tablets KBr (1%); the results of UV-absorption spectra in 0.1 M hydrochloric acid solution, absorption peaks were recorded for sulfamethoxazole with $\lambda_{max}$ = 265nm (A = 0.394, c = $1.57 \cdot 10^{-4}$ mol / $dm^3$), for trimethoprim with $\lambda_{max}$ = 270nm (A = 0.612, c = $2.7 \cdot 10^{-5}$ mol /$dm^3$).

Chromatography sulfamethoxazole solution in methanol plates «Silufol» in the system chloroform-isopropanol-diethylamine (6:5:1) revealed the manifestation spot UV light, $R_f$ = 0.33. For trimethoprim in the same conditions $R_f$ = 0.52. Sulfamethoxazole was identified in qualitative reaction on the primary aromatic amine (the formation of the diazonium salt, followed by coupling, with a solution of β-naphthol in alkaline medium); additional test was performed which was proposed by the British Pharmacopoeia on Trimethoprim using 2% solution of $KMnO_4$ in 0.1 M NaOH, formaldehyde solution, sulfuric acid at reflux. When adding chloroform its layer under UV light acquired green fluorescence.

To confirm the authenticity of the drug "Co-trimoxazole" the method of thin layer chromatography in a solvent system of chloroform-isopropanol-diethylamine (6:5:1) was tested in the presence of standard samples of substances witnesses - substances sulfamethoxazole and trimethoprim that meet regulatory requirements.

# DEVELOPMENT OF METHOD QUANTITATIVE DETERMINATION FOR PHENYLEPHRINE HYDROCHLORIDE IN NASAL DROPS

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Phenylephrine hydrochloride belongs to a group decongestant – nasal vasoconstrictor drugs systemic or local (topical) action. Phenylephrine stimulates a greater extent α1-adrenoreptory. As a result of activation of alpha-blockers pre- and post-capillary developing vasoconstrictor effect, which reduces congestion, vascular permeability and mucosal edema, nasal reduce secretions and helps to restore the outflow of mucus from the paranasal sinuses. This docked runny nose, nasal breathing improves and disappears feeling of nasal congestion. In addition, reducing swelling of the mucous in the mouth of the auditory tube pharyngeal promotes adequate aeration of the middle ear.

Stimulating α-adrenergic vascular vasoconstrictor phenylephrine promotes severe action. Vasoconstrictor effect is a decrease in blood flow, decrease swelling of the mucous membranes of the nose, sinuses and eustachian tube. Thereby recovering breathing through the nose, which was disturbed by the flu, colds and allergic diseases.

As decongestant topical action, phenylephrine hydrochloride used in nasal drops, such as "Nazol Baby", "Gripocitron Rinis", "Vibrocil" and others. All these dosage forms except phenylephrine contain other active and additional ingredients. The aim of our research was to develop a spectrophotometric method of quantitative determination of phenylephrine hydrochloride in nasal drops which allows to determine mezaton in the presence of others APIs.

To resolve this objective, we have developed a method of spectrophotometry in the visible spectrum, which is based on formation of colored products phenylephrine hydrochloride with 4-Aminoantipyrine. The reaction was performed in alkaline medium, in presence of potassium ferricyanide. Absorption of colored in the red color product was measured at 499 nm wavelength We found that the reaction of the test solution is stable for 30 minutes. Other APIs and excipients in nasal drops do not interfere the determination of phenylephrine hydrochloride in these conditions.

Methods has been tested on nasal medical products "Nazol Baby" and "Gripocitron Rinis". Established quantitative content of phenylephrine hydrochloride in these medical products is 92% and 95% respectively.

# THE INFORMATION ANALYSIS OF POISONING CASES OF GLICLAZIDE

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Sulfonylurea derivatives (SUD) – glibenclamide, gliclazide and glimepiride form the basis of treatment for diabetes mellitus type 2. Among them – the second generation drug Gliclazide were produced in many countries by various trade names as mono-drug (Diaglizide, Diaglizide MR, Gliclazide MR, Diabeton MR) in tablets of 30, 60 and 80 mg and in the combination with metformin (Glimecomb, Dianorm-M). Lifelong application, growing number of patients with diabetes mellitus 2 type, side effects, combined therapy with other antidiabetic drugs, OTC available – are factors of toxicological hazards of uncontrolled usage of this drug.

The aim of this paper is to conduct the information analysis of poisoning cases of gliclazide and developed methods and techniques for chemical-toxicological analysis of biological objects of this drug poisoning.

Obtained results: according to the dates of conducted informational analysis of websites FDA and patientsville.com it has been found that the number of reported cases of gliclazide poisoning in the period 2008-2012 were 274, including 21 – lethal. In particular, in Europe – 180, North America – 31, Asia – 14, South America – 26, Africa – 2, Australia and New Zealand – 21. The most frequently registered poisonings of this drug have been observed in the North America, South America and Australia, owing to the availability of FDA database and the widespread application in recent years. High index of SUD poisonings in the Western Europe related to the «aging of the nation», which, in turn, is caused by an increasing number of elderly patients with diabetes mellitus type 2. If all cases of SUD poisonings will be registered in other countries, including Ukraine, their number may be much higher. The main causes of acute SUD poisoning noted with side effects of the treatment of SUD in therapeutic doses, while lethal poisoning most frequently due to intentional (suicide) and unintentional drug overdose, which depending on the circumstances in doses that are several times higher than therapeutic ones with further development of hypoglycemia, lactic acidosis, cardiovascular events, and other pathological complications. However, the available literature sources have not contained any data regarding to the developed methods and techniques of chemical-toxicological analysis of gliclazide. Conclusions: results of the conducted information analysis approve the advisability of the development of methods and techniques of chemical-toxicological analysis of biological objects at poisoning of gliclazide.

# INVESTIGATION OF CHLOROPYRAMINE IN THE ROTTING BIOLOGICAL MATERIAL

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One of the important areas of forensic toxicological examination is the study of putrid corpses and exhumed corpses on the presence of substances that could be the cause of poisoning. Organic substances in the putrescent biological material subjected to chemical transformations, they can not be found in the observations. Only a fraction of substances stored in cadavers unchanged for a long time, so study the term storage of the substance in biological material during its decay is an actual problem.

Chloropyramine hydrochloride (suprastin) belongs to the group of antihistamines. This drug is characterized toxicity, in overdose, self-medication can cause intoxication. For the diagnosis of poisoning antihistamines is important to apply the results of chemical and toxicological studies. The aim of this work is to develop techniques isolating, purifying extracts, assay of Chloropyramine in biological material in its decay, depending on the term of storage.

The model mixtures 10,0 g of liver tissue with 1000,0 μg Chloropyramine hydrochloride and a control samples were used for investigation. They were left deposited at a temperature of 5 ° C - 7, 14, 21 and 28 days. Isolation of Chloropyramine was performed by a modified method of Stas-Otto - with ethanol acidified with acid oxalate. This method is recommended for forensic toxicological analysis of biological material in its decay. Chloroform extracts were purified by extraction of impurities with hexane and TLC-method: stationary phase - plates Sorbfil PSTH-AF-A, the system of organic solvents - ethylacetate – methanol - 25% solution of ammonia hydroxide (85:10:5), reagent for the detection - Dragendorff reagent (sensitivity of reagent -1-3 μg in the samples); $R_{f\,\text{Chloropyramine}}$ = 0,60-0,63.

Quantitative determination of Chloropyramine was performed UV spectrophotometry after TLC purification. Optical density values were measured on an SF-46, cell thickness 10 mm; $\lambda_{max}$ 312 ± 2 nm, reference solution – extract from control sample. Isolation of Chloropyramine with ethanol acidified with acid oxalate from biological material to determine – 35,2 ± 4,5 % of the substance.

Research term storage of Chloropyramine for 7, 14, 21 and 28 days was performed by the developed technique. It was established that after 21 days of storage of the substance in the decay of the corpse in the liver can detect 13,8% Chloropyramine; after 28 days storage discover Chloropyramine impossible.

# USE OF TEST "DISSOLUTION" FOR ESTIMATION OF QUANTITY OF ISONIAZID IN MEDICINAL FORMULATIONS

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In the pharmaceutical industry drug dissolution testing is routinely used to provide critical in vitro drug release information for both quality control for example to assess batch-to-batch constancy of solid oral dosage forms such as tablet and drug development.

Tablets taken orally remain one of the most effective means of treatment available. The effectiveness of such dosage forms relies on the drug dissolving in the fluids of the gastrointestinal tract prior to absorption into the systemic circulation. The rate of dissolution of the tablet is therefore crucial.

One of the problems facing the pharmaceutical is to optimize the amount of drug available to the body, its bioavailability. It is a subcategory of absorption and is the fraction of an administered dose of unchanged drug that reaches the systemic circulation, one of the principal pharmacokinetic properties of drugs. Inadequacies in bioavailability can mean that the treatment is ineffective and a worst potentially dangerous.

It is known, that even nowadays tuberculosis is still widely spread, but is a treatable and curable disease. Active, drug-sensitive disease is treated with a standard six-month course of four antimicrobial drugs that are provided with information, supervision and support to the patient by a health worker or trained volunteer. The vast majority of cases can be cured when medicines are provided and taken properly. Medicinal preparations are divided into basic remedies (isoniazid, rifampicin, pyrazinamide and ethambutol) and reserve remedies. For our researches, we have chosen substance from the basic remedies –isoniazid.

Our researches are devoted for comparison of generic preparations containing isoniazid on the base of test "Dissolution". Investigations were carried out according to the demands of the State Pharmacopoeia of Ukraine, test "Dissolution", using Pharma Test–DT 70 and spectrophotometer "Evolution 60S". For researches were taken isoniazid tablets 0.3 of two Ukrainian trademarks Lugal and Darnitsa.

Calculations of the quantitative content of isoniazid were carried out by UV-spectrophotometry by the method of standard.

As it has been stated, in 45 min isoniazid contents is not less than 90% of the nominal one. Test "Dissolution" can be used for comparison of quality for generic isoniazid-containing medicinal formulations.

# COMPARATIVE CHARACTERISTIC OF QUANTIFICATION METHODS FOR PYRAZINAMIDE IN TABLETS USING SPECTROPHOTOMETRY

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As it is known, tuberculosis represents a chronic infectious disease, which remains the most large-scale problem not only from medical, but also from social viewpoint for the present day, too. Annually, owing to tuberculosis about 3 million people dies all over the world and approximately 8 million events of first registered tuberculosis are observed every year. That is why constant research, which is aimed on improvement of the known methods of analysis for antituberculosis compounds either in pure condition or in medicinal formulations, is still a current task of pharmaceutical and medical care. So, medicinal preparations are divided into basic remedies (isoniazid, rifampicin, pyrazinamide and ethambutol) and reserve remedies (cycloserine, kanamycin, ethionamide, etc.). For our researches, we have chosen substance from the basic remedies – pyrazinamide.

The aim of our research is to carry out quantitative estimation of pyrazinamide contents in tablets of various trademarks using various techniques for quantitative determination by UV-spectrophotometry method; and on the base of the data obtained to make conclusion about quality of medications and possibilities of the tested techniques in quantification of substance.

Researches were carried out on spectrophotometer “Evolution 60S”; into quantification were put calculations by the method of standards, calculations by the graph and calculations using specific absorbance. For investigations were taken tablets of pyrazinamide 0.5 of two Ukrainian trademarks –“Borshchahivskiy chemical pharmaceutical plant” and Darnitsa.

As it has been stated in the result of our researches, the most preferable technique for quantification of pyrazinamide in the composition of tablets by UV-spectrophotometry is the method of standards; both trademarks’ remedies are of appropriate pharmacopoeial quality.

# THE REACTIVITY OF 6,9-DICHLORACRIDINES DERIVATED

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Substituents of 9-chloracridine are widely used as starting substances for obtaining various biologically active 9-amino-, 9-alkylamino-, 9-arylamino-, 9-hydrazineacridines; markers in genetic engineering; luminescent indicators in analytical chemistry.

The aim of the research is to study of reactivity of substituted 6,9-dichloracridines because the reactivity of compounds of this homologous series has not been investigated in details.

The constants of ionization $pK_{BH}^{+}$ of substituted 6,9-dichloracridines have been determined in the mixed ethanol-water solvent (50 mole percent of ethanol) at the temperature of $25^0$C by the method of potentiometric titration. It has been shown that these compounds are weak bases ($pK_{BH}^{+}$ of the corresponding associated acids is in the range of 3.71-3.95). It has been proven that their basicity depends upon the nature and position of substituents in the heterocycle. Introduction of 9-chlorine substituent to the molecule of acridine leads to significant weakening of basic properties ($pK_{sub}^{+}$ = 0.82) due to decrease of electron density on the atom of nitrogen (reactive centre). The appearance of 9-chloracridine of chlorine atoms in the molecule in 2-, 4-positions also decreases basicity of the heterocycle, but approximately 6.5 times less ($pK_{sub}^{+}$ = 0.13 (2-Cl), $pK_{sub}^{+}$= 0.14 (4-Cl)). On the contrary, the donor substituents increase basicity. The quantitative assessment of the substituents influence has been performed within the principle of available energy linearity according to the Hammet equation by the correlation analysis method. The equation obtained, which includes $pK_{BH}^{+}$ of all experimental compounds, proved to be statistically uncertain. On the plot of $pK_{BH}^{+}$- f(σ) dependence, the value of $pK_{BH}^{+}$ for 4-methoxy substituent is supposed to be out of the linear dependence. Elimination from correlation of $pK_{BH}^{+}$ for 4-methoxy substituted 6,9-dichloracridine allowed to obtain the correlation equation of $pK_{BH}^{+}$- f(σ) relationship with reliable statistic characteristics. This equation allows to predict reactivity of other members of this homologous series. The low value of the reaction constant is ρ = 0.86 and testifies a slight sensitivity of the reactive centre (heterocyclic atom of nitrogen) to the influence of substituents in the molecule of substituted 6,9-dichloracridine. It is notable that the reactive constants ρ for 6,9-dichloracridines, 5-nitro-9-chloracridines within the limits of experimental error coincide, and it indicates the single mechanism of the electronic influence of substituents on the reactive centre.

# DETERMINING FERUM IN RAW MATERIALS AND READY MADE FOODS

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Ferum(Fe), as a microelement, is present in the organisms of all plants and animals. The main biological function of Ferum is participation in transportation of oxygen and oxidizing processes.

Human daily need for Ferum makes up 10-30 mg. This dosage is supplied with the daily food regimen owing to animal and vegetable products. Major sources of Ferum are grains, liver and meat.

People with the excess of Ferum suffer physical weakness, lose weight, are ill more often. At the same time to get rid of the excess of Ferum is much more difficult than to fill up its deficit. The toxical dosage for a human being is 200 mg, and lethal makes up 7-35 g.

Because of shortage of Ferum in the organism Ferum deficient anaemia (ischemia) develops. Fatigue is the first symptom of Ferum deficiency and anaemia caused with it.

The aim of this work was to determine the presence of Ferum in vegetables, fruit and juices.

During the preparatory stage the most often used techniques of determining Ferum with chemical (gravimetry, redox reaction) and physical-chemical methods (photocolorimetry, potencymetric redox reaction) have been studied.

The preference has been given to the method of photocolorimetry with the use of graduated diagram . The advantages of this method are high sensitivity, accuracy and speed.

Photometric determining of Ferum means that dyad ions of iron interacting with 1,10-orthophenanthroline make up an orange-red complex. Previously the whole of Ferum in the sample has been reduced to Fe(II) with hydroxylamine hydrochloride. The on-stream length of the wave is 490 nm.

The main stages of the conduction of the experiment:

- preparation of original standard and booster solutions;
- the choice of on-stream length of the complex under investigation;
- preparation of a range of standard solutions, measuring their absorbance with the help of photocolorimeter CPhC – 2MP, creating a graduated diagram;

- preparation of probes of the samples under investigation and determining the presence of Ferum(II) in vegetables, fruit and juices.

The results of determining Ferum(II), received while photometric examination of food products of vegetative origin are as the following:

| Food product | The presence of Ferum(II) mg/100mg |
|---|---|
| potato | 1,30 |
| carrot | 0,83 |
| kiwi-fruit | 0,63 |
| honey | 0,52 |
| tomato | 0,48 |
| apricot | 0,47 |

| Food product | The presence of Ferum(II) mg/100mg |
|---|---|
| orange | 0,33 |
| lemon | 0,31 |
| apple | 0,21 |
| raspberry | 0,18 |
| apple juice | 0,10 |
| apple-grapes juice | 0,12 |

It should be reminded that Ferum assimilation from the food products makes up about 10%.

So, according to the results of the conducted investigation, the following conclusions can be made:

1) The technique of photocolormetric determining of Ferum with 1,10-orthophenanthroline in the foods of vegetative origin is not difficult to perform in the laboratory conditions and can be used for laboratory practice and for further going investigations.
2) The disadvantage of this very determination is long lasting preparation of probes of the samples under investigation(vegetables and fruit). To get some transparent juice it's necessary to get it filtered for many times. Moreover, if red or dark coloured juices are to be analyzed it's necessary to get them decolourized (to work them up with the solution of hydroxylamine hydrochloride and boil on a waterbath).

In future it is planned to go on the investigation connected with the seasonal differences of Ferum maintenance in vegetative food products.

# METHOD DEVELOPMENT ALLOCATION OF URINE TRAMADOL

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Tramadol (tramadol gidrohlorid, Melanate, Limadol, Tradonal Retard, Tramal, Tramundin Retard, Ultram, Zydol, Biovail, Crispin) - RR, SS-trans-2-[(dimethylamino) methyl] -1- (m-methoxyphenyl) cyclohexanol gidrohlorid.

Tramadol is inferior to the activity of morphine, but virtually no therapeutic doses depresses respiration. In the case of long-term use may develop drug dependence. Excreted urine excreted within 3 days, about 90% of the dose, including about 30% - unchanged, metabolites are excreted as conjugates.

The aim of this work was the development of detection techniques of tramadol and its metabolites in urine.

To 10 ml of urine was added to 1 ml of aqueous solutions tramadol containing 100, 200, 500 and 1000 mg of the drug, leaving a day with periodic stirring. In parallel, put "idle" experiment. A day model mixture was acidified with 0.1 M hydrochloric acid to pH 2 - 3 and extracted three times with new portions of diethyl ether 5 ml. Essential layers rejected. Aqueous layers basified 50% sodium hydroxide natrium solution to pH 10 - 11 and extracted three times with new portions of 10 mL of chloroform. The resulting chloroform extract was filtered through a paper filter with anhydrous sodium natrium sulfate (0.5 g). Identification tramadol and his major metabolites in the urine we conducted one is the most affordable methods chemical - toxicological analyza- by tonkosloynoy chromatoghrafy. Assay preparation was performed specially designed extraction-photometric, ionometrychnoyu methods.

| № | Of the drug, mcg | Highlight drug mcg | Highlight drug,% | Metrological specifications |
|---|---|---|---|---|
| 1 | 1000,00 | 675,00 | 67,50 | $\overline{X} = 64{,}60$ |
| 2 | 500,00 | 290,00 | 60,00 | $S = 4{,}77$ |
| 3 | 200,00 | 106,00 | 63,00 | $S_{\overline{X}} = 2{,}13$ |
| 4 | 100,00 | 65,50 | 65,50 | $\Delta\overline{X} = \pm 5{,}90$ |
| 5 | 100,00 | 67,00 | 67,00 | $\varepsilon = \pm 9{,}16$ |

The table shows that the method can provide 60,00-67,50% of tramadol urine. In parallel, to identify the most effective method of isolation of tramadol in urine were tested following extractant 4: 1-chloroform (60,16 ± 0,48); 2-mixture of solvents chloroform-n-butanol (9: 1) (80,06 ± 0,65); 3- mixture solvent of chloroform - isopropanol (9: 1) (84,53 ± 0,50); 4- solvent mixture of diethylether - etilatsetat (1: 1) (39,30 ± 0,44). The most effective solvent mixture is 2 and 3, which allows to allocate 84% of the tramadol.

# THE STUDY OF PHYSICAL AND CHEMICAL INTERACTIONS OF FOOD DYES WITH MEDICINAL SUBSTANCES

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Every manufacturer wants to attract the largest number of consumers to his product in an evolving competitive environment. A lot of attention is paid to the improving of consumption properties and the visual appeal of the goods along with the safe, effective, and high quality drugs. To achieve the similar purpose for the pharmaceutical market is possible by applying of various excipients, such as dyes, aromatic and flavoring additives etc. Food dyes is the one of the widely used groups of excipients in food and pharmaceutical industries. It is believed, that food dyes enter to the body in quite small quantities, but their interaction with each other and with different groups of substances has not been sufficiently studied. Over the past decade the number of allergies and other adverse reactions to the synthetic substances, entering into blood, has significantly increased. Food colors are poorly absorbed from the gastrointestinal tract, but getting into the blood, can bind to proteins and in this way become full antigens.

We have studied the chemical structures of synthetic food azo dyes and suggested, that they may react with organic amines, their salts and quaternary ammonium compounds to form ion associates. A series of experiments was carried out and proved, that the food azo dye carmoisine can form ion associates with some organic amines and such medicinal substances as lidocaine hydrochloride, chlorpheniramine maleate, and myramistin. Physical and chemical properties of formed ion associates are differ from the original dyes; in particular, they are soluble in organic solvents (chloroform, butanol, ethyl acetate etc.) and some fatty oils (peach oil). This fact suggests that the dye in composition of associates can directly absorbed from the gastrointestinal tract in the form of oil solutions or emulsions.

Also, we have studied the properties of formed ion associates - the partition coefficients for different solvents, the stoichiometric ratio of the components in ion associates, the dependence of the extraction of associates from the pH of the aqueous solution, extraction time, the effect of salting-out agents to be complete extraction.

Methods for identification and quantitative determination of carmoisine and tartrazine, contained in medicines, were developed on the basis of the obtained results. It is also planned the development of control methods of completeness cleaning the process equipment after using this group of dyes in the drugs and food production.

# SYNTHESIS AND STUDY OF METRONIDAZOLE COMPLEXES WITH $Fe^{2+}$ AND $Fe^{3+}$ SALTS

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Interaction of drugs with each other, with food and drinks is an important aspect of pharmacotherapy of diseases that physicians should consider in the case of simultaneous prescription of two or more drugs since it's not always possible to predict the nature of its consequences. Thus, obtaining products of drug interaction, together with a further study of their effects on the human organism, is promising as it will provide us with an opportunity to experimentally prove the expediency or impermissibility of concurrent medication use.

The aim of our paper was to synthesize metronidazole (MTZ) complexes as a ligand with divalent and trivalent iron salts and the study of the obtained compounds.

MTZ represents 5-nitroimidazoles containing two conjugated nitrogen atoms, which, due to non-bonding electron pairs, can enter into the donor-acceptor bond with metal cations containing free orbitals, such as $Fe^{2+}$ and $Fe^{3+}$ cations, and are also capable of complexation.

The MTZ complexes with $Fe^{2+}$ (MTZ-$Fe^{2+}$) and $Fe^{3+}$ (MTZ-$Fe^{3+}$) salts were obtained by boiling in methanol for several hours. For the synthesis of the MTZ-$Fe^{2+}$ complex, ligand and iron (II) sulphate salt were taken at a ratio of 2:1, and in order to synthesize the MTZ-$Fe^{3+}$ complex, the samples of MTZ and iron (III) chloride were at a ratio of 3:1 respectively. The obtained substances have the form of crystals of orange (MTZ-$Fe^{3+}$) and brown (MTZ-$Fe^{2+}$) color.

The melting point of MTZ-$Fe^{2+}$ is 156-158 °C whereas that of MTZ-$Fe^{3+}$ is 160 °C.

The research into the spectrum nature of the obtained compounds relative to the original substance of MTZ was performed by absorption spectrophotometry in the ultraviolet light in the wavelength range from 230 nm to 350 nm. 0.001% aqueous solutions of these substances and MTZ reference solution were prepared for this study.

The nature of complex compounds spectra correspond to the reference solution spectra, with the absorption maxima observed at the wavelength of 320 nm. In contrast to the pure substance spectrum for both complexes there is a significant hypochromic effect.

In the course of the experiment the chemical interaction of MTZ with $Fe^{2+}$ and $Fe^{3+}$ cations was confirmed, with its products isolated. We have also planned to continue working towards establishing the composition of the synthesized compounds and confirming their structure.

# DEVELOPMENT AND VALIDATION OF METHODS OF QUANTITATIVE DETERMINATION OF LISINOPRIL DURING THE "DISSOLUTION" TEST IN TABLETS

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The "Dissolution" test is one of the major pharmaceutical and technological tests used for formulating and analyzing medications (drugs) of solid dosage forms. The "Dissolution" test is intended to determine the amount of the drug, which shall release from solid dosage form into the dissolution medium during the certain period of time under the conditions specified in the normative documents of quality control. In accordance with the requirements of the State Pharmacopoeia of Ukraine (SPU) the methods for quantification of drugs, which are introduced into the methods of quality control of drugs, shall be validated. The main objective of validation of analytical methods is experimental evidence that this technique is suitable to achieve the purposes for which it was intended.

The aim is to develop the conditions of the "Dissolution" test and also development and validation of methods of quantitative determination of lisinopril during the "Dissolution" test in drugs in tablet form (10 mg of active ingredient in one tablet).

Methods of study. The degree of release of lisinopril tablets during the "Dissolution" test is proposed to control in accordance with the requirements of SPU, general article 2.9.3. Dissolution under the following conditions: device with a paddle (rotation speed – 50 rev/min); dissolution medium – 0.1 M solution of hydrochloric acid (900 ml); dissolution time - 30 minutes.

Results. Quantitative determination of lisinopril, which passed into the dissolution medium, should be carried out through liquid chromatography (SPU, 2.2.29) with the use of chromatographic column of octadecyl silica gel (XTerra RP8 size (250x4.6) mm with a particle size of 5 microns), column temperature – 40 °C, detection at a wavelength of 215 nm. As a mobile phase the following mixture is optimal to use: solution of 1.0 g of sodium hexanesulphonate in 820 ml of buffer solution pH 2.0 with 180 ml of acetonitrile at a speed of 1.0 ml/min. Chromatography time for one sample is 10 minutes, retention time of lisinopril peak is about 7.3 minutes. Rationing by "Dissolution" is set according to the SPU requirements 1.2, p. 139, 2.9.3.-1 – Q = 80%.

Proof of applicability of chromatographic determination conditions is provided by introduction of the "Test on chromatographic system applicability" into the technique. To dissolve the standard lisinopril sample, such conditions of applicability chromatographic system for lisinopril peak are used: efficiency of the

chromatographic column must be not less than 2000 theoretical plates; relative standard deviation (RSD) must comply with SPU requirements 2.2.46; symmetry factor of the peak should not exceed 2.5.

The specificity of chromatographic methods has been proven by the following: the retention time of lisinopril peak in the chromatogram of the test solution coincides with the retention time of the corresponding peak in the chromatogram of the blank solution accurate to ±2%; there are no peaks with the retention time in the chromatogram of the placebo solution, which coincides with the retention time of lisinopril peak in the chromatograms of the blank solution and test solution, i.e., placebo components do not hinder quantity determination of lisinopril; the degree of lisinopril peak division into the closest peaks meets the applicability of the chromatographic system.

According to the SPU requirements, article 2.2.N.2 "Validation of analytical methods and tests" the range of application of the proposed technique can be at least 25% of the standard (Q = 80%) value of dissolution, we have selected a range of 50-130%. As a result of analysis of model compounds and their statistical treatment it was found that the method of analysis is characterized by sufficient convergence. The found value of the relative confidence interval (0.22%) is less than the critical value for the convergence of the results (3.0%). The technique is characterized by sufficient accuracy, as the criterion of insignificance of the technique bias error is performed. Technique bias error equals to 0.16% and meets the requirements of the practical insignificance in the whole concentration range from 50% to 130%. Calculation of parameters of the linear relations is made using the least-square method and the following regression equation is obtained: Lock Y = 0.99927 + 0.18822 • X. The high correlation coefficient (r = 1.0000) satisfies the requirements of acceptability (r = 0.9984) and confirms the linear relations between the accepted ("true") and found amount of lisinopril in the range from 50% to 130% from the nominal value. To confirm the accuracy of the technique when reproducing in other laboratories, the calculation of total indeterminacy of the technique is made. The expected total indeterminacy of the analysis (ΔAs,%) is 1.20%, which does not exceed the maximum permissible indeterminacy of analysis 3.0%, i.e. the technique will give the correct results in other laboratories in terms of "Dissolution".

Conclusions. The method of quantitative determination of lisinopril during the "Dissolution" test in drugs in tablet form using liquid chromatography method that can be introduced into methods of quality control for drugs is developed. The conducted validation studies confirm specificity, linearity, precision (convergence), accuracy, intralaboratory precision and the range of application of the proposed technique. The technique may be proposed further on for the quantitative determination of lisinopril during the studies on the kinetics of «in vitro» release in the pH range 1.2-6.8.

# DEVELOPMENT AND VALIDATION OF THE HPLC-PROCEDURES OF DOXYLAMINE DETERMINATION IN BLOOD IN THE VARIANT OF THE METHOD OF STANDARD

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The purpose of the paper is developing the set of HPLC-procedures of doxylamine quantitative determination in blood using different variants of sample preparation, carrying out validation of the offered methods for choosing the optimal procedure of sample preparation provided effective doxylamine isolation from blood and low content of co-extracted substances in the obtained extracts at the minimum value of the method uncertainty, and also estimating the possibility of the method of standard application for doxylamine HPLC-determination in blood.

The HPLC-method for doxylamine determination using the system of HPLC-analyzer «Милихром А-02» was developed previously – the retention time of doxylamine was 11.85 min. We have suggested to carry out doxylamine isolation from blood using amphiphylic solvents with subsequent separation of organic layer under the conditions of aqueous phase saturation by electrolyte; this approach enjoys wide popularity in modern forensic and toxicological analysis. Such amphiphylic solvents as isopropanol, acetonitrile and methanol have been used in the experiment; ammonium sulphate has been applied as electrolyte for saturation of aqueous phase.

Isolation has been carried out in the alkaline (pH = 11) and weak-acid medium (pH = 5); carrying out isolation of analytes from biological objects in the weak-acid medium results in decreasing of co-extraction processes of biological matrix components in a number of cases. It is necessary to note that application of amphiphylic solvents and saturated solution of ammonium sulfate allows to maintain the isolation efficiency of substances of base character in the weak-acid medium at the same level as in the alkaline medium – it is conditioned by shift of pH real value in alkaline side for mixtures of electrolytes saturated solutions with amphiphylic solvents.

For choosing the optimal method of doxylamine determination in blood we have carried out validation of all developed procedures by such parameters as specificity, recovery, linearity, accuracy, repeatability and intermediate precision in the variant of the method of standard.

The methods validation has been carried out at the first stage using model solutions. The total results of this stage allow to point to the conclusion about acceptable linearity, accuracy and repeatability of the HPLC-procedure of doxylamine quantitative determination in the variant of the method of standard that

gives the possibility to recommend it to further application in forensic toxicology with the purpose of development of the methods of biological objects analysis for doxylamine quantification.

At the second stage the methods validation has been carried out using model samples.

For specificity investigation for the developed procedures as for the components of biological matrix we have determined the sum of peaks areas on the chromatograms of blank-samples within $11^{th}$ and $12^{th}$ minutes – $S^{\Sigma blank}_{t_R \pm 0,5 \min}$.

The maximum peak area for doxylamine is observed in the case of detection at the wave length of 210 nm, but at the same wave length the sum of peaks areas is maximum on the chromatograms of blank-samples. At the same time the less intensive doxylamine peak at $\lambda$ = 260 nm (this wave length is the nearest to characteristic line of doxylamine in UV-range of spectrum) is accompanied by the absence of peaks with the retention time, which is coincident with (or near to) the doxylamine retention time, on the chromatograms of blank-samples for all variants of procedures of analyte isolation from blood that points to the conclusion about acceptable specificity of the developed methods as for the components of biological matrix when using 260 nm as a working wave length.

The absence of peaks with the retention time, which is coincident with (or near to) the doxylamine retention time, on the chromatograms of blank-solutions for all wave lengths used for detection in the described HPLC-system is the evidence of the correct choice of sample preparation procedure for all considered cases.

It is necessary to note that in all cases carrying out doxylamine isolation from blood at pH = 5 provides lower sum of peaks areas on the chromatograms of blank-samples than in the case of alkaline pH using; at the same time by the results of recovery study small decreasing of doxylamine isolation efficiency from blood – within 3 – 5% – is noted under these conditions. The procedures with acetonitrile application are characterized by the best extraction efficiency.

The reproducibility of recovery values satisfies the acceptability criteria for all variants of methods.

Taking into account the data about specificity of the developed procedures the investigations of linearity, accuracy and precision have been carried out only for the set of procedures with application of the weak-acid medium for doxylamine isolation from blood.

All examined methods are characterized by the acceptable parameters of linearity, accuracy and precision, but high efficiency of doxylamine extraction from blood and low value of the method uncertainty allow to consider the method with acetonitrile application in the weak-acid medium as optimal for sample preparation of blood to further HPLC-determination of doxylamine.

# DEVELOPMENT OF METHODS OF QUANTITATIVE DETERMINATION OF HYDROCHLOROTHIAZIDE IN COMBINED PHARMACEUTICAL PRODUCTS CONTAINING ANGIOTENSIN CONVERTING ENZYME INHIBITOR RAMIPRIL

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The aim of our study was experimental confirmation of the possibility of using the methods of quantitative determination of hydrochlorothiazide in tablets using the method of absorption spectrophotometry in the ultraviolet and visible regions of the spectrum in the combined drug products containing thiazide diuretic gidrohlortiazid and inhibitor of angiotensin-converting enzyme (IACE) ramipril. The spectrophotometric method of determination of hydrochlorothiazide is contained in the monograph “Gidrohlortiazid tablets” and included in the II edition of the State Pharmacopoeia of Ukraine (SPU). To use the methods in the presence of other active pharmaceutical ingredients (API), we studied the effect of ramipril and excipients on the quantification of hydrochlorothiazide.

Objects of research: tablets "Ramizes com" series 10315, standard samples of hydrochlorothiazide and ramipril. Research methods: absorption spectrophotometry in the ultraviolet and visible ranges. Analytical equipment: spectrophotometer “Evolution 60S”, analytical balance “Axis” model 200 ANG, measuring utensils, class A, reagents and auxiliary substances that meet the requirements of SPU.

The method of preparation of the investigated solutions.To accurate sample of powdered tablets, equivalent to 50 mg of hydrochlorothiazide, or to precise linkage of standard samples, add 10 ml of 0.1 M solution of sodium hydroxide, shaken for 20 min, the volume was adjusted solution with water to 100.0 ml, stirred and filtered. 2.0 ml of the resulting solution was adjusted with 0.01 M solution of sodium hydroxide to volume of 100.0 ml. Optical density of the resulting solutions was measured at a wavelength of 273 nm, compensation solution is 0.01 M solution of sodium hydroxide.

When recording the UV spectra of the solutions of a model mixture, extraction from tablets and standard samples of hydrochlorothiazide and ramipril in the region from 220 nm to 350 nm is established that the maximum absorption of hydrochlorothiazide is observed at a wavelength of 273 nm. At this wavelength, ramipril practically does not absorb.

Our studies show that in combined dosage forms which contain ramipril, hydrochlorothiazide, can be quantified by spectrophotometry at a wavelength of 273 nm. It is established that neither ramipril nor excipients do not interfere with the course of the analysis.

# THE MOST IMPORTANT TRENDS IN MODERN ANALYTICAL CHEMISTRY DEVELOPMENT

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Nowadays specialists assert that modern analytical chemistry has its roots in physics, biology, in information of theory, in electronics and many others branches of science and technology. Except chemical methods more often physical, biochemical methods are applied. About 40 years ago was born the term “analytics” that often is used in the titles of periodicals, scientific conferences and other.

The purpose of our work was to pick up trends in modern analytical chemistry development on the importance of these trends attract their attention the recognized scientists in this branch according to different estimates more than 10-15 important trends are numbered.

Now more and more analytical analyses are done out-of a laboratory. It is a mobile laboratory, analysis at home, in a hospital ward, on board at a ship, in field conditions and others.The development of analytical non-destructive methods of analyses is being continued. It is mainly by X-ray methods, neutron activation analysis, electron paramagnetic resonance, Mossbauer spectroscopy.

For automation of analytical identification, x-ray fluorescence, atomic emission spectrometers, continuous flow analysis are often used.

The tendency creation small (portable) analytical devices and miniaturization analysis in general is been observed.

Origins of the most analytical spectral methods or gas sensors are in physics; biosensors were created on the base of biochemistry and molecular biology. Pattern recognition. Nowadays such identification we can do with modern devices “electronic nose”, “electronic tongue”.

Hybridization of methods and devices takes place (injection analysis, analytical chromatography, capillary electrophoresis).

Importance of methods is changed. From 2010 most of the publications are about chromatography-mass spectrometry. Recently increase requirements to analytic because you have to master besides chemical methods physical, biochemical and other methods. Changes in analytical community take place too. Tools for remote analysis and control are developed and increased.

Conclusions. Analytical chemistry is the branch which has dynamic development, its potential increases quickly. It is one of the fundamental disciplines for preparation specialist of pharmacy.

# IONOMETRIC ANALYSIS OF VITAMIN B1 IN SOLUTIONS FOR INJECTION USING THE THIAMINE-SELECTIVE SOLID CONTACT ELECTRODE

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The most well-known methods for the quantitative determination of vitamin B1 (thiamine bromide) described in the literature include spectrophotometry, fluorometry, photocolorimetry; alkalimetric titration is also widely used in pharmaceutical analysis. These methods are time-consuming, less sensitive. For that reason, it was necessary to develop a sensitive express method for the determination of thiamine bromide in solutions for injection. Ionometry is the most promising method for such analysis.

Thiamine-selective solid contact electrode for the potentiometric determination of thiamine bromide in solutions for injection, which is a thick-walled polyvinyl chloride tube with graphite rod as a current collector pressed in it, has been developed. The membrane composition is applied on the ground edge of graphite rod. The membrane composition (wt%) is: 26 ± 4 of polyvinyl chloride, 50 ± 5 of dibutyl phthalate, 17 ± 3 of thiamine tetraphenylborate, 4 ± 1 of activated charcoal.

The linear range of the electrode function is 1·10-1 – 1·10-5 mole/dm3, the slope of the electrode function is 53 ± 2 mV. The detection limit is 3·10–5 mole/dm3. The response time of electrodes is 20 - 30 seconds, the reproducibility of the potential is 2 mV. The drift for the potential of the proposed electrode for a week does not exceed 3-5 mV, endurance is not less than 3-5 months.

Ionometric analysis of thiamine bromide in solutions for injection with concentration of 3% and 6% has been developed. Our specially designed thiamine-selective solid contact electrode was used as an indicator; the EVL-1 M3 silver-chloride electrode was used for comparison. EMF measurement was carried out on the I-130 ionomer. The analysis was performed by two-point narrow range calibration curve.

The results of obtained ionometric analysis of thiamine bromide in solutions for injection are characterized by precision and reproducibility. The proposed method of analysis is characterized by simplicity and rapidity. Relative error of the analysis is not more than 2%, which complies normative-technical documentation for dosage forms.

# THE REACTIVITY OF N-[(2-OXOINDOLIN-3-YLIDENE)-2- OXIACETYL] AMINO ACIDS

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N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl] amino acids and their derivatives possess various types of biological activity, that is why, this class of compounds is intensively used for purposeful search of active pharmacophores. Pharmacological activity depends on the pharmacophore capacity of forming complexes with biological receptors which, in turn, is determined by the pharmacophore reactive ability, particularly, its acid-base properties. Therefore, the investigation of reactive power of the biologically active substances homological series represents undoubting scientific and practical interests which are connected with the strong possibility of optimization of these xenobiotics artificial synthesis and their active pharmacophore abilities modeling improvement.

The compounds ionization constants were determined by potentiometric titration method. The titrant was 0.05 M potassium hydroxide aqueous solution which did not contained $CO_2$. The concentration of the titrated solutions was 0.005 M at the point of neutralization. The measurements were performed by EV-74 ionomer with the usage of two electrodes: a glass (ESP 43-074) indicatory one as well as a saturated chlorine-silver one. The latter was applied as a comparison electrode. The determinations were carried out at $25^0$C in triplicates. The precision of the obtained results was evaluated by small selections mathematic statistics method (confidence probability - 0.95). The mixed solvent dioxane - water (60 volume % of dioxane) was prepared of freshly bi-distilled water free from $CO_2$ and of 1,4-dioxane (very pure) which did not undergo an extra purification.

The experimental compounds were proven to be weak dibasic acids. Their pKa magnitudes were determined by Noyers method. The correlation of these magnitudes to both of the reactive sites (COOH- and OH-groups) was performed. Each $CH_2$-prolongation step of the polymethylene chain length was shown to weaken acidity at both reactive sites ionization. Hammett correlation equations ($pKa_{1,2} - f(\sigma)$) were calculated for N-[(2-oxoindolin-3-ylidene)-2-oxiacetyl] amino acids which allows to predict acid-base properties of these homological series compounds. Low susceptibility of the reactive sites towards polymethylene chain prolongation was established. The obtained results are being used to QSAR-analyze the compounds of these iso-structural series by mathematical modeling.

# RESEARCH OF VALIDATION PARAMETERS OF THE SPECTROPHOTOMETRIC QUANTITATIVE DETERMINATION METHOD OF PARACETAMOL BY SPECIFIC ABSORBANCE

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Paracetamol belongs to the group of non-steroidal anti-inflammatory drugs, it is a nonselective COX inhibitor, and over 50 years it has already been used as an antipyretic and analgesic. Monocomponent formulations based on paracetamol tablets, capsules, solutions, suppositories, suspensions, granules, gel are produced by pharmaceutical industry.

Quantitative determination of paracetamol in the substance according to the monographs of the State Pharmacopoeia of Ukraine (SPhU), European, British pharmacopoeias and Pharmacopoeia of the Republic of Belarus is carried out by the ceriometry method, American, Japan Korea pharmacopoeias by the spectrophotometric method (by standard), China – by specific absorbance. UV-spectrophotometry by standard and specific absorbance methods, HPLC are used for pharmacopoeial quantitative assessment of paracetamol tablets.

The aim of this research is to research of validation parameters of spectrophotometric quantitative determination of paracetamol in tablets by specific absorbance, which is recommended by the British Pharmacopoeia (BPh).

Characteristics and criteria of acceptability of quantitative determination method of paracetamol have been theoretically calculated. The linearity parameter was studied at 9 points. The linear dependence graph was constructed in normalized coordinates. Values of b, sb, a, sa, $RSD_0$ and r comply with the parameters of the linear dependence. In the study of the accuracy of parameter systematic error made $\delta$=2.06%, which meets $\delta \leq 2.30\%$. The study of convergence of the relative confidence interval $\Delta As$=2.60% does not exceed the critical value for of convergence results $\Delta As^{10.0\%}$=3.20%.

The validation characteristics of the spectrophotometric quantitative determination of paracetamol in tablets by specific absorbance according to the British Pharmacopoeia have been evaluated. We have suggested to make such changes at the stage of the sample preparation as "… place the flask in an ultrasonic bath for 30 min…" instead of "…shake for 15 minutes…". The spectrophotometric quantitative determination of paracetamol tablets by specific absorbance is recommended to use for quantitative determination of API in the drug with the permissible limits of ±10.0%.

# MEDICATIONS USED IN DOPING AND METHODS FOR ITS DETERMINATION

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The aim of our study was the review of medications, which were used as doping and determination methods.

Doping – substances of different pharmacological groups, both natural and synthetic origin, used in sport for achieving best results. Such substances could extremely raise activity of nervous and endocrine system and muscular strength for a short time. Nowadays the number of doping drugs varies from 400 to 11004. The usage of such medicines can cause serious side-effects of healthy person and unexpected fatal outcome. Thus, most doping medications were prohibited by World Antidoping Agency (WADA) and Medical Commission of the International Olympic Committee (IOC). But doping drugs were also popular in amateur sport. The list of prohibited medications and doping methods of WADA contents such groups of preparations: stimulants (amphetamine, ephedrine), anabolic steroids (synthetic derivate of testosterone), actoprotector (bromantan), beta-agonists (salbutamol, salmeterol), peptide hormones (erythropoietin, insulin), psychotropic drugs, cannabinoides, narcotic analgetics (morphine, opiate), antiestrogen drugs (clomiphene, cyclophenil), diuretics (furosemide, acetazolamide) and other. Vitamins, antioxidants, antihypoxants, nootropic and adaptogenic were permitted preparations.

For rapid, accurate and effective determination of medicines and its metabolites in blood and urine samples gas (GC), gas-liquid (GLC), liquid (LC), high-performance liquid chromatography (HPLC), isoelectric focusing (IEF), mass-spectrometry (MS), isotope ratio mass spectrometry (IRMS) and combination (LS-MS, HPLC-MS and other) of this methods were used. The most widely applicable were combined methods. A preliminary isolation of substances from biological samples by solid-phase and liquid-phase extraction spends before the analysis. Chromatographic methods allow separating a mixture of substances, and mass spectrometry was used for determination structure of its compounds. Proteins (erythropoietin) can be determined by GC-MS. LC-MS was often used for analysis of diuretic substances, some anabolic steroids and corticosteroids. The analysis should be carried out in the presence of a standard sample. However, chromatographic methods do not allow to distinguish endogenous testosterone between injected from the outside. In such situations isotope ratio mass spectrometry or carbon isotope ratio method used.

# LUMINOL INDICATOR PAPER FOR HYDROGEN PEROXIDE DETECTION

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Luminol (hydrazide 3- aminophthalic acid) in the presence of minimal quality of hydrogen peroxide ($H_2O_2$, HP) shows high brilliance chemiluminescence, moreover this reaction are observed only in case of pH medium is more than 8 (Ponomarenko A.A., 1955). Light intensity could be raised significantly by adding of catalyst, as an example – hemoglobin. Because of high sensitivity of this reaction to HP it was possible to use it for the opening trace of HP in biological objects.

For the manufacture of luminol indicator paper 0,5% solution of luminol in 0,05 mol/L of aqueous sodium hydroxide was applied to the chromatographic paper by either wet-out process or by spray. By the same way hemoglobin solution with additive of disodium EDTA and trisodium phosphate in 0,05 mol/L of aqueous sodium hydroxide was applied. After that the paper was dried at the temperature approximately 40°C in a baker. For the HP detection the drop of investigated solution was applied. Because of that the bright blue chemiluminescence was observed. But such paper shows the less chemiluminescence in time that has been observed, which for real is enhanced by additive applying of drop of sodium hydroxide solution. Because of the damaging effect of the sodium hydroxide to the paper which has been made by abovementioned technology, subsequently, for the removing of hydroxide solution after the luminol had been apply the paper was placed in exsiccator which contained formic acid. After that the paper was removed and dried as usual.

For the HP by luminol indicator paper, produced by abovementioned technology, the next solutions was applied on a strip of paper: drop of the sample of HP and drop of sodium hydroxide solution. Very bright luminescence has been observed only after the sodium hydroxide solution had been added.

Prepared luminol paper during the storage for 1 year in different storage conditions didn't change their properties. During the test has been proved that HP in 0,0005-30% solutions might be detected by luminol paper. In this case peroxide's solutions with a concentration from 30 till 0,005% show the bright chemiluminescence after being applied to the luminol paper. At a 0,0005 % concentration of HP the faint, but absolutely clear luminescence was observed.

Thus, using the luminol indicator paper the HP in drop of solution at a dilution of 1:200 000 might be detected.

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*Research has been conducted under supervision of Prof. M.Ye. Blazheyevskiy

# THE SYNTHESIS AND SPECTROSCOPIC INVESTIGATIONS OF FLUOROQUINOLONES METAL ION COMPLEXES

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Molecules of antibacterial agents of fluoroquinolone's group are produced by chemical synthesis. In the case of drug interactions with antacids or iron preparations fluoroquinolones form metal complexes due to their capacity to bind metal ions. Complex formation occurs in molecules of fluoroquinolones by the carboxyl, ketone group and azoheterocyclyc fragment. Interaction with metal ions has some important consequences for the solubility, pharmacokinetics and bioavailability of fluoroquinolones, and is also involved in the mechanism of action of these bactericidal agents.

Considering the mentioned above information the purpose of this work was the complex compounds synthesis of ciprofloxacin hydrochloride with ferrous sulfate and ferric chloride salts in a medium of 0.1 M sodium hydroxide solution

and a medium of purified water for further study of biological properties of their complexes and determination of the influence of interaction for the effect of antibacterial therapy.

For the complex compounds formation a weighed substance of ciprofloxacin hydrochloride was dissolved in 0.1 M sodium hydroxide solution and then to the solution was added an iron salts in the ratio 2: 1 for ferrous (II) sulfate, and 3:1 - for ferric (III) chloride. The solution was stirred for 10 hours. The same research was performed in a medium of purified water with added 0,1 M NaOH to pH =8.

A further research of obtained complexes was performed by UV absorption - spectrophotometry in a medium of purified water and in 0.1 M solution of hydrochloric acid. The solution was prepared at a 0.0005% concentration. Measurement has been shown that there was no significant difference between the absorption maximum when the antibiotic was given alone and when given with the iron salts, absorption maximum of the complexes was observed at the same wavelength. The absorption maximum of the investigated complex compounds remained unchanged, but there was a significant change of the absorbance intensity of the studied complexes.

The next stage of our work is planned to be determination of the structure of obtained complex compounds, the study of bioavailability and biological activity of those.

# DEVELOPMENT AND VALIDATION OF UV-SPECTROPHOTOMETRIC METHODS OF METRONIDAZOLE QUANTITATIVE DETERMINATION IN URINE

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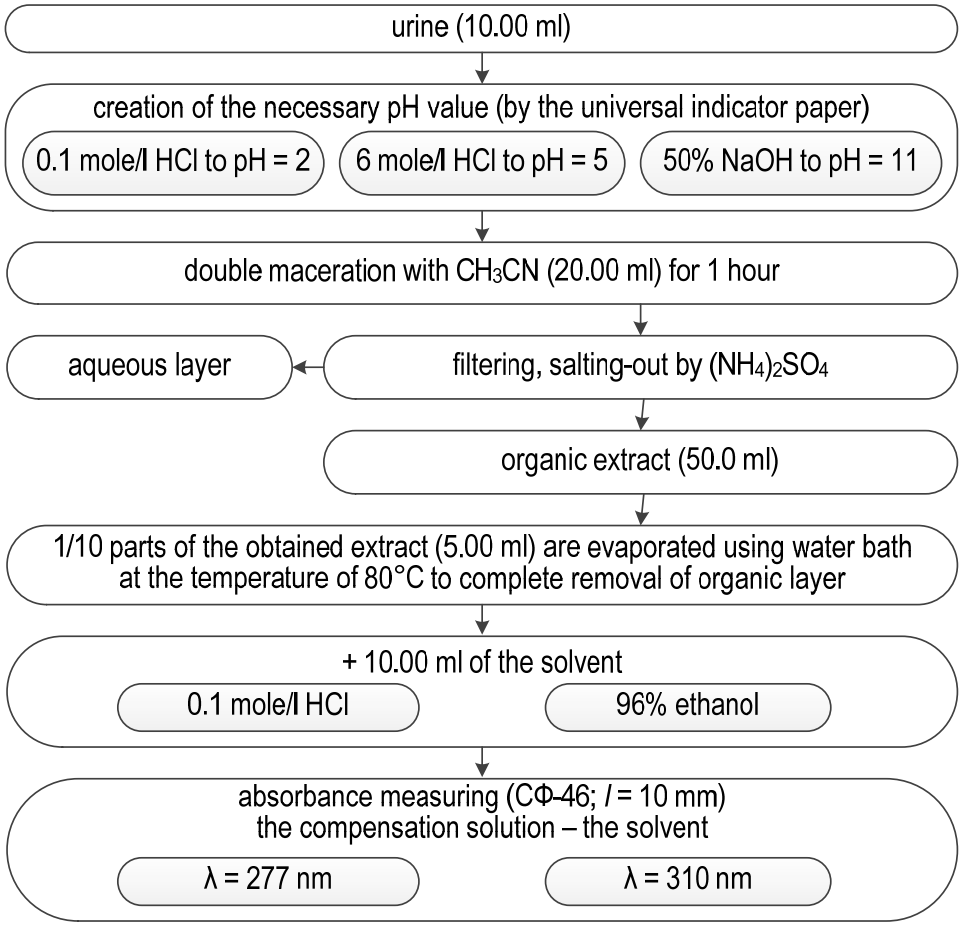
Metronidazole is attributed to the group of antiprotozoal medicines and widely used for treatment of infectious diseases, at the same time it is possessed of quite a number of side effects showed by classic symptoms of acute intoxication, especially when interacting with other medicines and alcohol.

The purpose of this paper is to develop UV-spectrophotometric procedures of metronidazole quantitative determination in urine and to validate the developed procedures using the offered before approaches to the determination procedure and acceptability estimation of specificity, recovery, linearity, accuracy and precision of UV-spectrophotometric methods of analytes quantitative determination in biological liquids applied in forensic and toxicological analysis.

It has been suggested to carry out metronidazole isolation from urine using acetonitrile with subsequent separation of organic layer under the conditions of aqueous phase saturation by ammonium sulphate according to the scheme.



Isolation has been carried out in the acid (pH = 2), weak-acid (pH = 5) and alkaline medium (pH = 11).

The development and validation of procedures of metronidazole quantitative determination was carried out according to the following scheme: application of the normalized coordinates (normalization by the reference solution); the application ranges is 25 – 175%; the number of concentration levels is $g$ = 7 in constant increments of 25%.

The metronidazole concentration in urine corresponding to the point of 100% in the normalized coordinates – 80 mcg/ml – was chosen as the mean metronidazole concentration in urine for acute poisoning.

Validation of the developed procedures by model solutions was carried out earlier and their acceptability for further application in forensic toxicology was shown.

Validation by matrix samples has been carried out by such parameters as «specificity/selectivity», «recovery», «linearity», «accuracy» and «precision».

The results of specificity study show that carrying out metronidazole isolation from urine using acetonitrile provides low contribution of biological matrix components into the absorbance of the sample to be analysed for both variants of the solvents used for analysis, and the lowest value was observed when carrying out the experiment in the weak-acid medium.

It is possible to point to the conclusion about high efficiency of metronidazole isolation from urine under suggested conditions – not less than 90% – by the results of recovery study. The method with acetonitrile application in the weak-acid medium is characterized by the best extraction efficiency.

The values of reproducibility for recovery (≤ 20.00%) and blank-samples absorbance (≤ 6.71%) satisfy the acceptability criteria for all variants of the methods.

All examined methods are characterized by the acceptable parameters of linearity ($RSD_0 \leq 6.01\%$; $R_c \geq 0.9884$), accuracy ($\delta \leq 6.40\%$) and precision (within-run

≤ 14.14%; between-run ≤ 20.00%), and the obtained data are the evidence of application possibility of the developed methods for metronidazole spectrophotometric determination in urine.

We have developed the set of UV-spectrophotometric methods of metronidazole quantitative determination in urine using acetonitrile for analyte isolation from matrix under the conditions of aqueous phase saturation by ammonium sulphate and 0.1 mole/l HCl solution and 96% ethanol as solvents for spectrophotometric measurements. Acetonitrile application in the weak-acid medium (pH = 5) is optimal – contribution of matrix components into the absorbance of the sample to be analysed does not exceed 10%, extraction efficiency is ~95%.

# DEVELOPMENT AND VALIDATION OF THE HPLC-PROCEDURES OF EFAVIRENZ DETERMINATION IN BLOOD IN THE VARIANT OF THE METHOD OF STANDARD

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**Purpose.** To develop the HPLC-procedures of efavirenz quantitative determination in blood and to validate the developed procedures using the approaches to the determination procedure and acceptability estimation of specificity, recovery, linearity, accuracy and precision of methods of analytes quantitative determination in biological liquids applied in forensic and toxicological analysis.

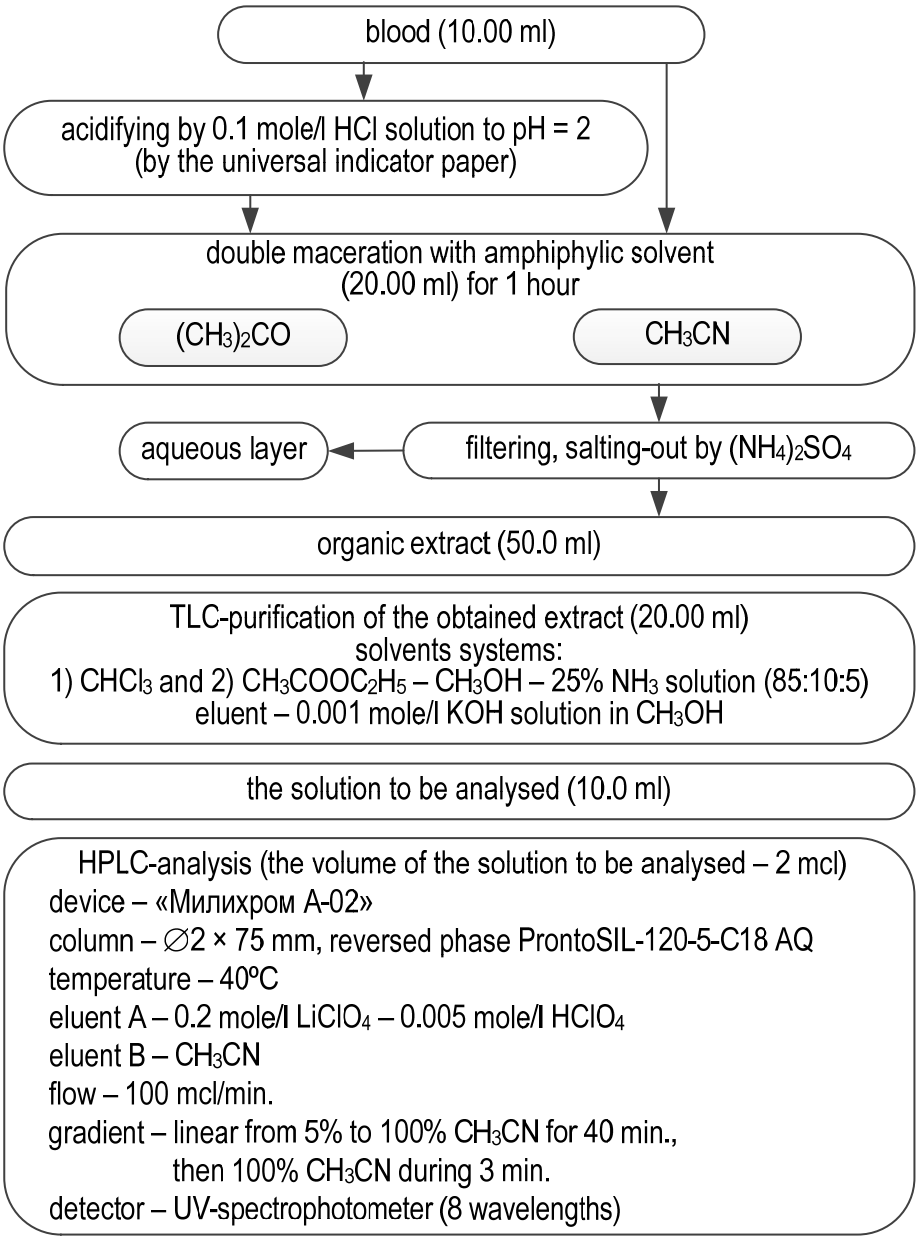
**Materials and methods.** The design of experiment on development of procedures of efavirenz determination in blood by the method of HPLC is presented on the scheme.

**Results.** The set of HPLC-procedures for efavirenz quantitative determination in blood has been developed by its maceration with amphiphylic solvents and subsequent separation of organic layer under the conditions of aqueous phase saturation by electrolyte for increasing the efficiency; this approach enjoys wide popularity in modern forensic and toxicological analysis. Such amphiphylic solvents as acetone and acetonitrile have been used in the experiment; ammonium sulphate has been applied as electrolyte for saturation of aqueous phase. Isolation has been carried out in the acid medium (pH = 2) and without previous blood processing.

For choosing the optimal method of efavirenz determination in blood we have carried out validation of all developed procedures by such parameters as specificity, recovery, linearity, accuracy, repeatability and intermediate precision according to the approaches offered before in the variant of the method of standard.

The methods validation has been carried out at the first stage using model solutions – the results allow to point to the conclusion about acceptable linearity, accuracy and repeatability of the HPLC-procedure of efavirenz quantitative determination in the variant of the method of standard.

At the second stage the methods validation has been carried out using model samples. The results of analysis show the absence of peaks with the retention time, which is coincident with (or near to) the efavirenz retention time, on the chromatograms of blank-samples for all variants of procedures of analyte isolation from blood that points to the conclusion about acceptable specificity of the developed methods as for the components of biological matrix.




By results of the recovery study the best efficiency of efavirenz isolation from blood is noted in the case of the experiment carrying out at pH = 2 and using acetonitrile. The reproducibility of recovery values satisfies the acceptability criteria for all variants of methods.

On the whole, all examined methods are characterized by the acceptable parameters of linearity, accuracy and precision, but high efficiency of efavirenz extraction from blood and low value of the method uncertainty allow to consider the method with acetonitrile application in the acid medium as optimal for sample preparation of blood to further HPLC-determination of efavirenz.

**Conclusions.** Four procedures of efavirenz quantitative determination in blood by the method of HPLC using amphiphylic solvents have been developed. Validation of the developed procedures has been carried out and the possibility of application of the method of standard for determination of efavirenz has been shown.

# THE ASPECTS OF IDENTIFICATION OF SULFANILAMIDE PREPARATIONS WITH THE HELP OF TEST-KITS WITH THE HEAVY METALS SALTS

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In the modern world, the express methods of investigation are getting used more and more often in different spheres of science and everyday life. Relatively simple, cheap methods and means of analysis, called test-kits, are used. Using test kits for quality control is promising and can significantly reduce the time and substances, while maintaining a sufficient level of quality. At present, a test-kit based on $FeCl_3$ has been introduced to the pharmaceutical practice. The development of other test-kits with the salts of heavy metals ($CuSO_4$, $CoCl_2$) is being conducted.

The aim of our work was to check the possibility of using test-kits for identification of sulfanilamide preparations while conducting the pharmaceutical analysis of extemporal medicines (EM). The role of sulfanilamide preparations in medicine is hard to overestimate. Being used in many spheres (ophthalmology, otolaryngology, etc.) even now, in "the era of antibiotics", they haven't lost their value and popularity. While conducting the experiment reagents responding to the requirements of the State Pharmacopoeia of Ukraine, "F" brand filtration paper, proper substances of medical preparations: sulfacylum-natrium, norsulfazolum natrium and aethazolum natrium, have been used. The choice of substances we justified in that sodium salts of sulfonamides give clear analytical colorful effects and do not require the addition of alkali during the reaction with $Cu^{2+}$, $Co^{2+}$, $Fe^{3+}$.

The results of the investigation of sulfanilamide preparations with the test-kits based on the filtration paper, modified $FeCl_3$, $CuSO_4$, $CoCl_2$ have been compared to the results in test-tubes and object plates, and with the results of blank experiments where the substances under investigation have been replaced by purified water.

After the experiments have been conducted it was determined, that the test-kit based on $FeCl_3$ gives an opportunity to identify the presence of sulfanilamides in the substances, however, due to the same analytical effect on the three medical preparations under investigation they can't be distinguished. With the help of the test-kits of modified $CuSO_4$ and $CoCl_2$ chemist analyst can easily distinguish one sulfanilamide from another one: with $CuSO_4$ sulfacilum-natrium provides bluish green colouring, norsulfazolum natrium – dark purple, aethazolum natrium – green; with $CoCl_2$: norsulfazolum natrium provides bluish purple colouring, aethazolum natrium – pinkish white and sulfacilum-natrium doesn't provide a certain analytical effect with the given analytical tool.

Test-kits based on filtration paper with the salts of heavy metals can be used to identify sulfanilamide preparations in aqueous solutions of EM. Test-kits made of copper (II) sulfate are preferable as they help to distinguish different sulfanilamide preparations. Test-kits made of cobalt(II)chloride can be used to identify aethazolum and norsulfazolum natrium, and test-kits made of ferum(III) chloride aren't optimal for identification of the given sulfanilamide preparations.

**ANALYTICAL CHEMISTRY TODAY AND TOMORROW. PITTCON 2012 - 2015**

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In 1949, in Pittsburgh (USA) held a scientific conference, initiated a non-profit Corporation, United Pittsburghese spectroscopic society (SSP) and the Society of analytical chemists of Pittsburgh (SASP). Since 1968, when the number of participants exceeded 5.000 people each year the conference was held in large U.S. cities. However, the title of the conference «PITTCON» remained.

The aim of our study was to analyze the scientometric data conferences «PITTCON» 2012-2015. In programs conference presents all modern methods of analysis. During the conference, an exhibition of the latest analytical instruments. «PITTCON» -2015 will be held March 8-12 in New Orleans.

In 2014, «PITTCON» the number of reports was dominated by chromatographic methods of analysis - 390 (120 chromatography - mass spectrometry). In General, methods of spectroscopy was dedicated 172 report. All types of sensors have been reported in the 140 reports. Electrochemical methods of analysis were presented in 128 reports, mass spectrometry (without chromatography) in 93, capillary electrophoresis 42, chemical analysis 20.

According to the statistics 40-50% of all analytical determinations performed chromatography methods (petrochemical up to 70%). The most commonly used HPLC (83 report), UHPLC (34), HPLC-MS and HPLC-MS/MS (84), hydrophilic (10), ion (30), chiral (16). 90 papers presented at various gas chromatography.

Among spectroscopic and related techniques – Raman spectroscopy - 50 reports, infrared spectroscopy (45), fluorescence (30), UV-visible spectroscopy (16), inductively coupled plasma (12), atomic absorption-NMR (9) and other.

Proposed and investigated many of the newest sensors - electrochemical, chemical and biosensors, sensors based ionic liquids, microfluidic, other.

Many of the scientific sessions at the conference took place from pharmacy (158), biochemistry and medicine (152), food analysis (94), environmental control (92), industrial analyses (214), clinical methods of analysis (70) and other.

Among the new scientific sessions select nanotechnology, nanomaterial's (52 reports), proteomics, metabolomics, glycomics, lipidomics, peptidomics and others (36 reports), microfluidics (65 reports), ionic liquids (as a fixed phase in gas chromatography, solvents, standard electrodes) -15 reports.

Conclusions. «PITTCON» is the signature event in the world of analytical chemistry in the number of papers and participants. Conference materials permit comprehensive scientometric data with modern development methods, analytical chemistry, applied spectroscopy, and analytical instruments.

# UV-SPECTROPHOTOMETRIC ASSAY SOTALOL HYDROCHLORIDE IN BULK AND TABLET FORMULATION

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Beta-blockers are used by tens of millions peoples to treat high blood pressure and other heart ailments. They are effective, life-saving medicines with decades of widespread and generally safe use.

Sotalol hydrochloride is a hydrophilic non-selective β-adrenoreceptor antagonist used for treatment of hypertension, cardiac arrhythmias, and angina pectoris. It is a racemic mixture consisting of equal amounts of the D and L forms, with the D enantiomer having solely antiarrhythmic class III effects and the L enantiomer having both antiarrhythmic class III and beta-blocking effects.

In this regard, the aim of our work is to develop the UV spectrophotometric methods of assay of sotalol hydrochloride. In medical practice, sotalol hydrochloride is used in the form of tablets and oral solution. In Ukraine registered tablets under the trade name “Sotalol Sandoz” of 40, 80, 160 mg and “Sotalol APO” Borshchahivskiy HFZ of 80, 160 mg.

Sotalol hydrochloride substance and formulations based on it included many foreign pharmacopoeias. Literature survey revealed that very few methods have been reported for the analysis of sotalol hydrochloride dosage form which includes UV spectroscopy the absorption index, reverse phase high performance liquid chromatography methods, thin-layer chromatography, gas chromatography, infrared spectrum, mass spectrum, colour test (Liebermann's reagent – brown; mercurous nitrate – black).

The aim of our work is to develop methods for the spectrophotometric determination of sotalol hydrochloride for its further use in the analysis of its dosage forms, particularly tablets.

In order to achieve this objective we have removed the ultraviolet spectrum was 0.05% aqueous solution and 0.1 N HCl solution of sotalol hydrochloride, maximum is observed at a wavelength of 228 nm and a shoulder at 261-265 nm region and 0.05% solution of aqueous alkali – 249.0 nm. Therefore, quantitative determination of sotalol hydrochloride in a solvent 0.1 N NaOH. Calculation of the content of the active substance in a quantitative spectrophotometric determination was carried out by standard.

As the results of research, obedience to the law of Bouguer-Lambert observed in the concentration range $5.0 \cdot 10^{-4}$ to $2.0 \cdot 10^{-3}$ g/ml at length wave 249 nm.

Approbation methods performed on the tablets “Sotalol Sandoz” containing 0.08 g of sotalol hydrochloride in one tablet. Found that auxiliary substances do not affect the character of the spectrum.

The developed methods has been used by us determination of sotalol hydrochloride commercial pharmaceutical formulations as tablet “Sotalol Sandoz” were prepared mixture model and determined the content of the active ingredient.

## SECTION № 4

## TECHNOLOGY PHARMACEUTICAL PRODUCTS

# TECHNOLOGICAL ASPECTS OF EXTEMPORAL TECHNOLOGY OF PREPARATION SUPPOSITORIES WITH SEA BUCKTHORN OIL FOR HAEMORRHOIDS TREATMENT

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Haemorrhoids are a very common disease that affects 50 % of the human population throughout the world. This pathology is met in adults of all ages and in children from birth.

Medicines of herbal origin are better tolerated by patients, have significantly fewer side effects, high bioavailability and a wide range of therapeutic action.

Among the offered range of phytomedicines for haemorrhoids treatment suppositories with sea buckthorn oil by LLC “Fitolik” were chosen as an object of research, as they show a significant anti-inflammatory, reparative (healing) effect due to membrane and antioxidant effects of sea buckthorn oil. Also, this medicine is suitable for treatment both adults and children above 6 years. But it contains hard fat as a suppository base, while usage of suppositories in children requires natural components. Pharmaceutical compounding gives an opportunity to develop extemporal technology of preparation suppositories with sea buckthorn oil with the use of natural suppository base – cocoa butter.

As cocoa butter has a low melting temperature and the chosen active ingredient is in the form of the fat oil in quantity of 33.33 %, the sealant is required. For a number of reasons, the most suitable sealant is set as beeswax.

To determine the suitable percentage of beeswax in suppositories, the relevant investigation was conducted. Suppositories with 3, 4, 5 % (samples 1, 2 and 3, respectively) of beeswax were prepared and studied by such physical and chemical property as melting temperature (by the by the method of State Pharmacopoeia of Ukraine, 1 ed., section 2.2.15.). Research was conducted for 3 series, for each sample, of 10 suppositories with sea buckthorn.

The obtained results showed that samples 1 and 2 have melting temperature lower than 34 °C, which means that they will melt at the hand of the patient at once. Such circumstance attests to the impossibility of their successful administration. Melting temperature of sample 3 provides good consumer quality of the medicine and meets the requirements of State Pharmacopoeia of Ukraine.

Therefore, the most rational quantity of sealant beeswax was set as 5 %. The obtained results were used in development of extemporal technology of preparation suppositories with sea buckthorn oil.

# MODERN PREPARATION OF MEDICINES AT PHARMACIES OF UKRAINE

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Compounding is the creation of a drug product by mixing ingredients. For hundreds of years this was the exclusive way pharmacists practiced. However, as professional manufacturing developed, compounding decreased. Fifty years ago, about 60% of medications were compounded. Today, only about 1% of new prescriptions are compounded, but compounding may be undergoing a resurgence.

Moreover, medical representatives of different pharmaceutical companies, who promote their products to the market, exert a significant influence on prescribing of medicine by doctors.

January 18, 2013 on the website of the Ministry of Health of Ukraine on medicine has been posted a draft order of Ministry of Health of Ukraine "On amendments to the license terms of an economic activity in manufacture, whole- and retail sale of medicine" concerning the requirements to activity of pharmacies. The document also noted that every tenth pharmacy must manufacture extemporaneous medicine. As of 29.01.2013, the total number of pharmacies in Ukraine made up 15092. On conditions that each tenth pharmacy must have a license of extemporaneous manufacture, according to the draft order, then there should be about 1.5 thousand pharmacies that manufacture extemporaneous medicine in Ukraine.

On 01/01/2013 the total number of pharmacies, which have a right to an extemporaneous manufacture made up 433. The leader of this index is the capital, which represents 69 pharmacies that have a license of extemporaneous manufacture. Among the regional centers 19 and more of such pharmacies are presented in Lviv and Kharkiv. It is worth being noted that there are pharmacies in all regions of Ukraine that manufacture medicine.

Manufacturing pharmacies of Ukraine make various medicines prescribed by doctors and at the request of medioprophilactic institution. Depending on the establishments being served (clinics, hospitals, health resorts, orphanages, etc.) a range of extemporaneous medicine in each pharmacy is individual. If there is an orphanage or a care establishment next to a pharmacy, then the major part in receipt occupy solid dosage forms for oral use. When hospitals are being served – dominate parenterale medicines. If institute of dermatovenerology is being served - soft and liquid forms for external use are made more often.

# RESEARCH OF THE LIQUID NETTLE LEAVES EXTRACT OBTAINING BY PERCOLATION METHOD

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It is known that nettle grows like a weed, but it refers to the medicinal plant raw material and has a complex of valuable substances such as vitamin, carotenoids, chlorophyll, vitamin C, flavonoids, tannins, and others. Stinging nettle has hemostatics, diuretic and tonic effect, showing weak choleretic activity. Nettle leaves are part of the species with gastric, laxatives, vitamin and other effect. From the leaves of nettle prepared tincture, liquid and dense extract. Dense extract part of the drug Alohol, which has a choleretic effect.

Long been and till present day by decoction of nettle leaves rinse hair to strengthen the roots and structure of hair, liquid extract is part of the therapeutic shampoo "Fitoval."

Therefore, we consider that the development of topical medicinal shampoos containing a set of extraacts from several types of raw materials, one of which is the nettle leaves is relevant.

Preparation of a liquid extract made by percolation, as extragent used 50% water alcoholic mixture, extraction conducted at room temperature. 100 g of raw material loaded into a percolator, to eliminate formation of voids (dead zones) pouring of extragent was carried out from the bottom up to a "mirror" level. Raw material was infused within 24 hours, and then started the process of percolation, that is selection of extract at a rate of 110 drops per 1 minute and at the same rate feeding by fresh extragent.

In order to establish the dynamics of the extraction process was carried out selection of extract samples in the amount equal to the weight of the loaded material. In all collected consistently extracts was determined the dry residue at a temperature of 105°C on hygrometer of «Sartorius» company (Germany). Also was calculated yield of extractives.

As a result of studies, it was found that for complete exhaustion of raw materials needed to use a ten-fold amount of extragent relative to the weight of the raw material. The obtained liquid extract was evaporated on a laboratory vacuum evaporator up to 100 mL, to achieve a ratio of raw material: extragent 1:1. Thus there was obtained liquid nettle extract, which will be used in our futher work at development of a therapeutic shampoo.

# THE INFLUENCE OF NEW MEDICINES FROM THE DRONE BROOD AND THE MOTH LARVAE OF BEE ON THE BODY'S DEFENSES

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The larvae of drone brood and bee moth are beekeeper products, which are used as raw materials for the development of new medicines will broad-spectrum pharmacological action. In folk medicine, medicines of the moth larvae of bee and the drone brood are used to treat cardiovascular diseases (ischemia, angina, heart attack, etc.), the respiratory system, tuberculosis, inflammation of the joints, lymph nodes, prostate, prostate adenoma, menopause, infertility in women and other diseases. On department pharmacy-basis technology of drugs from biomass drone brood larvae obtained the freeze-dried substance. On the basis the moth larvae of bee developed tincture. New medicines having antimicrobial, antiinflammatory, antioxidant action. The breadth of the pharmacological effects of medicines due to a variety of biologically active compounds, as contained in beekeeper products, includes the larvae of drone brood and bee moth. From scientific sources people knows, that the using of beekeeper products in food increases the protective forces of the body due to their positive effect, of the immune system.

The objective of this work studies the effect of the influence of new medicines on the immune system. The influence of medicinal substances on cellular immunity use the reaction of delayed type hypersensitivi. Also studied the effect of tinctures and lyophilized powder for humoral immunity (the number of spleen cells antibody producers purebred mice's and hemagglutinin titer of serum blood). This method of determination of antibodies in the serum agglutination test lies.

Studies to assess the actions immunotropic infusion of moth larvae bee indicate that the medicines tends to increase the functional activity of T-lymphocytes in delayed-type hypersensitivity, increased the number of spleen antibody producers and increasing hemagglutinin titer. The results of scientific studies have shown that freeze-dried substance drone brood has a strong immunomodulating-cial action. Substance stimulates T-cell responses immuno-eignty and production of antibody producers spleen. In tincture of biomass moth larvae bee this biological asset-ness is less pronounced. Performed experimental studies showed a trend of positive influence of bee moth larvae tinctures for immunity. The results can be used to study of this mechanism action new medicines. Lyophilized Nye substance from biomass drone brood can be used in the development of new medicines to enhance the body's defenses therapeutic and preventive action.

# DEVELOPMENT OF CAPSULES WITH JERUSALEM ARTICHOKE POWDER

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One of the most important ways to solve the nutrition imbalance problem is the use of certain biologically active supplements. To improve the health condition, productivity and life expectancy of the population it is necessary to ensure its proper nutrition with a balanced set of amino acids, to eliminate the deficiency of vitamins, minerals, trace elements, and also to develop and improve production technology, providing high quality of food products. One of such promising sources for food additives is Jerusalem artichoke (Helianthus tuberosus L.), which tubers comprise 15-20% of inulin, 2.5-3.5% fructose, about 2% of protein, pectin, hemicellulose, fats, iron and phosphorus compounds, potassium, magnesium, B vitamins, carotene, pantothenic acid, vitamins E and C.

In this context, the aim of the work was the development of hard capsules with dried powder of Jerusalem artichoke tubers.

As an object of research used fresh tubers of Jerusalem artichoke, which were purified from dirt, crushed and dried in an oven. When selecting the composition of excipients to develop capsules conventional methods according to the recommendations of the State Pharmacopoeia of Ukraine have been used.

Dried parts of tubers milled in a coffee grinder. The resulting powder is light gray in color, has a sweet taste and characteristic smell. The substance has low technological parameters on the flowability and bulk density. To eliminate these drawbacks binders should be used.

As binders for the given powder 2, 5 and 10% starch paste and 96% ethyl alcohol were chosen. The composition humidified with abovementioned binders and granulated through a sieve of diameter 1000 mm, and then dried at a temperature of 40 ° C. Studied the technological characteristics of the resulting mass. As a result it has been found that the mass does not meet the requirements for disintegration. Therefore, in the encapsulation mass added dry starch in an amount of 5% which provides the required hard capsules disintegration rates.

Furthermore, we have studied the amino acid and trace element composition of Jerusalem artichoke tubers.

# OINTMENT DEVELOPMENT FOR WOUND HEALING ON NATURE AFI

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Successful treatment of a particular chronic wound requires a detailed understanding of the molecular and cellular components present within each wound. Currently, chronic (and acute) wounds of different etiologies are treated using a multistep approach based on contemporary knowledge of wound healing. First, nonviable tissues from within and around a wound are removed using surgical debridement or debriding agents, such as bacterial collagenase. Second, infection and inflammation are minimized with antibiotics and anti-inflammatory preparations. Next, moisture imbalance is corrected, generally with carefully selected dressings. Finally, epithelialization and granulation tissue formation are promoted by the application of specific therapies, such as growth factors.

The use of time strategy is not always sufficient, however, and some wounds remain nonresponsive to current therapies.

The relevance of medicinal plants and herbs use, especially growing in Ukraine, modern medicine has increased significantly in recent years. Effectiveness of the modern drugs which contains herbal ingredients higher than most of synthetic drugs in terms of complex action exerted by keeping the amount of biologically active substances. Due to the following advantages: low toxicity, hypoallergenic, complex action and the possibility of long-term use without significant side effects it is expedient to use substances derived from medicinal plants. The most common active pharmaceutical ingredients obtaining from medicinal plant materials used for the production of ointments are extracts. Hydrophobic or hydrophilic fractions of extracts are prepared depending on the used extracting agent.

Among the drugs that have active influence on the course of reparative processes hydrophilic fraction of the Poplar Chinese leaves extract of was chosen. This active pharmaceutical ingredients has reparative, antimicrobial, inflammatory activities.

Despite these successes in the treatment of inflammatory processes, including combined ointments, most drugs in Ukraine are more active in the first phase of wound healing, and they has limited range, so creating effective ointments for the treatment of purulent wounds remain relevant, especially containing natural ingredients.

# STUDY DISPERSION AND AVERAGE WEIGHT IN A SINGLE DOSE SPRAY FOR USE IN ENT PRACTICE.

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Upper respiratory tract infection (VMD) is undoubtedly the most common diseases with which modern man is found throughout the period of life.

One of the urgent problems of modern pharmaceutical technology is creating a new generation of drugs for topical application, providing local and comparable ravnomirne release of active substances from the dosage form, creating high concentrations of therapeutic agents at the site of application without a significant increase of antimicrobial agents into the systemic circulation.

These drugs today are sprays that are used in the treatment of many inflammatory processes empty cavity and upper respiratory tract. In sprays, sprays having advantages, not disadvantages associated with the use of bottles under pressure increase and the use of propellant gas as a carrier.

The department supervisor developed in ATL combined spray composition for use in ENT practice.

We investigated some technological characteristics of the spray dvuma types of mechanical pumps from different manufacturers: JSC "Stoma" (Ukraine) and the company «Coster Technologic Special Spa» (Italy) - type 20DR 376/100/0-PT.

Because of the quality of the valve-spray system depends on the work of all aerosol packaging, we conducted a comparative study of several indicators of technological nature. We determined the average weight of the drug in a dose and dispersion.

An average weight was determined at (20 ± 2) ° C by pressing on the valve stem spray 5-6 times to get dispersed current. Then spray bottle was weighed to the nearest 0,01 (m1), nazhymaly on the valve stem from 1 to 20 times and weighed again (m2).

To determine the dispersion of aerosol particles is fixed on a slide.

On the slide Apply a thin layer of petroleum jelly mixture of oil and vaseline (1: 1) to fix the aerosol particles. The drug nebulize by mechanical valve, pressing the valve stem until the aerosol cloud formed. He made particle test solution. The particle size determined by microscope in which the ocular insert special mesh size of 20 mm at magnification (10 x 8). Definition carried out in 25 fields of view. Particle size is determined along the longest axis.

The average weight of a single dose, which vychavlyuvalas two valves is about the same, but the deviation from the weight of the valve AO "Stoma" is 3%, and for the valve «Coster Technologic Special Spa» 0,6%.

To determine the dispersion, the results of experimental studies it appears that 60% and 70% are particles of dispersion, which is satisfactory for this purpose sprays. Dispersion of airborne particles less than 100 microns.

Based on the research results can be concluded that an advantage of valve-spray system imported. Nevertheless, both systems provide the required dispersion quality and cutting, and can be used in aerosol drug technology as a spray.

# RESEARCH OF TECHNOLOGICAL PROPERTIES OF PLANTAGO MAJOR, HEDERA HELIX AND SALVIA OFFICINALIS AND THEIR MIXTURE

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Cold diseases or acute respiratory infections are the most common diseases, which stipulates their medical and social significance. Acute respiratory infections account for more than 90% of human infections. The characteristic symptoms of this diseases are sore throat, rhinitis, cough and fever. For the rational therapy choice attention should be paid to the effectiveness and safety of medicines. Over the past decades, significant demand have gained herbal products.

As the plant material have been chosen leaves of Plantago major, Hedera helix and Salvia officinalis. As it is known, the leaves of the Plantago major contain polysaccharides and flavonoids, among the latter determine, rutin, apigenin, luteolin. Expectorant action of plantain leaves is due to the presence of polysaccharides. Saponin glycosides of Hedera helix determine its secretolytic effect, hydroxycinnamic acids exhibit immunostimulatory and anti-inflammatory effect. Hydroxycinnamic acids, flavonoids and tannins of Salvia officinalis exhibit anti-inflammatory, antimicrobial and astringent effect.

The aim of this work is to investigate technological properties of these plants separately and mixture of these plants.

The relative density, the bulk density, the porosity raw, the free volume of the plant layer, the absorption coefficient (purified water), the humidity, the flowability, the angle of repose, the content of extractives (purified water), the content of polysaccharides were studied for each plant separately. The results of the studied parameters were sufficiently close to other plants and did not have large deviations.

The next step was to prepare the mixture of Plantago major leaves, Hedera helix leaves and Salvia officinalis leaves in the ratio 5:1:1. The following are some of the parameters that have been studied for the mixture. The relative density - 1,36 g/ml, the bulk density - 0,21 g/ml, the porosity raw - 0,37, the free volume of the plant layer - 0,82, the absorption coefficient (purified water) - 1,90 ml/g, the humidity - 9,61%, the flowability - no value, the angle of repose - 45°, the content of extractives (purified water) - 38,72%, the content of polysaccharides - 13,83%.

The obtained technological parameters will be used in the development of the extraction drug technology of this mixture.

# STUDIES ON DEVELOPMENT OF COMPOSITION AND TECHNOLOGY OF SETATIVE BLEND

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The problem of creation of effective herbal remedies from medicinal plants is currently relevant.

This is due to the fact that the medicines based on natural bioactive compounds have advantages over their synthetic analogues, since the breadth of therapeutic effect in them is combined with minimal side effects. Of particular importance are blends, which contain a complex of biologically active compounds responsible for the multivalent effect on various body systems.

The aim of this work was to develop and study a sedative blend. As objects used the following types of medicinal plants - hop cones, motherwort herb, hawthorn fruit, mint leaves and elderberry flowers.

To determine the optimum extraction conditions extracts with 70% ethanol and purified water were obtained. Each of the extracts was sampled fractionally with DER increments of 1:1. For each sample was conducted quantification and calculated the main parameters of the process dynamics. The extraction process carried out in a laboratory filtration extractor.

It has been established that the maximum number of stages for extraction of the extract should be considered equal to 4, since further increase of the extractant portions does not lead to a significant increase in the yield of finished product. Considering the duration of the extraction process and the power consumption it is rational to obtain total extract, although its yield is slightly less than at extraction of a single plant material. The best yield of extractive and active substances is observed when used as extractant purified water.

A comprehensive study of the blends has been conducted. The presence of flavonoids, phenol glycosides, floroglucides, tannins, anthracene derivatives, saponins, water-soluble vitamins in blends has been established. The main biologically active compounds of blends: flavonoids, tannins, ascorbic acid have been quantified. The coefficients of water absorption and total loss of extractant have been determined.

The optimal dosage form for extemporal manufacture is determined to be an aqueous decoction, filtered without cooling.

# BIOPHARMACEUTICAL RESEARCH EXTEMPORAL OINTMENT FOR THE TREATMENT OF ECZEMA

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One of the main directions of development of biopharmaceutics is the choice of optimal type and composition of the dosage form to ensure high safety and therapeutic efficacy.

The main terms of the action of drugs is their release from the dosage form, absorption through biological membranes and transport to the place of impact with blood, lymph. It depends mainly on a combination of pharmaceutical factors. The therapeutic activity of drugs in the form of ointments related to the properties as drug substances and excipients, pH, viscosity, which render effect on bioavailability of drugs through the skin. One of the important indicators of quality of ointments, like any other dosage form is its ability to provide optimal bioavailability of the drug. As you know, the rate of absorption of drugs affect a variety of factors pharmaceutical and pharmacological order.

Of pharmaceutical factors affecting bioavailability of drugs should be allocated as follows: degree of grinding, polymorphism, solubility and other physical and chemical properties of the medicinal substance.

To provide the necessary dosage form pharmaco-technological characteristics chosen excipients, such as optimal media for drugs. The use of any additive in each case requires special studies to ascertain its impact on the process and bioavailability.

As the original carrier of pharmacologically active substances foundations themselves have certain physical and chemical properties. Therefore, in each case, a combination of drugs and assisted in the appropriate dosage form should be individualized based on the pharmacokinetics of drugs

Ointment bases cannot be seen only as a neutral environment of drugs administered to them. Properties ointments, its ability to be absorbed and hence therapeutic effect largely depend on the nature of ointment bases. Given the foregoing, to increase the therapeutic action we proposed the use of combination of hydrophilic ointment base, which differs from the usual fat basis - vaseline.

In order to assess the degree of increase therapeutic effect was evaluated the degree of release of drugs (streptocide and anaesthesin) ointment bases with different composition by "agar plates." It is proved that the rate of release depends on the nature of the base and the degree of dispersion of the drug.

# MODERN PROBLEMS OF TREATMENT OF SKIN CANDIDIASIS

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Doctors keen interest in the study of skin candidacies in recent years due to a significant increase in their frequency. This is due to a sharp increase in the number of risk factors for fungal infections (active antibiotic therapy, resuscitation, use of glucocorticoid and immunosuppressive drugs, etc.).

The number of antifungal agents that are "in service" doctors constantly updated. Now it includes about 10 dozens of local and systemic drugs.

Existing drugs are mainly fungstatics not effective in treating such patients. In this regard, the acute problem of development and introduction of new drugs with fungicidal original mechanism of action, such that no cross-resistance with existing drugs.

However, in the last century to treat fungal infections could use only potassium iodide, which is also used in our days, and local funds - only preservatives, many of which (liquid Castellane et al.) Have been established only later. The situation has not changed until the mid XX century, when the antifungals different chemical groups to treat fungal skin lesions.

Their implementation in practice dermatologists changed in views on the nature of the treatment of fungal infections of various origins. The emphasis in their treatment became gradually shift towards systemic therapy, but local therapy still remains the main treatment. Some methods of topical treatment, those who today seem inappropriate (hair removal, removal of nails, etc.) Were slow to give the combined therapy with antifungal agents.

Modern Ukrainian market of antifungal drugs fully meets the current needs in this group of drugs. However, their relatively high cost in low solvency of the population cannot meet the needs of patients with mycosis. One way to solve this problem is to develop new and improve existing composition of extemporaneous preparations antifungal action.

Given the foregoing, one way to solve this problem is to develop new and improve existing composition of extemporaneous preparations antifungal action.

The analysis of extemporaneous formulations to treat this class of diseases has shown promising development structure highly topical administration of drugs with complex action (antifungal, antiseptic, and dry action) that will help improve medical and preventive care to patients.

# VISCOSIMETRIC STUDIES OF METHYLCELLULOSE DERIVATIVES

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Currently are widely used soft dosage forms in the form of gels, due to a number of benefits such as efficiency (well absorbed through the skin and mucous membranes), usability (easy to apply and spread over the surface), simplicity and efficiency of preparation technology. As a gelling agent carbopol of different brands is often used. Of great interest is the study of hydrocolloids, as which may be used methylcellulose and its derivatives, carrageenan, gums, pectins to create new drugs based on them.

We have studied 0.5%, 1%, 1.5%, 2%, 2.5% and 3% solutions of sodium carboxymethylcellulose, hydroxypropylmethylcellulose, hydroxyethylcellulose, ethylcellulose. The samples were prepared by the gravimetric method, dispersion of methyl cellulose derivatives in purified water performed with a homogenizer POLYTRON 2500 E of company "KINEMATICA AG" (Switzerland). Prepared samples were subjected to rheological (structural-mechanical) research on the device "Rheotest-2" (Germany) with the H set of coaxial cylinders. Rheological studies allow to judge of the viscous-plastic properties of solutions of methyl cellulose derivatives and their thixotropy. To compare the data of the dynamic viscosity of the methylcellulose derivatives solutions carbopol solutions were prepared at the same concentration. Samples which viscosity did not allow carrying out rheological studies were subjected to determination of kinematic viscosity using the viscometer 2-VSL.

As a result of experiments it was found that in all the samples with increasing concentration value of the dynamic viscosity increased. In the concentration range of 0.5 - 1.0% solutions have low viscosity, systems are approaching Newtonian liquids. In samples with a concentration of 2.5 - 3% viscosity increases sharply, but does not exceed the viscosity of the gels prepared with Carbopol.

On the other hand incorporation of salts into the hydrocolloid lowers the viscosity thereof. Thus, the next stage of our work will be to study the dependence of viscosity of hydrocolloids solutions from introducing into their composition of solutions of salts and other substances.

# THE DEVELOPMENT OF THE COMPOSITION AND TECHNOLOGY OF THE NEW PLANT PARODONTOPROTECTOR

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Statistical studies of the last years indicate the high rate of prevalence of inflammatory diseases of parodontium and of mucous membrane of the oral cavity in different age groups. Moreover, the indicated diseases have a negative influence on the quality of life, that is why they belong to the socially important diseases in medical practice. Therefore, at present the development of new drugs for the pharmacotherapy of inflammatory conditions in dentistry is a topical interest for the scientists who work in the pharmaceutical field, the solution of which should be based on the phased researches.

The purpose of our work was a theoretical and an experimental justification, the development of composition, technology and quality control methods of a new remedy in the form of herbal collection for the treatment of inflammatory diseases of parodontium and those of mucous membrane of the oral cavity. The objects of study included medicinal plant raw materials, tincture of Japanese Sophora, the collection «Denta-Phyt». The research was conducted by using organoleptical, pharmaco-technological, microbiological, biological, physical, chemical, mathematical methods.

Among the drugs for dentistry registered on the pharmaceutical market of Ukraine the limitation of complex phytomedicines, which include collections, was established and this factor indicates the prospects of their development for the further introduction into the medical practice.

According to the data on the use of collections for the treatment of inflammatory dental lesions in folk and official medicine in prescriptions the most widespread medicinal plants were selected and stable combinations with other plants in the composition of each collection were defined for them. As a result of analysis it has been noted the objects frequently combined with each other and perspective medicinal plants, the raw materials of which due to the content of biologically active substances, may be incorporated into the complex dental preparations. The microbiological screening of the infusions of raw materials of selected plants for the purpose of the experimental substantiation of MPRM-components of a new collection was carried out. The research was conducted by using the method of diffusion in agar in the modification of "wells". The medicinal plant raw material with the most expressive antimicrobial activity was defined due to the obtained values of the diameters of the zones of stunted growth of microorganisms S. aureus, E. coli, P. aeruginosa, B. subtilis, P. vulgaris, C. albicans and five MPRM-ingredients of the collection were selected: sage leaves, marigold flowers, St. John's wort herbs, linden flowers, peppermint leaves. The impact of the tincture of Japanese Sophora on the antibacterial and antifungal activity of modeling samples of the collection and also the content of the given component in the preparation were defined on the basis of microbiological studies, besides the substantiation of the optimum ratio of ingredients in phytopreparations. The rational composition of the new plant medicine for the local use in dentistry was established and it was conditionally called "Denta-Phyt"

(to 100.0): St. John's wort herbs (29.0), linden flowers (29.0), mint leaves (14, 0), marigold flowers (14.0), sage leaves (14.0), the infusion of Japanese Sophora (10.0).

The technological parameters of each medicinal plant raw material of phytomedicine and of the developed collection, which should be taken into consideration when making the drug, were studied with the help of pharmaco-technological researches. A rational technology of the new plant medicine was substantiated on the basis of analysis of the influence of regimes of getting infusions from the collection and the stage of dividing the components up to the value of solid residue, which indicates the content of extractive substances. The three separate fractions of the collection "Denta-Phyt" were studied with a particle size of 1.2 mm, 2.3 mm and 3.4 mm, for which the aqueous extracts were obtained by using different modes: the infusion time in a water bath (from 2 to 28 min in increments of 6.5 min) and the infusion time at room temperature (from 15 to 60 min in increments of 15 min). Two fractions of the collection of herbs - 1.2 mm and 2.3 mm, which can be combined into one with a particle size of 1-3 mm, were chosen according to the results of the study. The infusion time during 15 min in a boiling water bath and during 45 min at room temperature was selected as a rational mode of obtaining the aqueous extract from the phytomedicine.

The development of the project of the quality control methods for the new collection "Denta-Phyt" was based on a series of physico-chemical studies, as a result of which the parameters, by the following indicators such as appearance, identification, the loss of weight on drying, total ash, ash insoluble in hydrochloric acid, microbiological purity, a substance extracted, quantification of the active ingredients, were established. The main functional groups of components of the phytomedicine such as flavonoids, essential oils, polysaccharides, phenolic compounds were defined by using qualitative reactions. With regard for the different methods of tests based on for the identification of flavonoid compounds and essential oils in the composition of ingredients of collection ingredients (according to the monographs of the State Pharmacopoeia of Ukraine), it has been developed the unified methodology for their identification. So, the biologically active substances such as flavonoids (rutin, hyperoside, caffeic and chlorogenic acids) and essential oils (menthol, thymol, cineole) were detected by thin-layer chromatography analysis. The quantitative determination of active substances of the phytomedicine was carried out by the spectrophotometric method according to which the content of amount of flavonoids was established. The spectrum of pharmacological activity was defined on the basis of several studies. The anti-inflammatory influence of the infusion of the collection of herbs on the model of an acute aseptic inflammation caused by injection of carrageenin was detected. According to the method of Althauzen, the presence of a moderate hemostatic action was established. Also, on the model of the experimental periodontitis, the specific parodontoprotecting activity of the collection "Denta-Phyt", which has a more expressive effect of the herbal preparation in comparison with the collection "Elekasol", was defined.

Thus, according to the results of studies conducted sequentially, the optimum composition, a rational technology and quality control methods of the new parodontoprotector – the collection "Denta-Phyt" were developed.

# THE RELEVANCE OF THE CREATION OF PHARMACEUTICAL PRODUCTS CONTAINING METALLIC NANOPARTICLES

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In development of modern medicine the vital part belongs to exploration of the potential of metallic nanoparticles. This is specified, first of all, by a wide range of their application, and also by the high effectiveness of the drugs that contain nano-particles.

Changing the size of particles has been shown to have the direct impact on changing of physical and chemical properties of substance, parameters of the crystal lattices, melting points, electronic structure and also catalytic and other properties.

Changing the following properties may cause changing of their usage in the pharmaceutical industry.

The given size of nanoparticles causes the subsequently modification of physical and chemical properties of metallic, which can become a background for creation of nanomaterials and nanocompositions that are able to change the methods of diagnosis and treatment.

Nowadays, scientists describe the broad application of various metallic nanoparticles. Gold, Bismuth and Silica nanoparticles have been extensively studied for enhancing efficiency and reducing side-effects of therapy of oncologic diseases.

Ferum nanoparticles are widely used to treat various types of anaemia and also for diagnosis of diseases, in particular for higher sensitivity of Computerized Axial Tomography . Zinc and Gold Nanoparticles facilitate regeneration and rejuvenation of skin cells and mucous membranes, but also possess proper antimicrobial activity.

Silver also plays an essential role in nanomedicine. A study on Argentum nanoparticles has made significant progress which caused an in-depth exploration of their application for pharmaceutical purposes.

It was proven the antiviral and antifungal activity; antiviral, anti-inflammatory, immune-modulatory effects of the given drugs.

In vitro and in vivo the bactericidal and antiviral activity of given silver nanoparticles was proved. Used externally, it was observed fast regeneration of the affected skin areas. Thus, it was established that metallic nanoparticles possess healing components and stimulate regenerative processes.

From the above, we could conclude that the development of new drugs on the basis of nanoparticles remains an extremely valuable and timely issue due to the constant progress of modern medicine. This applies particularly to antiviral and antimicrobial drugs, which will make it possible to resolve the problem of antibiotic resistance.

# STUDY PROCESS DATA ANTIULCER DRUGS BASED ON BEE PRODUCTS

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To ensure high efficiency of drug action and minimum side effects when applied a large value has a correct selection of pharmaceutical factors, including excipients and production technology. In connection with the above goal was to develop a rational technology combined drug of natural origin based on bee products and plantaglyutsid having anti-ulcer effect.

Study drug technological properties revealed that it has a good bulk density ((1,00 ± 0,01) g/cm3), and poor flowability (2.18 g/s); plantaglyutsid has good bulk density ((2,51±0,01) g/cm3) and poor flowability. In this connection the mixture of starch were used and aerosil and talc, lactose, microcrystalline cellulose and glucose. The study of the technological properties of the granular mass showed that the best indicators has to include a mixture of starch and aerosil: bulk density - (0,92±0,02) g/cm3; flowability - (1,26 ± 0,03) g/s.

Investigations were carried out according to the SPU I Publishing (article" granules"). Experiments showed that the granules satisfy the requirements of particle size 0.3 to 0.4 mm which have an excellent flowability, and the disintegration time in an acidic environment Granlie was much smaller (less than 12 min). This is crucial, as granules developed primarily intended for the treatment of gastric ulcer , the secrets of which are acidic environment.

Determination of abrasion resistance by the standard procedure, as a result of studies , it was found that the indicator satisfies the requirements

(minimum 97 %) and is 99.36 %.

Thus, as a result of the research established a number of technological melon which give granules with high pharmaceutical availability.

# RESEARCH MEDICAMENT FOR THE TREATMENT OF PROSTATITUS

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Prostatitis is one of the most common inflammatory diseases of the male urogenital area. Prostatitis - an inflammation of the prostate gland. There are about 7 types of prostatitis: acute catarrhal, follicular or acute suppurative focal acute purulent diffuse parenchymal or abscess of the prostate.

Prostatitis suffer from 35 to 58% of men over 50% of them are patients from 20 to 40 years. After 45 years, the number of patients increases to 75% after 60 years - up to 85%. At present, the disease is much "rejuvenated".

Socially and economically important area in modern pharmacy is to expand the range of safe and effective drugs that normalize the condition of the urogenital tract of man.

For the treatment of prostatitis use different kinds of therapy: massage, physiotherapy, acupuncture, metallotherapy, laser therapy.

In the pharmaceutical market of Ukraine registered more than 120 drugs for the symptomatic treatment and etiopatogeneticheskogo different types of prostatitis. Most of them are represented by foreign agents, quite expensive.

For the treatment of prostatitis use different groups of drugs. We analyzed prostatoprotektorov on the dosage form. For treatment of prostate using various forms: capsules, tablets, powders for preparation of injectable solutions, suppositories, granules, drops, infusions.

The drugs of choice are the fluoroquinolones (ofloxacin, ciprofloxacin, pefloxacin), macrolides (azithromycin, clarithromycin, spiromitsin), and tetracyclines (doxycycline, methacycline). The efficacy of rectal administration of several drugs (nitrofurans, analgesics).

The prostatitis problem is growing and requires new research and new technologies for production of drugs to combat the disease. Thus, we can conclude that the drugs analyzed in this study are effective in the treatment of various types of prostatitis, but should not be treated as the last point in the research work of scientists in the field. Pharmaceutical science priority is to improve and further identificate new active substances to expand the range of innovative medicines and its successful implementation in clinical practice.

# THE RELEVANCE OF CREATION DENTAL GEL BASED ON NATURAL RAW MATERIALS FOR TREATING OF STOMATITIS

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Now it is considered that the stomatitis is a general term which includes inflammatory diseases, degenerative lesions of the oral mucosa of both infectious and non-infectious nature.

Stomatitis may occur in patients of all ages, but each age group has the specific form of this disease of the oral mucosa. For example, in childhood are more common acute aphthous and fungal stomatitis. In adolescence dominates catarrhal stomatitis. After 40 years the most frequently aphthous stomatitis is detected.

Considering the current approaches to the treatment of stomatitis, it should be noted that when the development of drugs for their treatment, they must possess antimicrobial, antiviral, anti-inflammatory and wound-healing pharmacological activity.

Today more and more dentists are advised to use in the treatment of stomatitis drugs based on natural plant material, the advantage of which is wide focused therapeutic action and the almost complete absence of side effects

Analyzing the current pharmaceutical market of drugs for topical treatment of stomatitis based on natural plant materials, it is worth noting that most of them are represented by liquid dosage forms (tinctures, solutions for external use, etc.). However, following the instructions on their use, the use of these drugs should be carried out at least 5-6 times a day, which affects the patients' compliance.

More modern dosage forms, such as dental gels based on natural compounds, are represented only by a few drugs. However, the herbs in their composition are only combined with synthetic substances; that in turn causes the relevance of development the new dental gel based on natural plant raw materials.

After examining the range and pharmacological properties of medicinal plants that can be used in the treatment of stomatitis, as active ingredients for development a dental gel for the treatment of this disease, we have chosen dry extract of licorice root and essential oils of sage and peppermint. These active ingredients have necessary antimicrobial, antiviral, anti-inflammatory and wound-healing pharmacological activities for the treatment of stomatitis.

Further aim of our work is to develop composition and technology of a new dental gel based on natural raw materials for treating of stomatitis.

# PROSPECTS OF CREATION OF EXTEMPORANEOUS PREPARATIONS OF COMBINATION ACTION FOR TREATMENT OF ECZEMA

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Eczema - a chronic, relapsing disease with sharply inflammatory symptoms presented polymorphism morphological elements, which formed as a result of a complex set of etiological and pathogenetic factors. Eczema is 30-40% of the multitude of all dermatitis.

So today in terms of the immediate needs of practical medicine should be given great importance to the study of different variants of clinical course of different types of eczema, optimization approaches for the treatment of severe and complicated forms of the disease and the development of complex combined action of drugs (anti-inflammatory, antimicrobial, keratolytic, reparative) that to be highly effective, easy to use and have given the least amount of side effects. The aim of this work was improving the structure of the public extemporal prescription ointment for the treatment of microbial eczema, which usually is the hardest course and many complications.

It is known that most of the essential oils have antimicrobial properties, actively inhibits the growth of different groups of microorganisms and pathogenic fungi. It is also known that microorganisms prolonged contact with essential oils produce virtually no resistance to them. The combined use of certain essential oils with antibiotics and sulfonamides increases bactericidal activity of the latter. These properties are more inherent in the essential oil of tea tree. It is because of the ointment was asked to enter the tea tree oil.

Usually eczema observed destruction of the epidermis and dermis, so we proposed to enter into the ointment preparation Ayekol. It has metabolic and antiulcer effect, stimulates reparation and speeds healing. With its antioxidant and anti-inflammatory effect, it restores capillary permeability and tissue and capillary circulation. Microbial eczema differs significantly from other forms of dermatitis is characterized by the appearance of affected skin areas that are covered by sero-purulent crusts and bloody, and the surface free of crusts layers, easily wets. Given this fact, it is appropriate to use drugs with possesses drying effect. Such properties have macrogols hydrophilic base with the addition of propylenglycol.

Thus, on the basis of the research was proposed improved composition of complex action extemporal ointment for the treatment of microbial eczema.

# CLAY MATERIALS AND THEIR PROPERTIES

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Medical and pharmaceutical scientists are increasingly turning to the use of natural materials to treat diseases of internal organs and skin. The interest of scientists to the unique properties of clay minerals is not only reduced today, but is growing. The peculiarity of clay application is its efficiency and availability.

Clays are fine sediments consisting of small crystalline particles of clay minerals (montmorillonite, kaolinite and mixed-layer formations of size less than 0.01 mm and the largest aleurite (0.01 - 0.1 mm) and sand (0.1 - 1.0 mm) grains of quartz, feldspar, calcite, gypsum, iron oxide films and other minerals. In clays there is more than 50% of fine particles. They lie as a layer and deposits are developed open-cast.

Clay is a silica-alumina mixture containing silicon, aluminum, manganese, titanium, potassium, calcium, beryllium, iron, gallium, copper, cobalt, molybdenum.

Montmorillonite dust by its chemical composition represents hydroxyl aluminum silicate, containing alkali and alkaline metals. Its structural formula is: $Al_2Si_4O_2$ (OH) $2H_2O$ where Al can be partially replaced for Na, K, Ca, Fe, Mg.

It has been proven that to obtain the necessary ointment-like consistency Na - form - 13%, K - form - 19%, Mg - form - 31%, Ca - form - 38%, and H - form - 40% are required.

Therefore, we have attempted to get Na – form of Bentonite from Ca - form of montmorillonite.

When using bentonite clay in pharmaceutical practice, great importance has the removal of sand and ballasts from clay. This is achieved firstly by more detailed selection of the cleanest samples, secondly,by sludging out, ie washing with purified water to completely remove coarse particles and sand from clay. Sludging out is conducted by a special technique (see. Table.)

Bentonite purification by sludging out.

| Coarse particles and sand content, % | | | | |
|---|---|---|---|---|
| Before sludging, % | Single sludging, % | Double sludging, % | Triple sludging, % | 4 times sludging, % |
| 19,2 | 6,4 | 31,1 | 0,2 | 0,2 |

n=5

The analysis has shown that 5 times sludging provides required purity. After that bentonite is filtered and dried at t° - 110°C.

Double-sludged fraction is taken for further investigation.

# THE ACTUALITY OF USING DRY EXTRACT OF COLTSFOOT IN TREATMENT OF ACUTE RESPIRATORY DISEASES

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Preparations of coltsfoot are traditional remedy for diseases of the upper respiratory tracts. Coltsfoot is an old drug against cough and breathlessness. Preparations of coltsfoot are used for acute and chronic laryngitis, bronchiectasis and selicose and tuberculosis.

In its structure coltsfoot contains active ingredients such as carbohydrates, tannins, flavonoids, organic acids, carotenoids, sterols, steroid saponins. In therapeutic doses coltsfoot has a slight stimulating effect on the sympathetic nervous system, which intensifies the secretion of bronchial glands, as the consequence there is a decrease of bronchospasm.

Preparations of coltsfoot have bronchodilator properties. It should be noted a very important property of a coltsfoot to dissolve infiltration, whereby coltsfoot is recommended for SARS, bronchitis, pneumonia, bronchial asthma. Grass has expectorant, emollient, enveloping, antiseptic and anti-inflammatory properties. These properties are caused by presence in its structure of inulin, carotenoids, sterols, organic acids. Inulin also allows the use of drugs of this plant in patients with diabetes mellitus.

In general a medicinal plant coltsfoot is used as a remedy for respiratory diseases. Extract of the herb is used for a cold, cough, high temperature. Also the using of dry extracts is good for bronchitis, laryngitis, tonsillitis and bronchial asthma.

Nowadays the assortment of drugs which are based on coltsfoot is quite narrow as this plant is not well known but in a folk medicine it is very popular. This fact shows us the possibility of further using of medicinal plants, which can allows the using of drugs with an extract coltsfoot in a wider range of treatment of various diseases.

At present among the drugs which are basis on using the coltsfoot in the treatment of acute respiratory infections are known only syrups and multipart fees. In order to improve the consumer properties it is more rationally the using of solid dosage forms. The development of composition and technology the tablets with an extract of coltsfoot is an important task of pharmacy.

# COMPARATIVE CHARACTERISTICS OF THE OINTMENT MADE AT A PHARMACY AND THE OINTMENT PREPARED AT A FACTORY

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The aim: To compare the characteristics of the ointment made at a factory and the ointment made at a pharmacy and make conclusions.

Since time immemorial medicines have been prepared at pharmacies. Today pharmaceutical business is growing in the market system so production of medicines at pharmacies and other traditions are left in the past. But experience shows that, despite the growing range of ready-made medical products, preparation of drugs by prescriptions at pharmacies does not lose its value. Besides, among individual prescriptions for preparing medicines received by the pharmacy, there are a lot of dosage forms for children where individual combinations of drugs and doses are extremely required.

Medicines prepared by pharmaceutical companies seem to be cheaper than their analogues prepared at a pharmacy. But comparing their costs shows vice versa results.

Thus, drugs prepared at a pharmacy are much cheaper than drugs prepared by the pharmaceutical industry. This fact contradicts the well-known economic statements that mass production is less costly than individual and serial.

We conducted the experiment that proved above mentioned arguments.

For comparison we took such medicinal product as Eucalyptus cold BALM Dr.Theiss and extemporaneous ointment made by the prescription.

Ointments (lat. Unguenta - ointment) are soft dosage forms used for application to the skin, wounds or mucous membranes. Ointments consist of a base and medical substances equally distributed in them. Also ointments may contain preservatives, surfactants and other subsidiary substances allowed for medical use.

Eucalyptus cold BALM Dr. Theiss contains such ingredients as:

- Eucalyptus oil
- Pine oil
- Camphor
- Tallow
- Oil corncobs
- Beeswax.

It has anti-inflammatory, locally irritant and expectorant action.

It is the ointment for external use and inhalation.

It is used for inflammatory diseases of upper and lower respiratory tracts.

We have prepared a homogeneous ointment for cough according to the pharmacy prescription:

Rp.; Camphorae 2.5
Olei Eucalypti

Olei Pini
Olei Abietis ana 3.0
Cerae flavi 12.0
Vaselini 4.0
Misce, fiat unguentum
Da. Signa. Rubbing for cough.

This ointment contains:

- Eucalyptus Oil - antipyretic, anti-inflammatory and expectorant action.
- Pine oil - stimulates circulation and activates the immune system.
- Camphor - warming and irritating properties.
- Beeswax - softens the overall clinical picture, reducing the severity of the symptoms.

The ointment can be used for cough by adults and children older than three years old, externally and for inhalation. It is better to use this medicine in a complex treatment of colds. The ointment is used externally, rubbing the skin of the back and the chest with massage movements.

The preparation of the ointment:

1. Prepare the workplace.
2. Take necessary amount of wax and place it in a porcelain cup.
3. Weigh Vaseline.
4. Melt wax in a water bath in a porcelain dish.
5. Add vaseline to the melted wax.
6. Melt wax with Vaseline.
7. Transfer the fusion into heated mortar.
8. Add vaseline oil.
9. Weigh camphor.
10. Dissolve camphor in the fusion.
11. Add essential oils.
12. Mix thoroughly.
13. Transfer to a jar for delivery.
14. Prepare for delivery.

The ointment should be keep out of the reach of children, at a temperature not exceeding 25 C. It can be used during 3 years. Qualitative characteristics of our ointment are the same as the characteristics of the ointment made at the factory. Density, color, uniformity, smells correspond to the national standards. The cost of the extemporal ointment is 22.33 UAH. Its weight is 20.0 g.

It is known that factories use advertising services, the cost of which is also included to the price of the finished medicinal product. Pharmacies do not use advertising to sell their products. Thus we see that the ointment prepared at a pharmacy is cheaper than the ointment prepared at the factory.

Conclusions: Today, almost all the pharmacies have become sales outlets. But it is wrong because the traditional pharmacy is, first of all, the place of production of extemporaneous preparations, and just then the place for selling of finished dosage forms. Despite the significant development of industrial pharmacy and decrease of pharmacies making extemporal preparations, there is a growing need in preparation of all dosage forms. Extemporaneous production is extremely important for the pharmaceutical industry.

# TECHNOLOGICAL AND MEDICAL ASPECTS OF PRODUCTION OF DRUGS IN THE FORM Of RODS

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One of the important directions in the development of Biopharmaceutics is the choice of optimal type and composition of the dosage form (DF), which ensures high safety and therapeutic efficacy of the finished product (FP).

Unjustly forgotten and almost completely absent in the pharmaceutical market and in the arsenal of modern medicals are drugs in the form of rods, the use of which may be effective in the treatment of diseases of ear and number of urological diseases.

Topical application of drugs in the form of rods gives opportunity to effect directly on the affected target tissue avoiding, in most cases, fluctuations in the concentration of active substances in plasma, which is typical during the second administration of drugs that are excreted quickly, and to avoid primary passing through the liver that occurs after absorption in the gastrointestinal tract.

SPU, 1 ed., Ext. 2 contains general pharmacopoeial article "Rods", which provides a definition of the DF and the requirements of their quality control. The main reasons that hinder the use of drugs in the form of rods are technological, physical and chemical problems associated with their production and standardization, and problems of informational nature related to the coverage of the main aspects of drug therapy of various diseases using these drugs.

The purpose of this work is to highlight the important technological aspects of rods, and the development of methodological approaches of improving of technology and quality of the DF according to modern biomedical requirements.

Suppository are the closest to rods DF and they are the most studied in all aspects (structure, technology, test). So when we described this material the basic approaches to production and standardization of this group of drugs with emphasis on features that are unique for drugs in the form of rods were taken as the basis.

According to the Pharmacopoeia rods usually have the form of a cylinder with a pointed end and a diameter of 10 mm. Their length varies, but may by no more than 10 cm and a weight of 0.5 to 2.0 g.

The composition of rods, other than active ingredients, includes the base, which in most cases provides the necessary physical, chemical, technological and consumer properties of the DF. For the manufacture of rods used almost all bases used in technology of suppositories except gelatin-glycerol and soap-glycerine basis due to insufficient mechanical stability. According to the nature of the distribution of active ingredients in basis, rods can be in a variety of dispersed systems. Heterogeneous systems are formed in all cases where the active ingredients are distributed on the basis of the type of suspension or emulsion, homogeneous - when drugs are dissolved in the base.

By analogy with rods suppositories can be made by 3 methods: hand-formation, moulding and pressing.

The use of a method depends on the properties of the base, its ability to form a plastic mass, velocity of freezing and forming of structure. To obtain rods by hand-formation method, which is used mainly in the manufacture of extemporaneous, as the basis for cocoa butter is used only. Pressing and pouring into molds are the most versatile because they can be used in drugstores and pharmaceutical factories using almost all types of bases. Their physicochemical and technological properties can be adjusted by means of different groups of excipients (lubrication, increasing the hardness and melting point components, antioxidants, preservatives, etc.).

The determining factors that hinder the production of this group of drugs is the lack of social order, which can be formed by clinicians-consumers of this group of drugs, and lack of Pharmaceutical Manufacturers necessary equipment: special press tool for pressing rods and special shapes for their molding.

Thus, the solution of these problems together with urologists we see in the ground and create special forms for the production of rods and their molding technology development using different bases of different nature to treat the most common urological diseases.

**MODERN TOWARDS Of DEVELOPING Of INNOVATIVE DRUGS**

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During the last few decades special attention is paid to the creation of innovative medicines. Their introduction into medical practice increases the effectiveness of the treatment of diseases previously considered incurable, leads to the rejection of the use of less effective and obsolete methods of therapy, reduces the period of disability. Medication forms deserver special attention Among innovative products with improved pharmacokinetic parameters.

Currently, socially and economically important area in modern pharmacy is to expand the range of safe and effective medicines which, hase a tonic effect. Similar pharmacological effect to the greatest extent among adaptogenic plants. Milk thistle, Echinacea purpurea and others has, a group of phenylpropanoids plants provides this effect, causing also hepatoprotective properties of its products. Phyto extraction drugs in pharmaceutical preparations much attention, is attracted which combine the breadth of therapeutic action and the harmlessness at the reception, so that they can be assigned to the treatment of many chronic diseases, as well as health-care compositions. Gradually, ditterent drinks and concentrates for their manufacture are gaining popularity in the pharmaceutical market. Functional properties of plants or functional ingredients may be antioxidant, soothing, immunostimulant, increases vitality and exciting, and others. At the same time, of course, in no case organoleptic qualities should not suffer. Because functional drinks are primarily food, are not drugs. Many such beverages contain large amounts of synthetic flavoring taste, color or odor, which greatly reduces their effectiveness. For the preparation of beverages offered convenient and rational form of use of food supplements in the body in the form of a modern and comfortable shape to correct syrup. Proper selection of extractant and extraction process is of great importance for the pharmacological effectiveness, as individual components can alter the bioavailability of the active ingredients, and sometimes to conduct reduction or complete loss of therapeutic effect. To this the extractants as water, ethyl alcohol and alcohol-water solutions were studied, the raw material was crushed to particles passing through a 3 mm sieve.

The extraction was carried out by maceration. As a result of this study we saw that increasing the ethanol concentration increased content of flavonoids and anthocyanins, but organic acid content is reduced.

# THE URGENCY OF DEVELOPING DENTAL MEDICATIONS IN THE FORM OF MEDICATED CHEWING GUMS

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**Aim.** Nowadays, dental diseases are among the most common diseases in modern society.In thislist leading positions are occupied by inflammatory periodontal diseases.

**Materials and methods.** Recently, there is a tendency in dental practice of using an integrated approach for the treatment and prevention of diseases of the oral cavity. Enzyme preparations are one of the most interesting groups of medicines in this case, because of the variety of different directions of their multifunctional properties. In this work, we proposed a mixture of proteolytic enzymes of animal – lysozyme and vegetable origin – papain. At the present stage of development of dentistry among the selection of active pharmaceutical ingredients (APIs), another important issue is finding the optimal dosage form.Another important method is the possibility of localized delivery of drug, the duration of action and constant concentration of the active substance.

**Results.** Today such dosage form as a medicated chewing gum (MCG) is gaining popularity owing to its advantages and opportunity to be used for local treatment of diseases of the oral cavity and for systemic delivery by direct absorption through mucous membrane.To date, the relevance of the use of MCG in dentistry is proved by many researches which were carried out by many scientists all over the world. However, very small number of national scientific research devoted to the study of this dosage form.

In dental practice proteases, which include lysozyme and papain, are used in complex treatment of pyonecrotic, inflammatory and degenerative processes in the oral cavity. They have antimicrobial, antiinflammatory, antiedematous, wound healing properties and prevents the formation of plaque (both microbial and pigment).Moreover, an important role has their particular effect on the microflora of the mouth as one of the key factors in the emergence of dental diseases.Drugs based on lysozyme and papain are represented mainly toothpastes, foam for oral hygiene and tablets. Medicated chewing gums with this APIsdo not existin the pharmaceutical market of Ukraine.

**Conclusions.** All things consider, our further aim will be developing a composition and technology of dental medicament based on lysozyme and papain in the form of medicatedchewing gum.

# SUBSTANTIATION OF THE CHOICE OF THE BASE WHEN DEVELOPING A GEL

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When developing a soft drug for treating acne the choice of a base-carrier of medicinal substances is of great importance. First of all, this base must not overload the skin with the excess of fat and should have a moderate dehydrogenating power to provide the flow of the purulent exudate from the glands, besides, the drug itself should exhibit the antimicrobial, anti-inflammatory and reparative activity.

The combination of the propolis phenolic hydrophobic drug with the comlex therapeutic effect with the antimicrobial substance – azelaic acid will provide the multidirectional action on the affected areas of the skin.

Taking into account the previous studies on solubility of the propolis hydrophobic drug, which determined its solubility in polyethylene oxide-400 and propylene glycol, it is necessary to study the effect of the concentration of the given substances on the dehydrogenating power. The samples of 1.5% carbopol gel containing 30% and 60% of PEO and propylene glycol each, as well as their combinations of 15% and 30% each in comparison with “Skinoren” gel have been investigated.

As a result of the study of the kinetics of water absorption by the samples through a semipermeable membrane at the temperature of 37$^{o}$C it has been found that the sample with the PEO-400 content of 60% has the maximal dehydrogenating power at the level of 110% on the 24-th hour of observation. The least dehydrogenating power was observed in 1.5% carbopol gel containing neither PEO, nor propylene glycol (10%). “Skinoren” gel had an insignificant dehydrogenating power that was 35% on the 24-th hour of observation. Based on the data of the studies the samples of the gel base containing PEO-400 and propylene glycol of 30% each with the dehydrogenating power of 60% and 40%, respectively, have been selected.

# RELEVANCE OF CREATING A DENTAL GEL OF THE DENTAL GEL-BASED RAW MATERIALS OF NATURAL ORIGIN

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Currently periodontal diseases are the most complex and important issue that gets not only medical but also social significance. Due to the high prevalence of dental diseases we conducted an in-depth study of the range of gels used in the treatment of this disease. In the pharmaceutical market of Ukraine gels used in dental diseases are mainly represented by the combination of metronidazole with chlorhexidine. Only 30% dental gel as active pharmaceutical ingredients contain a combination of active ingredients of natural origin and synthetic substances. Gels, which include the active ingredients of purely natural origin are absent in the pharmaceutical market of Ukraine.

A study of the range of dental gels showed that the development of gel-based substances of plant origin is an important task. In developing such drugs should be taken to create composite formulations that affect different parts of the pathological process and thereby increase the effectiveness of treatment and significantly reduce the risk of possible complications.

Aloe vera is one such product exhibiting multiple benefits and has gained considerable importance in clinical research. Dental uses of Aloe vera are multiple. It reduces bleeding, inflammation and swelling of the gums. It is a powerful antiseptic in pockets where normal cleaning is difficult, and its antifungal properties help greatly in the problem of stomatitis, aphthous ulcers, cracked and split corners of the mouth.

Drugs from Oak bark also are perspective for the treatment of dental diseases. Oak bark is widely used in medical practice in Ukraine and in foreign countries, but mostly used in medicine galene drugs of oak bark (decoctions, infusions) extemporal production. At the Department of Drug technology of National University of Pharmacy dense extract of oak bark are developed and put into production. Anti-inflammatory, antimicrobial, hemostatic properties are represented from it pharmacological activity. According this pharmacotherapeutic activity dence extract of oak bark with a complex of plant polyphenols, tannins and flobafen should be also add into composition of stomatological gel.

The combination of dense extract of oak bark with Aloe Vera in developed dental gel are provides comprehensive complex therapeutic effect.

# STUDYING OF ASSORTMENT OF VAGINAL MEDICINAL FORMS FOR THE TREATMENT OF INFLAMMATORY DISEASES IN GYNAECOLOGY

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A serious medical problem in gynaecology is made by the inflammatory diseases of muliebrias, caused by different causative agents transmissible a sexual way, or caused by a heterospecific microflora.

The aim of our research was realization of review of literature and generalization of data on inflammatory gynaecological diseases, and also study of assortment of the medicinal preparations of home and foreign production, presented at the pharmaceutical market of Ukraine for local treatment of foregoing diseases.

Medical statistics establishes that for the last 5 the amount of inflammatory gynaecological diseases for the women of our country grew on 30 % and it resulted in such heavy consequences, as violation of menstrual cycle (50 %) up to his complete freezing, sterility (14 %), unmaturing of pregnancy (15 - 20 %) and other

In many countries of the world a height of inflammatory diseases is investigation of migration of population, urbanization, change of sexual behavior.

Inflammatory diseases differ on the remoteness of origin and sharpness of clinical displays (sharp and chronic), by a causal factor (bacteria, viruses, fungi, simplest and other), at the place of forming of pathological process.

The clinic of these diseases is characterized by permanent excretions from a vagina, that can be with a specific smell, itch of genital organs, making more frequent of urination, sickliness and burning at urination, pain, at sexual intercourse.

For treatment of inflammatory diseases of woman sexual sphere use mainly local and antibacterial medicines.

The nomenclature of the medicinal facilities registered in Ukraine according to the State register of Ukraine counts 73 preparations.

The most stake of vaginal medicinal facilities is made by suppositories (pessaries) - 45,2 %, vaginal pills - approximately 34,2 %, creams - 9,6 %, capsules - 7 %, gels - 2,7 %, solutions for vaginal application - 1,3 %. Pessaries are made most stake from all medicinal vaginal forms, because they are the most comfortable form in application and possess the expressed local action.

The indexes of inflammatory gynaecological diseases are high enough both in home medicine and foreign, therefore a necessity of study of problem of treatment of these pathologies is very actual. The successive decision of this problem will assist the improvement of reproductive health of women.

# DEVELOPMENT OF GELS ANTI-INFLAMMATORY AND ANALGESIC ACTION FOR THE TREATMENT OF SPORTS INJURIES

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Diseases and injuries of the musculoskeletal system (OPA) is one of the most pressing reasons for limiting physical activity of people with active lifestyles. Inflammation musculoskeletal tissues occur usually during or after exercise, including overload associated with professional sports, extreme or work, accompanied by long stereotyped movements in the muscles and joints.

Most common manifestations of inflammatory diseases and degenerative tendons, muscles and joints are considered pain, seizures, tumors and soft tissue inflammation near the joint that significantly affect the pathological process and the quality of life of patients. In most cases, the success of the treatment depends not only on the correct choice of a drug in terms of the symptoms described in the instructions for use and evidence-based research on the effectiveness of the drug, but in general also how we stand unable to compare the clinical impact of medications means to the individual characteristics of the patient.

In modern conditions in pharmacotherapy OPA to eliminate inflammation and ease pain commonly used NSAIDs. However, currently remains unresolved a number of questions regarding the details of the pharmacological effects and adverse side effects of drugs of this group. Despite the fact that the range of drugs for the treatment of above named pathology is quite diverse, analysis of the pharmaceutical market of Ukraine demonstrates the need for the development of the domestic market sector preparations for the local treatment of diseases of OPA and the relevance of developing, manufacturing and medical practice new home, highly efficient and harmless drugs Local destination.

We have conducted research on the development in the new integrated drug in gel form based on compounds of synthetic and natural origin, including bee products to treat injuries OPA, which are mainly found in sports medicine. The structure of the drug includes active pharmaceutical ingredients – propolis phenolic hydrophobic drug (Praeparatum Propolis phenohydrophobum) (RP № UA/4505/01/01, order Ministry of Public Health of Ukraine of 07.06.2011 № 337 g.), a local anesthetic, menthol and rosemary oil, rational concentration which was established by the analysis of contemporary literature. Conducted research also studied the structural, mechanical and technological properties in order to choose the basis for investigational gel, the choice gel creators and its concentration, and provided indicators of quality control was included in the project is designed to quality control the drug.

# CONCERNING THE USE OF READY-MADE MEDICATIONS IN THE PREPARATION OF MEDICINES IN PHARMACIES

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An acute problem in Ukraine today is preserving the function of industrial pharmacy and improving their work. State pharmacopoeia of Ukraine GFU 1.2. includes article 5.N.1. "Extemporaneous medicines", which contains a provision allowing for the preparation of medicaments for oral and topical use with ready-made medicines, if it is specified in the doctor's order.

The preparation of drugs in pharmacies with the use of medicines of industrial production has some significant advantages for industrial pharmacies, as most of them are not able to buy a large amount of various substances but ready-made products are much easier to acquire for pharmacies.

In addition, these preparations contain precise drug concentrations and conform to requirements of GMP for their production, which ensures the high quality of products prepared in pharmacies on their basis.

But along with this, there are several problems. Doctors, not knowing perfectly the whole range of ready-made pharmaceutical products, prescribe them with inaccurate names, form of release or dosage. This in turn causes a pharmacist either to return the prescription, or do complex recalculations for the preparation of the drug.

Therefore, educational work is necessary among doctors and managers of medical-care institutions on the nomenclature of finished drugs which can be used in the preparation of extemporaneous medicines in the conditions of specific pharmacies.

To inform doctors the publication of standardized formulations collection is advisable, indicating their purpose with certain diseases or to place this information in electronic form suitable for doctor's use.

# RESEARCH OF TECHNOLOGICAL PROPERTIES AND EXTRACTION OF THE BIRCH LEAVES

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Birch is a broadleaved deciduous hardwood tree of the genus Betula in the family Betulaceae. They are typically rather short-lived pioneer species widespread in the Northern Hemisphere, particularly in northern temperate and boreal climates.

Nowadays birch leaves preparations are used in cases of avitaminosis, edema, urinary bladder inflammation, atherosclerosis, kidney disorders and as cholagogic and expectorant. Leaves decoction is tonic and restorative and is useful for wet eczemas and climacteric neurosis. Birch leaves are used for flushing kidney and bladder stones, and for urinary infections. Preparations made of them are good for bronchitis, gastritis, stomach ulcers, edema and gout. Birch leaves are also valuable for various skin problems and help in coping with pathogenic microbes, fungi and inflammations. Finally they are known also to stimulate hair growth.

The dried leaves of the birch tree are typically used to make supplements taken by mouth. The leaves are often used to make teas and tinctures. The usual dose is 0.6 g to 9 g of dried leaves, in divided doses, per day.

The aim of this work is to investigate technological properties of the birch leaves and factors of the extraction process.

Birch leaves were crushed and sieved to obtain a fraction with a size of 1-3 mm. It is known that this is the optimal particle size for extraction. Then the relative density - 1,28 g/ml, the bulk density - 0,16 g/ml, the porosity raw - 0,40, the free volume of the plant layer - 0,83, the absorption coefficient - 2,3 ml/g, the humidity - 7,15%, the flowability – poor value, the content of extractives - 24,23% were studied for this fraction.

The next step was to justify the choice of extractant for subsequent extraction. Based on the physico-chemical properties of the active ingredients of birch leaves we have chosen the 50% ethyl alcohol as an extractant.

As an extraction method, we chose percolation. This method has advantages over the method of maceration, extraction with reducing the time for pharmaceutical companies have percolators for this process.

According to the results of determining the content of extractives in the samples determined that the optimal conditions for the extraction in the laboratory is the infusion time – 24 hours, percolation time - 3 hours, the ratio of raw material - the extractant – 1:12.

# SELECT LUBRICATING COMPONENTS IN CAPSULE FOR TREATMENT URINARY TRACT INFECTIONS

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Urinary tract infections are the second most frequently form of infectious diseases, second only to respiratory infections. A major problem is recurrent urinary tract infections in patients who have ever suffered from acute cystitis. This problem makes a pronounced impact on the quality of life of patients and results in significant medical costs. In the global standards of treatment of urological infections direction proposed introduction regimens herbal products that complement the basic therapy, enhancing the action of antibiotics, reducing the risk of relapse and can be used as a prophylactic measure without the threat of negative effects on the body. Abroad are popular drugs based on cranberry and hibiscus to reduce the frequency of lower urinary tract infection due to the large number of organic acids and proanthocyanidins that change urine pH and show antyadhezive effects.

The aim of this work was the development of technology and capsules based on medicinal plants for the treatment and prevention of inflammatory urological diseases and the optimal choice of lubricant to ensure the process of filling capsules.

Materials and methods. As an active drug components used flowers hibiscus , cranberry fruit, herb chamomile and equisetum. To provide the necessary technological parameters added to a mixture of lactose monohydrate and had a wet granulation using 20% aqueous polyvinylpyrrolidone. As used lubricant magnesium stearate and aerosil. We determined the turnover, bulk volume granules before and after shrinkage, moisture content in the compositions. The technological parameters were determined by methods SPU.

The obtained results. To improve the yield rate and fix problems when filling capsules from plant material of the capsule weight added several types of lubricants. When using magnesium stearate granules turnover increases, but when administered in capsule weight aerosil its fluidity demonstrates better performance. What does the presence of colloidal silica in mass to 1.0% of its turnover increases, while increasing concentrations slowly decrease. High porosity allows syloyidu absorb moisture, which is important when used in mass of a drying plant material.

Conclusions. The structure was introduced filler caps lactose monohydrate, polyvinylpyrrolidone binding component and lubricant aerosil (in the amount of 1%), which provides optimal technological parameters necessary for filling capsules.

# EXAMINATION OF BIOLOGICAL PROPERTIES OF EYE DROPS "PROPOLIS"

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The bioavailability and the specific activity of eye drops was investigated in accordance with the MSS.

The object of this study is to determine the degree of exposure to the toxic eyedrops hydrophilic phenolic fraction of propolis on the weight of the animals, and the blood much less important organs gently with the route of administration - intravenous , since the commonly used method of applying eyedrops (instillation) was not found their side action.

For the experiment were selected 12 rabbits "Chinchilla", six of which served as controls. Three rabbits were administered 0.5 % solution, and the other three - solution of 1% concentration. Eye drops were administered to rabbits in a volume of 2-2.5 ml per 1 kg of animal body weight (within 10 sec - 1 mL) once per day. Blood sampling was carried out in dynamics before administration , then after 1 hour, day 10 and 20 days.

Biochemical and morphological analysis of the blood of rabbits during prolonged administration of 0.5 and 1% propolis solutions, eye drops was performed by the conventional method.

The data show that the eye drops of propolis when administered intravenously for 20 days did not have a material effect on the morphology of red blood cells . The number of erythrocytes and hemoglobin in the blood is not changed, and erythrocyte resistance ESR are normal. The drug has no toxic effect on the morphological composition of white blood animals. Besides that long-term intravenous administration in a double amount (1% solution) rabbits № 4-6 also does not increase the number of leukocytes in the blood and does not significantly affect the leukocyte formula. Harmlessness of 0.5 and 1% solution of propolis and proved virtually unchanged in blood sugar, total protein and its fractions.

The weight of animals in parallel, is also an important indicator of drug

indifference towards macroorganism.

The obtained results led to the conclusion that the eye drops do not show statistically propolis toxic effect on animal weight change even when intravenously ($P > 0.5$).

For a more objective assessment of the safety of eye drops "Propolis" was held Pathological and histological examination of the internal organs of animals.

At the end of the experiment (after 20 days), rats were sacrificed by decapitation, and were subjected to analysis of brain, liver, spleen, gastrointestinal tract, kidneys, heart, lungs.

Effect of 0.5% solution of hydrophilic phenolic fraction of propolis for intravenous administration (in grams) weight to rabbits

| № rabbits | Mass rabbits ( in g) before administration | After administration of the drug | | |
|---|---|---|---|---|
| | | 1 day | 10 days | 20 days |
| 1 | 1850 | 1840 | 1870 | 1910 |
| 2 | 1930 | 1925 | 1910 | 1910 |
| 3 | 1720 | 1730 | 1700 | 1770 |
| 4 | 2020 | 2035 | 2050 | 2090 |
| 5 | 1500 | 1495 | 1500 | 1330 |
| 6 | 1800 | 1800 | 1790 | 1820 |
| M | 1803 | 1803 | 1803 | 1803 |
| | 7,0 | 7,9 | 8,5 | 9,3 |
| | - | 0,5 | 0,5 | 0,5 |

Studies have shown that eye drops with the hydrophilic fraction of propolis did not cause toxic, inflammatory, degenerative changes or from the tissues of the eye or the internal organs.

The study of the specific activity of eye drops found their anti-inflammatory, antiviral, restorative, radioprotective effect.

# SAPROPEL - THE PERSPECTIVE RAW MATERIAL FOR MEDICINES AND COSMETICS

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Sapropel – substance of biological origin, that is formed under water, on the bottom of freshwaters from residues of planktons and bentons organisms, involving bacterial processes that occur in the surface layers of sediments at low oxygen access. Sapropel consist of silt solution, skeleton and colloidal complex. Silt solution consist from water and substances dissolved in it – mineral salts, low molecular weight organic compounds, vitamins, ferments. Skeleton of the sapropel represents the remains of plants and animals, colloidal complex – complicated organic substances, which is providing jelly-like consistency for sapropel.

Sapropel unique naturally occurring substance that finds its use as a source of organic minerals in traditional mud therapy, cosmetology and agriculture.

Given the wide range of pharmacological properties of sapropel – antimicrobial, anti-inflammatory, antioxidant, detoxic effects there is creation of medical and cosmetic products based on native raw materials and extractions from sapropel.

We was investigated chemical composition of sapropel from Pribich lake Shatsky district of Volyn region. Was indicated the presence of a wide range of amino acids, fatty and organic acids, microelements. Was getting aqueous, spirituous and oily extracts of sapropel. Was defined anti-inflammatory, reparative and antimicrobial activity of developed extracts. Was defined humidity, fractional composition, technological properties of native materials (bulk, volume, specific weight, porosity), was investigated dependent technological properties from humidity. Was soundly expediency of using native sapropel in cosmetics.

For the results of physico-chemical, structure-mechanical and microbiology researches was developed the composition of cosmetics masks for different types of skin. The using of the gelling agent was soundly for increasing adhesion to skin surface.

Research shows that in addition to the cost, an important factor for Ukrainian consumers is the naturalness of cosmetics. The demand for cosmetic products based on natural ingredients is growing every day. More and more consumers want to use quality products, which include natural ingredients and no synthetic substances.

There is no cosmetic or drugs on sapropel, so it is very actual topic.

# THE DEVELOPMENT OF LABORATORY TECHNOLOGY OF THE CONCENTRATED SOLUTION FOR HAEMODIALYSIS

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**Topicality.** The prevalence and incidence rates of kidney diseases are high in Ukraine and have a tendency to increase. The increase of providing patients with renal replacement therapy suffering from chronic kidney disease is one of the most important questions of the current nephrology. The treatment with methods of kidney replacement therapy (haemodialysis, peritoneal dialysis, and kidney transplantation) is extremely expensive. On 1.01.2013 there were 4952 patients registered in Ukraine who are treated by hemodialysis (HD). The HD procedure requires large amounts of a dialysis solution for 1 patient (about 120 L per procedure HD, 3-4 sessions per a week). It is necessary to have a wide range of available HD solutions to meet specific patient needs. The development of the technology and the introduction of solutions for HD in local manufacture is a perspective direction of pharmaceutics.

**The purpose of the study is** to develop laboratory technology of concentrated acid solution for bicarbonate HD.

**Research methods used in the work:** analysis, systematization, potentiometric, trilonotythrometrical, microbiological.

**The results and discussion.** Laboratory batches are employed for the development of drug products according to the Guide "Validation process" 42-3.5:2004. These batches are made at the initial stages of pharmaceutical development. The purpose of the production of the first laboratory batches of proposed composition solutions was: the experimental trial of the proposed composition and the relevant formulas for calculation of components weights, and laboratory technology; elaboration of quality control methods for components assay, determination of bacterial endotoxins for laboratory series, and quantitative enumeration of mesophilic bacteria and fungi that may grow under aerobic conditions. Because dialysis solutions are used in large volumes, it is advisable to produce them in the form of concentrated solutions. According to the European Pharmacopoeia, concentrated solutions for HD is non-sterile solutions, unless otherwise specified by the manufacturer, however, they must have a minimum level of microbiological contamination because they have a non direct contact with the blood and are used in large volumes. According to the the Guide "Water quality for use in pharmacy" purified water may be used in the

production of concentrated solutions for haemodialysis, if it is satisfactorily tested for bacterial endotoxins. In the clear areas of educational and industrial pharmacy of Lviv Medical University a laboratory batch of the acidic concentrated solution was producted. Water for injections of pharmacy production was used for the preparation of the acidic concentrated solution. For trial of the laboratory technology the composition of the acidic concentrated solution was used which after the appropriate dilution (1 L of acid concentrate : 1,225 L of 1 M solution of sodium bicarbonate : 32,775 L of water) gives a dialysis solution of the following ionic composition in mmol/l: $Na^+$ -138, $K^+$ - 2, $Mg^{2+}$ - 0,5, $Ca^{2+}$ - 1,5, $CH_3COO^-$ - 3.0, $Cl^-$ - 109, $HCO^{3-}$ - 32. The concentrated solution was prepared by dissolving salts of sodium chloride, potassium chloride, magnesium chloride hexahydrate, and calcium chloride hexahydrate with following adding glacial acetic acid ice at the room temperature. This solution was filtered and packed in glass bottles of 50 ml without further sterilization. Acetic acid in the composition of this solution performs the role of a pH regulator, and provides the necessary the pH of the dialysis solution (about 7.3) after dilution to prevent precipitation of calcium and magnesium carbonates. The pH of the obtained concentrate is of about 2.5. In the study of antimicrobial activity according to the pharmacopoeial method of the State Pharmacopoeia of Ukraine (SFU 1.4) 5.1.3 "the effectiveness of antimicrobial preservatives" it was found that the investigated concentrated solution exhibits antimicrobial activity against the following strains of microorganisms: Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, Candida albicans, Aspergillus brasiliensis. It might suggest that this antimicrobial activity is caused by the very low pH. In accordance with the requirements of the SFU 2.6.12 "Microbiological examination of non-sterile products: microbial enumeration tests" method of determining the microbiological quality of the concentrated solution for HD was developed, set its suitability. Having used this method it was determined that the total aerobic microbial count (TAMC) is less than 1 (<1).

The method of determining the sum of the amount of calcium and magnesium ions was elaborated. This method helps on the stage of laboratory technology to establish their quantitative content in the absence of atomic absorption spectrophotometer.

**Conclusion.** During research the laboratory technology of the concentrated acid solution for HD and methods for determining the microbiological quality, antimicrobial activity, the quantitative content of the sum of the amount of calcium and magnesium ions were developed.

# RESEARCH OF SYRUPS VISCOSITY DEPENDING ON THE CONCENTRATION OF HYDROXYMETHYLPROPYLCELLULOSE

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One of the major tasks of pharmaceutical science is the creation of new medicines. Syrups are most convenient dosage form for internal application for children and adults. Such popularity of syrups explains in addition biopharmaceutical aspects related to the regularity and absorption speed medicinal substances, their distribution and excretion, exception pain when taking drugs, metering accuracy.

Medicinal syrups is concentrated solutions of sugar, to which was added active pharmaceutical ingredients and auxiliary substances, such as fillers, sweeteners, preservatives, dyes, stabilizers, pH regulators and flavors.

Syrup bases are presented by solutions of sucrose, polyol or their mixtures. Sucrose is standard of taste purity and sweetness. All other substances, having sweet taste, called - sweeteners.

The study of structural and mechanical properties of syrup is necessary for the development and improvement of production processes, determining the optimal conditions for storage. Rheological properties affect on therapeutic and consumer indicators such as the release of medicinal substances, dosage and stability.

The aim of our work was to study the indicators of sucrose syrup viscosity depending on the concentration of hydroxymethylpropylcellulose.

Previous research physical and chemical and technological parameters of sucrose samples was found that stable high indicators samples of granular sucrose under the brand name Compri Oh, that is white granules with good flowability properties; different by composition (pure sucrose or mixed with other auxiliary substances), structure, particle size and bulk density. So, for samples research was used sucrose syrup mark Compri O, solution of which was adjusted to the desired viscosity by thickener HPMC, that dissolves in cold water and forms a transparent liquid solution. Characteristics of HPMC include good moisture retention, thickening, adsorption and surface activity, has no taste and smell, are not toxic.

The objects of study were Compri O samples with HPMC concentration of 0.5%, 1%, 1.5%, 2%, 2.5%, 2.5%, 3%.

Viscosity measurements were carried out on viscometer MYR V2R 3000, by the Brookfield method. Temperature of measurement was 20˚C. Recorded readings - viscosity and temperature.

The research results show that the viscosity of syrup with 60% content of Compri O is 40 mPas. HPMC was injected 0.5%, 1%, 1.5%, 2%, 2.5%, 2.5%, 3% Adding of 0.5% HPMC allowed to increase the viscosity of almost 20%. Next adding of HPMC within the limits of 0.5% allowed to increase viscosity in 4 times (165 mPas), without changing appearance and consumer characteristics.

The results suggest that for further research should be used HPMC in the amount of 3% of the total weight.

**STUDY EXCIPIENTS REQUIRED TO CREATE GRANULES BASED PERGA**

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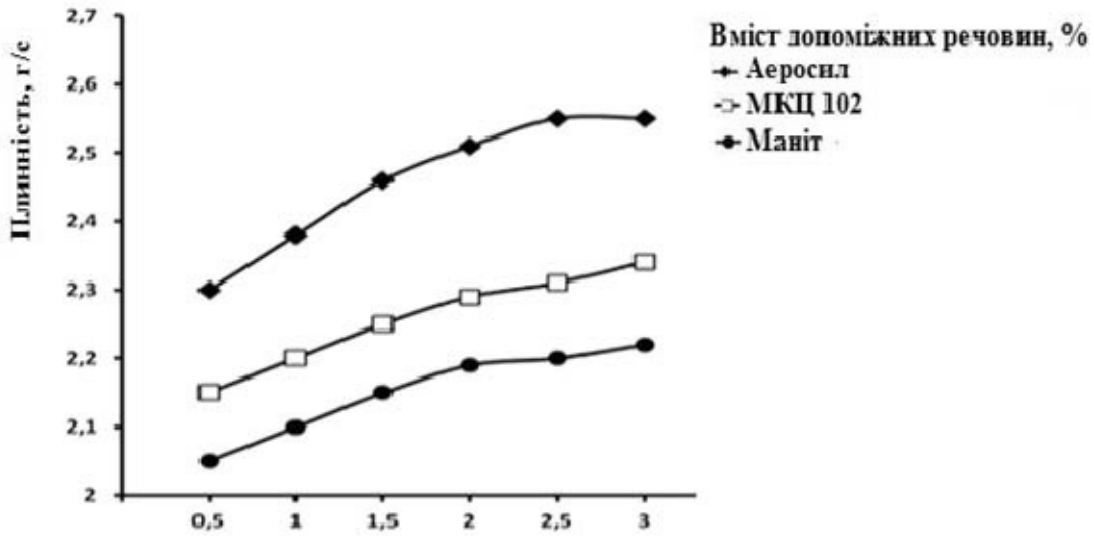
Perge - product processing bees pollen (bee pollen).

To create pellets with high properties should be included in the composition of the drug friction material to improve strength, such as aerosil, microcrystalline cellulose and mannitol.

Through the use of these substances have achieved a significant improvement in yield mix. The results of research are presented in the picture.




The dependence of yield cerago content excipients .

It should be noted that management is adding the drug excipient such as succinic acid. The substances positively affect the absorption of active substances developed the drug, and improves immune-modulating properties cerago, which is very appropriate, as pellets of ambrosia be used as a drug to boost the body's immune.

In a filler in the manufacture of pellets we use lactose, which also serves as an additional and sweetener.

In the future we plan to conduct a study of the physicochemical properties of the granules with ambrosia to create high-quality immune-modulating drug action.

# STUDY THE ASSORTMENT OF PREPARATIONS TO ANTIFUNGAL AND ANTIMICROBIAL ACTION

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Today the vital problem of midwifery, gynecology, venereology and urology are urogenital fungus and bacterial infections. This is connected with the wide acceptance of these illnesses, the frequent complications and the relapses.

The preparations for the local application appoint for treating the infectious diseases in midwifery and gynecology together with the preparations of system action. Local treatment is more effective, and the development of side effects considerably decreases.

We carried out the study of the assortment of the preparations of antifungal and antimicrobial action in the drugstores g. Kharkov. For treating the pathologies pointed out above use various forms: tablet (18,7%), capsule (16,4%), pessaries (17,2%), creams (14,2%), solutions for infusions (6,7%), ointment (5,2%). Preparations of domestic manufacture on the market g. Kharkov they comprise 31,3%, foreign production - 68,7%. Among the foreign firms the firms of India (26,9%), Germany (6,7%), Russia prevail (5,2%).

The assortment of the domestic preparations in the form of vaginal suppositories represented it is not very wide, but foreign preparations little are accessible through the high cost.

The preparations of the group of the azoles are the most effective antifungal preparations for the local application: bifonazol, klotrimazol, ekonazol, ketoconazole, the group of allylamines: naftifine, terbinafine and other.

Are most widely represented the preparations, into composition of which as the acting substances enter flukonazol (21,6%), klotrimazol (14,2%), terbinafin (12,7%). The preparations, into composition of which enter the substances of ketoconazole, nystatin, itraconazole, ornidazole occupy from 5 to 10%. The preparations, into composition of which enter the substances of sertaconazole chlorhexidine and bifonazol occupy of about 2,2%. The preparations, into composition of which enter substances of naftin, nitrofungin, synthomycin, isoconazol occupy near 1,5%.

Taking into account the variety of microflora (mikst- infection), their resistance to the traditional chemotherapeutic medicines, rational appears the creation of preparations with the active pharmaceutical substances, which have the wide spectrum of antimicrobial action, which will seize both the fungi and bacteria.

# RESEARCH OF THE EXTRACTION PROCESS IN THE PREPARATION OF CAMEL THORN DENSE EXTRACT

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Currently, an integral part of natural resources of Kazakhstan consists of wild medical plants. In many cases medical herbs is the only source of raw material for the preparation of dosage forms with high therapeutic activity. One of the known plants used in folk medicine of Kazakhstan, is a wild plant Camel thorn. Camel thorn (Alhagi Kirgisorum Schrenk) - is a plant of the pea family, popularly called Alhagi or Yantak. In medicine is used aerial parts (herba) of camel thorn, less than fruits and roots.

In official medicine camel thorn tea is used as a diuretic and diaphoretic. Sometimes it may used as drink at cough treatment. Often tea or fresh juice drink at gastro-intestinal diseases, mainly at chronic diarrhea and dysentery. Extracts from the aerial part of Camel thorn have antimicrobial activity, also bactericidal effect they have on streptococci, staphylococci, dysentery bacillus. Decoctions successfully used as a throat rinse at acute tonsillitis. In folk medicine decoction of camel thorn sometimes are used for the treatment of hemorrhoids (bath, washing) for topical treatment of eczema, abscesses, festering wounds and ulcers (washing, compresses). In the clinical setting decoction treated patients colitis, dysentery, used for gastric ulcer and gastritis, liver disease, as a choleretic, astringent, sometimes prescribed for colds and coughs immoderate.

Herbs of Camel thorn included in the State Pharmacopoeia of Kazakhstan.

Thus, is relevant obtaining of a dense camel thorn extract and study its chemical composition, microbiological and pharmacological properties, in order to develop drugs of different pharmacological groups.

Dense extract prepared according to standard technology, which provides for the liquid extract of vegetable raw materials, followed by evaporation to a thick. Taking into account physical and chemical properties of the basic active groups contained in the raw materials (flavans and tannins) as an extragent was chosen the

alcohol-water mixture. To determine the optimal concentration of the water-alcohol mixture, conducted research of the yield of extractives from the raw material by the standard procedure SP USSR XI, vol. 1. The dry residue in obtained extracts determined by the method of USP 1 ed. 1. Was investigated extracting the activity of 40%, 50%, 60%, 70%, 80% alcohol and purified water. As a result of studies, it was found that the maximum yield of extractives from camel thorns herb provides use of 70% aqueous-alcoholic mixture.

The next step was to produce a liquid extract, for this purpose we have chosen the classic method of liquid extracts and tinctures producing - percolation or filtration extraction. The essence of the method is that the raw material is loaded into the percolator and poured by extragent to form a "mirror", then there is standing out during the one day. For extraction was selected fraction of camel thorn herb with size of particles 1 mm. After the infusion process is taken place the selection and simultaneous feeding of raw material by the extragent with the same speed to create a high difference in concentrations in the extraction medium, which is the driving force of the extraction process. In our case percolation rate was 10 drops per 7 sec, 63 '. In order to establish the dynamics of the extraction process, and therefore the amount of extragent required for full exhaustion of raw materials were selected from the samples in the amount equal to the weight of the loaded material. The dynamics of the extractive substances yield from the selected samples determined by calculation of the dry residue.

We have found that for complete exhaustion of raw materials needed to use a ten-fold amount of extragent relative to the weight of the raw materials, the absorption coefficient is 1.25.

The resulting camel thorns liquid extract is concentrated using a laboratory rotary evaporator until the water content in the dense extract no more than 25%.

Thus, the dense extract obtained after standardization will be used for development of medicines of various pharmacological groups.

Research and production of liquid and dense extract is relevant and promising. Interest to camel thorn extract explains by a wide range of its biological action, widespread in nature and insignificant or absence of toxicological properties, i.e. the plant is not harmful, because until now there was no evidence of any adverse effects.

# ABOUT NECESSITY OF EXPANDING THE RANGE OF OINTMENTS FOR THE TREATMENT OF DERMATITIS WITH FUNGAL INFECTION

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At present the problem of treatment of allergic skin diseases is of particular relevance in connection with the growing number of patients and an increase in the prevalence of severe and occurring resistant to treatment of dermatitis.

Dermatitis is a group of inflammatory and allergic diseases that can affect the scalp, smooth skin of the body, nails, and soles of the feet, groin and face. This is the most common human pathology that occurs at any age and in almost all countries.

Quite often, today there are allergic dermatitis complicated by a secondary fungal infection. The main agents of this form of the disease are different types of Trichophyton, Microsporum, and several species of Epidermophyton, united under the common name of dermatophytes. Also, there are skin lesions by fungi of the genus Candida.

Parasites multiply in the skin and its appendages. This disease is characterized by itching; often large bright red, scaly plaques clearly limited less than 5 cm in diameter, located singly or in groups.

Today in Ukraine there are a variety of drugs with anti-allergic and with anti-fungal action, but the range of medicines with combined pharmaceutical action is limited only by one name - ointment “Fladeks”.

Treatment of allergic dermatitis complicated by a secondary fungal infection usually begins with the use of local drugs, namely, ointments, creams, solutions. Soft medicines provide the elimination of inflammatory and allergic processes, eliminate or reduce the symptoms of the disease. Drugs in the form of ointments have fewer side effects and act directly on the affected skin.

Thus, the aim of our future work is to develop an anti-allergic and anti-fungal ointment with such components:

- Licorice extract - natural phytoestrogen, which has an antimicrobial effect, but also in its composition contains glycyrrhizin acid that has anti-allergic properties. Its content also provides a skin-soothing effect.
- Terbinafine hydrochloride - allylamine antifungal agent whose mechanism of action is associated with inhibition of production of ergosterol.
- Lavender essential oil, which has antiseptic and antibacterial properties. In addition, promotes active wound healing effect.

# DEVELOPMENT OF COMPOSITION OF EXTEMPORANEOUS SPESCIE FOR TREATMENT OF MASTITIS

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Mastopatia is a dishormonal breast disease, which in breast tissue is proliferation of connective and glandular tissue from forming seal or formation of cysts of various sizes.

The main role in the occurrence fo mastitis owned of deficiency of progesterone and estrogen levels increase with the development hyperestrogenii, resulting in proliferation of the epithelium of the alveoli, ducts, connective tissue. Some role can be played by increased of production of prolactin, which regulates growth, development and functional state of the mammary glands.

Women with moderate cyclical or permanent form of mastitis and diffuse fibrous - cystic changes in the structure of the breast conservative therapy is carried out using both hormonal therapy and nonhormonal therapies.

In the treatment of mastitis commonly used herbs that have diuretic, sedative, hypotensive effect.

To date, topical herbal medicine market research and collections. Primarily, this is due to the increasing interest of the population to drugs based on plant material. The second factor is the population distribution of national traditions of herbal remedies. The basis for this choice is more active attitude of the population towards their own health and the risks involved in the use of synthetic drugs. And, of course, not to mention the fact that the modern consumer is increasingly inclined to buy herbs and charges not only for treatment but also for prevention of disease.

The aim of our work was to develop a multi-part collection for use in the treatment of mastitis.

During the work the literature data on the etiology, pathogenesis and pharmacological correction of mastitis was examined: market research domestic market hormonal, non-hormonal drugs and medicines was conducted. Analyzing the results of studies have found that consumers Ukraine under-economically affordable medicines for complex treatment of this pathology.

In view of the above, we theoretically and experimentally proved composition of multicomponent extemporaneous spescie for treatment of mastitis. Using modern technological methods of influence of the degree of grinding, packaging type and time insisting on quality indicators of developed spesie were studied.

# RELEVANS OF DEVELOPMENT OF COMBINED ANTIDIABETIC PREPARATION

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Solving the problem of the treatment of diabetes mellitus (DM) type 2 and the associated metabolic syndrome (MS) is an important task of modern medicine and pharmacy

To date, there is no consensus about the root causes of MS: is this state caused by genetic or develop exclusively due to the action of environmental factors.

A number of researchers believe that the development of MS due to the existence of one or a group of genes which interact with each other, which can simultaneously stimulate the development of all its components. However, despite significant advances in genetics and molecular biology, the question of the influence of genetic factors on the risk of developing MS and features of the course are still poorly understood

Acuteness of the problem in the first place due to the prevalence of MS (up to 20% of the population and 70% among patients with type 2 diabetes), which is defined by WHO epidemiological in nature, and secondly - the limited range of medicines that affect the basic pathogenetic links of the disease, and namely the elimination of insulin resistance (IR). Furthermore, derivatives of dimetilbiguanid (metformin) and thiazolidinedione (rosiglitazone), which increase insulin sensitivity due to side effects have limited application and therefore cannot solve the problem.

Given the many manifestations of MS component, promising event pharmacotherapy of the disease is the use of combined antidiabetic drugs on the basis of metformin and rosiglitazone without or in combination with glibenclamide. However, such drugs have some inherent side effects of their active substances.

In view of the above, development of the combined antidiabetic is the actual drug with metformin and medical substance the original diacamph, which developed in pharmacy, is the actual.

Due to its low toxicity and spectrum of pharmacological properties of diacamph, his pharmaceutical composition with metformin may have certain advantages over precursors of drugs.

# STUDY OF THE DEPENDENCE OF THE EMULSION DISPERSION FROM THE USED 1ST KIND EMULSIFIER AND EMULSIFICATION CONDITIONS

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In recent years, pharmaceutical technology has entered a new stage of development, characterized by intensive development of new adjuvants that enhance the technological properties of dosage forms. Increasing attention of specialists in creating soft dosage forms is attracted by emulsion systems. Creams which are based on emulsion systems have the cosmetic advantage over conventional ointments, into the creams may be incorporated both hydrophobic and hydrophilic nature substances with controlled release.

We have studied the emulsifying ability of 1st kind emulsifiers olivem 1000 emulpharma 165, mulsifan B20, ercawax BM1, Emulpharma ®V, Erkalan 75. As the 2nd kind emulsifier used cetostearyl alcohol. Oily phase - vaseline oil 20%. In all the samples emulsifying mixture consisted of 30% of 1st kind emulsifier and 70% of 2nd kind emulsifier. Samples were emulsified at a temperature of 65-70°C on a laboratory homogenizers POLYTRON 2500 E and POLYTRON 3100 D, of the "KINEMATICA AG" company (Switzerland). This equipment is characterized by dispersing due to different design of headpieces. Dispersing occurs through the rotor-stator. Rotating rotor creates a vacuum, the sample falls into the center of the system and is dropped to the periphery, passing between the teeth of the stator. Between stator and rotor (the annular gap) on the product act substantial tangential braking forces and radial acceleration. Individual droplets disintegrate and thus are reduced in size. As a dispersion result microscopic homogenized emulsions are obtained.

Samples of emulsions prepared in this way were stable, homogeneous creamy masses that were subjected to rheological studies on Rheotest 2 device (Germany) using a set of N cylinders, and dispersity analysis using a microscope Lyumam P1.

As a result of studies it has been found that the properties of emulsions directly depend on the type of 1st kind emulsifier and emulsification conditions. Emulsification of samples on POLYTRON D 3100 homogenizer results in emulsions of more uniform composition of the oil phase particles, which density is somewhat higher than in the homogenization on POLYTRON 2500 E.

# RATIONALE FOR OINTMENT ANTIMICROBIAL ACTION FOR THE TREATMENT OFTHE FIRST PHASE OF WOUND HEALING

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According to the Wound Healing Society, wounds are physical injuries that result in an opening or break of the skin that causes disturbance in the normal skin anatomy and function. They result in the loss of continuity of epithelium with or without the loss of underlying connective tissue. Wounds represent a significant burden on the patients and health care professionals worldwide. They not only affect physical and mental health of millions of patients but also impose significant cost on them. Current estimates indicate that worldwide nearly 6 million people suffer from chronic wounds.

Unhealed wounds constantly produce inflammatory mediators that produce pain and swelling at the wound site. Wounds are a substrate for infection and prolong the recovery of injured patients. Chronic wounds may even lead to multiple organ failure or death of the patient.

Many medicinal plants have been reported to possess wound healing activity and found useful in the treatment of wounds. This article outlines types of wound, factors affecting wound healing, mechanism of wound healing and properties of some medicinal plants that exhibit wound healing activity. The paper presents discussion of some patents relating to herbal products for wound healing management.

Medicinal plants are important sources of new chemical substances that have beneficial therapeutic effects. Extensive research has been carried out in the area of wound healing management through medicinal plants. Recent studies with significant findings involving Alternanthera sessilis, Morinda citrifolia, Lycopodium serratum, Sesamum indicum, Catharanthus roseus, Cecropia peltata, Euphorbia hirta, Ginkgo biloba, Clerodendrum serratum, Pterocarpus santalinus, Lawsonia alba, Napoleona Imperialis, Kaempferia galangal, Radix paeoniae, Prosopis Cineraria and Trigonella foenum-graecum and etc are emphasized here. The growing interest in herbal medicine stimulates the expansion and renewal of the range through the introduction of scientific medicine traditional medicine plants and the development of new herbal remedies based on them. Each herb is a source of essential to human body.

Given the above, creating a soft dosage form with phytoextracts and essential oils, meets all modern requirements for drugs for the local treatment of wounds in the first phase of wound healing and other diseases is important.

# UNTERSUCHUNG DER EIGENSCHAFTEN VON SILICONEMULSIONS

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Zu den viel versprechenden Gruppen Hilfsstoffe für die Herstellung von Cremes wurden berühmte Silikone und deren Derivate. Als Emulgatoren sorgen Silicone für optimale Orientierung von Molekülen an der Grenzfläche aufgrund der großen und flexiblen Molekülketten räumlichen Abstoßungsmechanismus beide Phasen. Als Komponenten der Ölphase, Silikone in der Lage, lange auf der Hautoberfläche zu bleiben, um Schutzfilm, ohne die Atemfunktion der Haut und das Gefühl der Klebrigkeit zu stören erstellen.

Das Ziel der Arbeiten war es, die Eigenschaften von Emulsionen auf Basis von Silikonpolymeren studieren.

Die Forschungsobjekte sind Emulsionen von SiliconpolymerenDimethicon und Cyclomethicon hergestellt und Emulgator PEG / PPG-19/19 Dimethicon und S13-16 izoparafin (and) izoparafin S10-13).

Emulsionen wurden unter Verwendung der folgenden Technik: Emulgator mit Silikonpolymer bei Raumtemperatur (Ölphase) und die resultierende Mischung vermischt wurde bei konstantem Rühren langsam gereinigtem Wasser zugesetzt. Sensorischen und sensorischen Eigenschaften, die thermische Stabilität, die kolloidale Stabilität, pH-Wert: Die resultierenden Proben wurden auf folgende Parameter getestet. Während der Serie von Proben wurde uns von der weiteren Forschung durch Trennung beim Kochen oder durch schlechte Testergebnisse auf thermoelektrische oder kolloidaleStabilität entfernt. In stabilen Proben, die strukturellen und mechanischen Eigenschaften in Brookfield-Viskosimeter HB DV-II PRO (USA) untersucht wurden. Im Zuge der Studie Proben wurden stabile Siliconemulsionen und dicke flüssige Konsistenz, die eine zufriedenstellende Verbraucher aufwies: leicht hinterlegt, verteilt und hinterlässt keine klebrigen Gefühl.

Die Ergebnisse ermöglichen es uns, Daten-Emulsion als Basis für die Erstellung von topische Medikamenten und Kosmetika empfehlen.

# TECHNOLOGICAL AND PHYSIC-CHEMICAL ASPECTS OF INTRAVAGINAL GEL WITH LACTIC ACID

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Summary.

Lactic acid is the natural content in the vagina. This acid is the result of vital activity lacto and bifidobacteria in vagina.

Lactic acid is a natural antibacterial barrier for pathogenic and transient microflora. The purpose is research the optimal concentration of the lactic acid (pH 4,0-4,5). As well the impact of lactic acid on the physic-chemical, rheological and technological properties of the different gels base.

Materials and methods.

Were selected for study such a gel base: apple pectin, hydroxyethylcellulose, carbomer, xanthan gum, sodium alginate. Lactic acid is introduced into the gel base as a dilute solution (1:50) in different concentrations (0.1%, 0.2%, 0.3%, 0.5%).

The organoleptic properties evaluated by visual analysis.

Consumer`s properties were evaluated by application to the skin. Rheological properties were determined using a viscometer HB BROOKFIELD DV-II PRO (USA). Determination of pH was researched on ionometry PH-150 MI.

Results.

Gel bases after the addition, lactic acid (0.1%, 0.2%, 0.3%) did not alter it`s organoleptic properties (color, smell, consistency), except carbomer bases - observed liquefaction system. Gel base did not lose stability - remained thermally and colloidal stability. Structural viscosity decreased with increasing percent acid.

The most acceptable performance structural viscosity at a concentration of lactic acid 0, 1%, 0.2%, 0.3%. pH 4.0-4.5 produces lactic acid in a concentration of 0.2%. Changing consumer properties observed when added to lactic acid based solutions of higher concentrations. They became not kept flowing on the surface.

Discussion.

Based on studies conducted (rheological, organoleptic, mechanical and other) were selected for further experiments such gellants: xanthan gum, hydroxyethylcellulose. Lined with the necessary concentration of lactic acid - 0.2%.

# SOME ASPECTS OF CREATION NEW NASAL GEL FOR TREATING OF ALLERGIC RHINITIS

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Now the problem of the prevention and treatment of allergic diseases is considered as one of the most important aspects that directly affect the quality of patients' life.

The basis of allergic rhinitis is an inflammation of the nasal mucosa, which is based on the reaction caused by contact with allergens. Most often provoke allergic rhinitis: pollen, mites, yeast and molds, some food, home (portrait) dust, some drugs. Symptoms of the disease are presented by copious mucus - rhinorrhea, nasal congestion, watery eyes, frequent sneezing, and general poor health.

Modern range of drugs for the treatment of allergic rhinitis in the pharmaceutical market is represented by a number of different pharmaceutical groups. Thus, the vasoconstrictor sprays and drops reduce swelling of the mucous, and make it easy to restore nasal breathing. However, it is important to remember that these drugs relieve the symptoms but not the cause of the disease.

Representative of the antihistamine drugs group is combined medicine "Sanorin-Analergin", which consists of antazoline - selective blocker of $H_1$-histamine receptors and naphazoline - with a strong vasoconstrictor action.

Homeopathy has been developing medicines to strengthen the body's defenses. The most frequently used representative of this group is "Sinupret" in different dosage forms.

But today more and more attention attract nasal gels. There are a number of advantages of this dosage form: fewer side effects, the presence of the dampening effect on the nasal mucosa, prolonged action.

One of the most commonly prescribed anti-allergic nasal gels is gel "Lorizan", but given its synthetic origin urgent task of pharmacy is to create a new domestic nasal gel based on natural compounds.

As active ingredients, we proposed to use dry licorice root extract and essential oils of eucalyptus and pine tree, which have strong anti-allergic, anti-microbial and anti-inflammatory properties.

Further aim of our work is to develop composition and technology of a new nasal gel based on natural raw materials for treating of allergic rhinitis.

# THE ROLE OF EMULSIFIERS IN MODERN TECHNOLOGY OF COSMETIC MEDICATIONS

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Actuality of the subject:

There are just a few investigations of the quality of hand creams being done nowadays and Ukraine is not an exception. According to the Internet resources they are generally held by a specific cosmetic company in a close mode. Of course, this information is very limited and it is very difficult and expensive for the average consumer to check it.

To make the right choice in the assortment of the hand creams and to have a good result after using it you should pay attention to the characteristics of a cream.

Therefore, having analyzed several hand creams of industrial production we made a conclusion that some components are almost useless, and some of them are even harmful. So, emulsifier Trytanolamin, which is a part of the tested cream, is a strong alkaline compound used in industry: in washing-up liquids, polishes and paints. The next questionable component is acrylate copolymer. It is water-soluble polymer used not only in cosmetics but also in production of varnish-and-paint materials, sanitary engineering, furniture and materials for nail modeling in nail salons.

The presence of useless components in the creams produced at factories motivated us to conduct the research with the cream of our own production.

The requirements, which were set up to the produced emulsion cream are colour and smell, weight homogeneity, absorbency.

An emulsion is a two-phase system. The principal components are an oil phase and an aqueous (water) phase. Emulsions are a fundamental product form for many cosmetic categories and these are made possible by careful selection of the optimum emulsifier system.

The aqueous phase is water plus any combination of materials which are polar and dissolve, at least to some extent, in water. The oil phase comprises one or more oily materials, or other ingredients which are non-polar and exhibit at least some solubility in oily materials.

It is known that the emulsifier is a substance that can mix water and oil – substances that never mix with each other under normal conditions. Emulsifiers are employed in cosmetics to prepare emulsions.

The efficacy of emulsifying agents depends on their ability to reduce surface tension, to form complex films on the surface of emulsified droplets, and to create a repulsive barrier on emulsified droplets to prevent their coalescence.

For the experiment we used a guar gum.

Guar gum is an odourless powder of white or yellowish colour. It is extracted from milled seed endosperms of guar beans. The seeds contain up to 70% of gum.

The composition of the cream of our own production includes olive oil, beeswax, mineral water, bitter orange oil. Beeswax contains esters (70-75%), free fatty acid (12-15%), carbohydrates (10%), and mineral flavors. The main chemical elements are carbon wax (80%), water (13%) and oxygen (7%). Wax is rich in vitamin A. It includes tocopherols (vitamin E) that have an antioxidant properties; carotenoids; flavonoids - bioactive substances involved in redox reactions; chlorophyll; squalene that protects from skin cancer and others.

Technology of production of emulsion creams of o /w type involves the following operations:

1. Preparation of the aqueous phase;
2. Preparation of the oil phase;
3. Both phases (water and oil) are placed into a water bath;
4. Emulsification;
5. Cooling;
6. An essential oil adding;
7. Cream packaging.

Evaluation of consumer characteristics was made with the help of students and teachers.

Conclusion:

According to the research, which was attended by 20 participants, the cream has positive evaluation. All participants who tested the cream said that its structure is quite oily, thanks to the presence of beeswax in its composition. Of course, we took into account the peculiarities and the skin type of the participants, on which the absorbency of the cream depended.

According to the point of view of the participants the cream has a light odour, delicate and soft structure, it is pleasant for the skin, its surface appearance corresponds to the demands required from factory produced creams.

Later we asked again the participants about the feeling on the skin and received the answer that the skin became softer.

Definitely the creams that contain natural components are useful not only for the skin, but also for the consumers' health.

It is profitable, useful and easy to prepare such creams yourself.

# THE DEVELOPMENT OF A DRUG FOR THE TREATMENT OF ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a chronic inflammatory disease of the skin of the allergic nature, which is characterized by dryness, reddening, rash and itch. AD is considered to be a children's disease – 65% of little patients with such diagnosis symptoms develop before the age of 1 year, 90% – at the age of 5 years, in rare cases, AD remains for the rest of all life. The wrong treatment of atopic dermatitis not only doesn't give to the patient relief, but also aggravates the course of a disease.

Local treatment of AD is an obligatory and important part of a complex treatment. Its goal is not only the preclusion of inflammation and itch, but also restoration of a water and lipidic layer and barrier function of the skin.

The aim of our work is the develop of a soft drug composition of moisturizing, anti-inflammatory, antimicrobial, reparative and antipruritic action for the treatment of atopic dermatitis. For this purpose as active pharmaceutical ingredients, we recommend to include into the developed soft drug the dry extract of green tea and D-panthenol (provitamin B5).

Green tea extract is considered as one of the most effective plant remedies for the prevention and treatment of skin diseases. Due to the complex effect of polyphenols, catechins and antioxidants the extract possess a good penetrating ability that allows biologically active substances to influence on the deeper layers of the epidermis, thus providing antibacterial, antiseptic, antifungal, anti-inflammatory, calming and antipruritic actions. Besides that, the green tea extract improves oxygen and water-salt exchange, moistens the skin, removes reddening and irritation, and also stimulates a regeneration.

D-panthenol has epithelizing, wound healing and anti-inflammatory effect, that determined its addition into the composition of the developed medicine for the treatment of atopic dermatitis.

The aim of our further work is exploring the physical-chemical and technological properties of the active ingredients, and also the choice of a rational basis, the kind of which affects the degree of release and absorption of the active ingredients from a soft dosage form, so and on getting a given pharmacological action.

# PERSPECTIVE FOR THE USE OF ALGINATES IN THE TECHNOLOGY OF SOFT DOSAGE FORMS

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"Alginate" is the term usually used for the salts of alginic acid, but it can also refer to all the derivatives of alginic acid and alginic acid itself. Most of the large brown seaweeds are potential sources of alginate. Alginic acid is a linear polymer based on two monomeric units, b -D-mannuronic acid and a -L-guluronic acid. Sodium alginate is the main form of alginate in use. Smaller quantities of alginic acid and the ammonium, calcium, potassium and triethanolamine salts are also produced. Calcium alginate and alginic acid are made during the calcium alginate process for making sodium alginate; each can be removed at the appropriate stage, and after thorough washing, can be dried and milled.

The uses of alginates are based on three main properties. The first is their ability, when dissolved in water, to thicken the resulting solution (more technically described as their ability to increase the viscosity of aqueous solutions). The second is their ability to form gels; gels form when a calcium salt is added to a solution of sodium alginate in water. The gel forms by chemical reaction, the calcium displaces the sodium from the alginate, holds the long alginate molecules together and a gel is the result. The third property of alginates is the ability to form films of sodium or calcium alginate and fibres of calcium alginates.

The ionotropic gelation of sodium alginate with calcium cations is conventionally described by the “egg-box” model, where calcium cations interact with guluronic acid monomers in the cavities formed by pairing up of the G sequences of the alginate molecular chains.

Several gelling systems based on alginates can be formulated, but the most frequently used are diffusion setting or internal setting.

Diffusion setting. In this system, a calcium salt which is insoluble at neutral pH, is mixed with the alginate. When an acid comes into contact with the surface of the mass, the calcium salt is solubilized. The soluble calcium will then react with the alginate and start the gelation process.

Internal setting. In this process, calcium is released within the product under controlled conditions. It employs the combination of alginate, a slowly soluble calcium salt and a suitable calcium sequestrant, such as a phosphate or citrate.

Thus, due to their properties alginates may be used in the technology of soft medicinal forms.

# DEVELOPMENT OF HEPATOPROTECTIVE ACTION TABLETS BASED ON PLANT BLEND

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A significant role in the prevention of exacerbations of liver disease and prevention of acute process transition in chronic can be played by herbal medicines. Their action is multifaceted: decoctions of herbs liquefy bile, simultaneously possessing choleretic and anti-inflammatory action, do not allow an infection to get in the biliary tract, restore the tone of biliary system. Herbal medicines therapy in liver diseases should be carried out systematically every 2-3 years.

The aim of the study was the development and study of plant blend, possessing hepatoprotective activity.

At development of a new drug the following substances were investigated: dry extracts of immortelle, mint and tansy.

In order to develop the optimum composition and technology of tablets based on powders of extracts from plant material pharmaco-processing characteristics of the active substances of the dosage form have been studied: bulk density, flowability, compressibility, moisture content, pressing disintegration in water.

As a result of studies on the creation of a new hepatoprotective action phytopreparation, composition and technology of tablets production by wet granulation has been chosen. As auxiliary substances have been tested milk sugar, potato starch, microcrystalline cellulose, croscarmellose sodium, talc and calcium stearate. For the preparation of tablets by wet granulation the optimal humidifier is 7% solution of potato starch, which provides a minimum disintegration time of the tablets obtained.

The effect of excipients on indicators of technological characteristics of the tablet mass and quality indicators of the resulting tablets has been studied. technological parameters have been grounded. In the development of this formulation technology it has been identified, that a significant influence on the quality indicators oftablets, in particular on the strength of tablets to crushing, has a residual moisture of the tablet mass.

The flow chart of the drug production has been composed.

# RESEARCH OF THE PHARMACOLOGICAL AND TECHNOLOGICAL PROPERTIES OF MEDICINAL PLANT RAW MATERIALS OF ASTRINGENT EFFECT.

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The frequency of all dysfunctional uterine hemorrhages is 60% of all gynecological diseases that may be classified the following way: juvenile, of childbearing age and climaterical. This pathology appears as a result of ovary hormone production malfunction. Usually hemorrhages are connected with malfunctions of pituitary-hypothalamic system function that regulates ovary work and menstruation function, and also with different inflammatory diseases of genitals.

One of the directions in pharmacotherapy of dysfunctional uterine hemorrhages is the use of synthetic hemorrhagic remedies that have a number of side effects: thromboembolism, hypotension, agranulocytosis, neutropenia, thrombocytopenia, allergic reactions, asthenia, fever etc.

For reducing side effects by treatment it is reasonable to take preparations of plant origin that have quite a number of advantages: they can be taken for a long time, have less quantity of side effects, have soft therapeutic effect, are nontoxic.

According to the foregoing the purpose of our work is study of pharmacological and technological properties of medicinal plant raw materials for the development of astringent effect preparation.

The objects of our work are the herb of yarrow and shepherd's purse. Research of humidity, dispersity, specific and volume density, bulk density of raw materials have been conducted according to methodologies given in State Pharmacopoeia of Ukraine.

Results of research testify that values of humidity of yarrow are 12,77% that significantly exceeds the content of humidity of shepherd's purse – 5,26% that corresponds to the specifications and technical documentation. Study of fractional structure of raw materials has showed polydispersion of samples: the size of particles fluctuates from 0,1 to 0,5 cm. In two samples the main fraction makes from 0,1 to 0,2 cm. Study of specific density has showed that for both examples the value is almost equal (≈ 0,97 g/ml). Volume density made 0,417 g/ml and 0,500 g/ml agreeable. The bulk mass is equal 0,147 g/ml and 0,164 g/ml. The results of specific and apparent density allow to predict uneven distribution of herbs when mixing. The obtained data will be used by developing a preparation of astringent effect from this type of raw materials.

# RESEARCH OF THE EXTRACTION PROCESS OF RUBIA TINCTÓRUM AT LIQUID EXTRACT OBTAINING

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Dyeing Madder (Rubia tinctorum) is a perennial, high enough (up to 2 meters), herb of the family *Rubiaceae*. In today's traditional, as well as in folk medicine, the plant gets popularity due to the pronounced diuretic, antispasmodic and litholytic action. The main effect of the plant is the ability to destroy calcium oxalate stones, phosphoric acid, oxalic acid salts of calcium and magnesium, ureates produced in the kidneys and bladder, at cholelithiasis. Has a diuretic, antibacterial, anti-inflammatory effect in pyelonephritis, nephritis, cystitis. Eject the salt from the joints of hands and feet at gout, osteochondrosis, arthritis.

As medicinal plants raw material used Rubia tinctorum root, and as it has the above properties. Root of the Rubia tinctorum very developed, branched, its bark is reddish-brown hue, partially peeled off. The roots of the Rubia tinctorum contain about 60 derivatives of hydroxymethyl anthraquinone, the main ones are alizarin, lutsidin,, rubiadin, purpurin-3-carboxylic acid, purpurin, ksantopurin etc. Extracts from Rubia tinctorum are in compose of the combined drug "Cystenalum."

Thus, is relevant the development and investigation of dense extract and solid dosage forms based on it.

For obtaining the liquid extract was used a method of percolation or filtration extraction. In the process of percolation conducted selection of samples of extract in amount equal to the weight of the loaded material. In all collected consistently samples was determined content of dry residue and extractives by the results was made a conclusion about exhaustion of raw materials. Was proved experimentally usefulness of 70% alcohol as extragent. For a complete exhaustion of raw materials needed to use a ten-fold amount of alcohol relative to the weight of raw materials.

# DEVELOPMENT OF DOSAGE FORMS WITH IMMUNOMODULATORY EFFECTS FOR USE IN PEDIATRIC PRACTICE

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In recent years there is a tendency for children born with weak and underdeveloped immune system, which reduces resistance to viral and bacterial agents, especially in preschoolers and school age children.

Thus, weak immunity negatively affects human performance later on in adulthood, which has negative consequences for the economy.

The immune capacity of the body can be enhanced by taking immunomodulators. Based on market research conducted, it has been found that a group of natural origin immunomodulators is presented in insufficient quantities. Therefore, the problem of developing an immunomodulating action drug of natural origin for children is relevant for the practical pharmacy.

The purpose of this research was the choice of optimal dosage form, substantiation of composition and technology of a drug with immunomodulatory effect.

As the main active ingredient lyophilized vegetable protein has been selected, which immunomodulatory properties have been established in previous studies.

As pediatric dosage form lozenges have been selected, because they are convenient to use, they are easily digested and cause no indigestion, have a pleasant taste.

The fluidity of initial sunflower protein powder was insufficient, so in order to improve this indicator, obtained granules by wet granulation. As a humidifier water was chosen. The resulting granules have been dried in the oven to the optimum level of residual moisture.

As a basis for lozenges gelatin was chosen. Also entered sufficient amounts of other excipients.

Choosing temperature modes proceeded from the properties of active ingredient and excipients. On the basis of thermogravimetrical studies conducted at the NUPh optimal temperature conditions lozenges production have been determined.

Quality assessment of the lozenges conducted according to the State Pharmacopoeia of Belarus and Germany.

Today preclinical studies of the vegetable protein lozenges in animals are in progress.

The results of research have allowed grounding of composition and technology of immunomodulatory action medicinal product in the form of lozenges for use in pediatric patients.

# APPLICATION OF HIGH FRMAGMENTOV FOR FLUIDS IN PROGRESS CHROMATOGRAPHY METHODS FOR DETERMINING THE QUALITY OF BEE VENOM

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Analysis preparations voderzhaschih lyophilised bee venom without anesthetic (Preparation 1) and in combination with lidocaine (Preparation 1) was performed by high performance liquid chromatography using a chromatograph Varian ProStar ( ProStar 210 pumps, a spectrophotometric diode - array detector ProStar 330; ProStar 400 autosampler volume dosing loop 20l; thermostat speaker ProStar 500). Chromatographic column Ascentis RP-Amide: 250 x 4.6 mm, the diameter of the sorbent particles 3 microns, pore diameter of 100 A (Supelco).

To identify components of bee venom were used apamin standards (Sigma-Aldrich, Cat. № A1289, pp. 111M4138), melittin (Sigma-Aldrich, Cat. № M7391, pp. 098K4131), phospholipase A2 (Sigma-Aldrich, Cat. number R9279, p. 032M4001V). The determination of the bee venom was used in the pre- lyophilized formulations standardized bee venom, analysis was performed by external standard method, reference solution used as a solution in bee venom standardized nominal concentration (1 mg / ml).

Chromatographic conditions: column temperature - 25 C°; mobile phase A - water trifluoroacetic acid (1000:1, v/v); mobile phase B - acetonitrile - trifluoroacetic acid (1000:1, v/v); mobile phase rate - 1 ml/min; detection - spectrophotometric at 210 nm; sample volume - 20l nm.

Gradient program :

| Time, min | MPh A, % | MPh B, % |
|---|---|---|
| 0-2 | 95 | 5 |
| 2-12 | 95 → 30 | 5 → 70 |
| 12-16 | 30 | 70 |
| 12-16 | 30 → 95 | 70 → 5 |
| 16-20 | 95 | 5 |

For the analysis of the respective solutions were prepared.

# TECHNOLOGY PARAMETERS DEVELOPMENT OF MAGNESIUM S-LACTATE DIHYDRATE PRODUCTION FROM TECHNICAL PRODUCTS

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Magnesium lactate is used as an active pharmaceutical ingredient in the form of R,R-; S,S- and R,S- isomers mixture in some medicines, that are represented at the pharmaceutical market of Ukraine and many foreign high-tech countries.

Usage of individual S,S-isomer is expected to have increased pharmacological efficiency because of improved affinity to the S-structures of biological objects. However, it wasn't found. The relevance of this compound and of its production technology also increases because of growing compared to euro dollar course, and especially growing compared to hryvnya. That's why such production can become competitive in Ukraine.

The main purpose of our work is the technology parameters development of magnesium S- lactate dihydrate production in order to obtain quality product with high yield.

As a basic substances we have used cheap and accessible water cleared (SPhU 1.4. p.389), technicals magnesium oxide and S-lactic acid.

Theoretical organic chemistry, quantitative calculation of possible admixtures, instrumental physicochemical, titrimetric types of analyses and technological methods were used as research methods.

As a result we have developed technology parameters of magnesium S-lactate dihydrate production. The technology is carried out in two stages, using water as a solvent, under heating, with subsequent filtration and product drying. Thus, all insoluble in hydrochloric acid admixtures from the orginal oxide, and also polilactic acids and products of their decomposition from lactic acid are removed from the end-product.

The quality of the obtained product corresponds to the requirements of the European standards (Ph Eur 2008, monograph 2322). At the same time some additional indexes were added to the analytical documentation project. Particularly, the determination of a specific optical rotation was added. The average magnesium S-lactate dihydrate yield was found out as 86,8% of theoretical one.

Therefore the developed technology is quite simple; it doesn't need any fire dangerous or explosive solvents. And it also posses high economic parameters. That's why this technology is offered to the Ukraine manufacturers in order to use it at the industrial production.

# PROSPECTS FOR THE USE OF IBUPROFEN IN THE TREATMENT OF OSTEOARTHRITIS

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Osteoarthritis (OA) occurs in 10-12 % of the population and is the most common diseases. Increase in the number of patients with OA noted with increasing age: at the age of 50 years, every second man has OA, at the age of 70 years or more clinical and / or radiological signs are defined in 80 ─ 90% of people. OA does not affect the vital prognosis, but the defeat of the "stress" of the joints significantly affects the quality of life of patients and leads to partial or total disability.

Therefore, based on pathogenic prerequisites for an effective pharmacotherapy is necessary to suppress inflammatory responses and pain as well as normalize cartilage metabolism. Nowadays, using rapid-acting symptomatic agents, which include analgesics, non-steroidal anti-inflammatory drugs, glucocorticoids. Drugs of choice for the treatment of OA, as a rule, are NSAIDs. The results of the multicenter study on the treatment of OA suggest proven symptomatic effects of NSAIDs. Ibuprofen is a medicine from group of non-steroidal anti-inflammatory drugs.

Has a pronounced analgesic, anti-inflammatory, anti-exudative and antipyretic effects. The mechanism of action of ibuprofen is based on its ability to inhibit the enzyme activity of cyclooxygenase and to disturbe metabolism arachidonic acid. Ibuprofen inhibits the synthesis of prostaglandins E and F, as in the tissues of the central nervous system as well as directly in inflammation. Moreover, when the metabolism of arachidonic acid disorder occurs lowering thromboxane. Ibuprofen relates to indiscriminate cyclooxygenase inhibitors, equally it blocks the action of cyclooxygenase-1 and cyclooxygenase-2. In recent years, special attention is paid to the safe use of NSAIDs. The most severe side effects in the appointment of almost all NSAIDs are disorders of the stomach, lung dyspeptic disorders to the development of gastroduodenal ulcers and bleeding. When topical use of NSAIDs are therapeutic concentration of the drug in the soft tissues directly under the place of application, and enter into the general circulation only small amount, that minimizes systemic adverse effects.

Thus, local therapy appropriate dosage forms of NSAIDs (ointments, creams, gels) is not only a reasonable addition to the system prescribe drugs to reduce their number due to the greater bioavailability of the drug in the inflammation, and in some cases to do without them. Local therapy in some cases can be considered as an effective alternative especially for patients with high risk of complications.

# MEDICATED LOLLIPOPS FOR THE TREATMENT OF ORAL THRUSH IN CHILDREN

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Oral thrush is a disorder caused by infection of the mouth due to fungus (yeast) candida albicans. In babies it may be a severe infection sometimes causing epidemics in schools by cross-infection. Candida albicans is a normal inhabitant of the oral cavity found in 30% to 40% of the population. Typically, oral candidiasis takes the form of an adherent white, curd like, circumscribed plaque anywhere within the oral cavity. There are many drugs dosage forms like lozenges, tablets, inhalers, and syrups, are in markets for the treatment of the same. The “lozenges are flavoured medicated dosage forms intended to be sucked and hold in the mouth/pharynx. Development of lozenges dates back to 20th century and is still in commercial production.

Most of the lozenge preparations are available as Over The Counter medications. Lozenge provide a palatable means of dosage form administration and enjoy its position in pharmaceutical market owing to its several advantages but it suffers form certain disadvantages too. The dosage form can be adopted for local as well as systemic therapy and a wide range of actives can be incorporated in them. Lozenges currently available in market are of four types: Caramel based soft lozenges, hard candy lozenges and compressed tablet lozenges.

The present review covers more or less all aspects associated with lozenge. It includes various researches performed till date, formulation and evaluation parameters adopted for the dosage form. Furthermore, it throws light on the applications of lozenges. These preparations are commonly used for the purpose of local effect or systemic effect”. Advantages of the lozenges as dosage forms include increase in bioavailability, reduction in gastric irritation, bypass of first pass metabolism and increase in onset of action.

New drug design to this area always benefit for the patient, physician and drug industry. There are several dosage forms like in the market, there is a need for more dosage forms which acts effectively and locally as well as systematically. Oral thrush is a disorder caused by infection of the mouth due to fungus (yeast) candida albicans. In babies it may be a severe infection sometimes causing epidemics in schools by cross-infection.

# THE CHOICE OF THE OPTIMAL AMOUNT OF "PROPOLIS" GEL FOR APPLICATION TO THE SKIN

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The aim of the present stage of the research was to determine the optimal amount of the test sample for cutaneous applications. The terms of this stage of the study is that the amount of the test sample is applied on the skin area of 4 $cm^2$ (2x2 cm) and is rubbed into the animal's skin for 30 sec. Assessment of the skin cover is carried out visually. That amount of gel after rubbing which the skin is without glitter and remains hydrated enough is optimal. If the skin is dry and is not moisturized, the amount of gel is insufficient; if the skin is shiny, the amount of gel is excessive.

Determination of the optimal amount of the test sample was conducted on male white rats. The hair in the skin area of 4 $cm^2$ (2x2 cm) was cut off on the right side of the animals 24 hours before applying "Propolis" gel; in group 1 of the animals the gel was applied in the amount of 40 mg, in group 2 the amount of the gel was 50 mg, and in group 3 – 60 mg. The testing of each amount of the gel was performed on three animals.

The results of the study on choosing the optimal amount for application to the skin of animals are presented in Table 1.

Table 1 – The results of the study of the optimal amount of "Propolis" gel, 2 %, for application to the skin of animals

| Test sample | The state of the skin cover in 30 sec after application of "Propolis" gel | | |
|---|---|---|---|
| | 40 mg/4 $cm^2$ | 50 mg/4 $cm^2$ | 60 mg/4 $cm^2$ |
| "Propolis" gel | the skin remains dry | **the skin is hydrated enough** | the skin is hydrated excessively |

Based on the data obtained one can conclude that the optimal amount of "Propolis" gel for skin application is 50 mg/4 $cm^2$, which is 12.5 mg calculated with the reference to 1 $cm^2$.

Thus, according to the results of the study conducted the optimal dose of "Propolis" gel for application to the skin of rats has been determined, it is 12.5 mg/$cm^2$.

# DETERMINATION OF TECHNOLOGICAL PARAMETERS OF PLANT MIXTURE FOR TREATMENT OF UROLITHIASIS

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The incidence of urolithiasis in the world is from 0.5 to 5.3% and is diagnosed in children and the elderly. However, in 68% of cases it develops in working age. Unfortunately, even after removal of stone recurrence during the first 3 years after treatment was 53%. Therefore, urgent measures are metaphylaxis using combined herbal preparations that provide not only a diuretic and anti-inflammatory actions and influence the pH of urine and provide antispasmodic effect. Preparations Rubia tinctorum promote urinary calculus loosening, reduce spasms and facilitate discharge of small calculus with urolithiasis.

The aim is to develop of technology and collection of litholytic activity for use in acute kidney stones, and a prophylactic measure for all forms of urolithiasis.

Materials and methods. In developing the collection of medicinal herbs has been used, which is widespread in Ukraine: the roots of Rubia tinctorum, Ammi visnaga grass, Chamomile flowers and Betulae burgeons. Technological parameters studied samples of plant materials and their mixtures: fractional composition, fluidity, bulk volume, the moisture content. Technological parameters indices were determined by methods SPU.

The obtained results. Our results revealed that all samples of plant material fraction (0.5, 1.0 and 2.0 mm) have satisfactory fluidity and is close to the value that indicates compatibility in this collection.

In determining the fractional composition of the mixture were the largest number of fractions with particle size less than 1 mm fraction and particle size of 1-2 mm. They totally make up 84.2%. Particle size significantly affects the yield of extractives of medicinal plants in the extraction. Therefore, the presence of plant collection of fractions with particle size of less than 2 mm should facilitate the rapid release of active ingredients. Therefore, further investigation was elected these fractions. After receiving the powder mixture held its pharmaco-technological analysis, which showed that the bulk density of plants is low. When she shrinkage varies considerably, and may cause a change in dose mass volume dosage collection.

Conclusions. Determined that all components of the mixture are compatible. Sieve analysis showed a high content of shallow fractions, which significantly accelerates the extraction. But a significant change in bulk density further expedient packing blend in filter bags or obtain granules to provide a more accurate receiving the necessary dose patient.

# FACTORS WHICH AFFECT THE DEVELOPMENT OF THE FLOATING TABLETS TECHNOLOGY

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Oral delivery of drugs such as tablets is the most preferable route of drug delivery due to the ease of administration. Oral sustained-release technology provides oral delivery for 24 h; however, in substances that cannot be well absorbed throughout the whole gastrointestinal tract, it may be disadvantageous.

Normal gastric residence times usually range between 5 min and 2 h. Gastric emptying is unpredictable in the presence of food and disease conditions, though drugs with a short half-life are eliminated quickly from the stomach. This has led to the development of oral gastro-retentive dosage forms.

Various gastroretentive techniques are used, including floating, swelling, high density, and bioadhesive system, have been explored to increase the gastroretention of dosage forms. Floating systems having low density systems that have sufficient buoyancy to float over the gastric contents and remain in the stomach for a prolonged period.

Hydrophilic polymers hydroxylpropylmethyl cellulose (HPMC) were found to be more beneficial to improving floating properties. Hydrophilic polymer slowly forms thick gel, which retains integrity of the formulation and promotes drug release through thick gel which controls the burst release. This polymer produces gel-forming matrices and, in contact with gastric fluid, possess sufficient structure to form a gel layer and achieve an overall specific gravity lower than that of gastric fluid.

The main purpose of a floating drug delivery system is to increase the gastric residence time of the dosage form by generating gas. Citric acid and sodium bicarbonate were found as effervescent base to generate the carbon dioxide and to enhance the buoyancy of the tablets.

Floating tablets may be prepared by direct compression or by wet granulation. In the second case it is necessary to use an alcohol solution instead of the aqueous binder to prevent interaction between citric acid and sodium bicarbonate.

The in vitro buoyancy of prepared tablets should be determined by floating lag time and total floating time. The time required for the tablets to rise to the surface and float is determined as floating lag time. The duration of time the dosage form constantly remained on the surface is determined as the total floating time.

# RESEARCH TO IMPROVE THE STABILITY OF VITAMIN EYE DROPS

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Most drugs for the topical treatment of cataracts contain medicinal substances that contribute to the activation energy and metabolic processes in the lens and cornea preservation electrolyte composition of the cytoplasm, the normalization of the function of cell membranes, providing antioxidant protection, enhancing the exchange of aqueous humor, which accelerates the leaching of toxic degradation products stimulate reparative and regenerative processes in cases involving disturbans of metabolism in tissues of the eye, reduces inflammation in the conjunctiva, cornea and other eye structures.

The majority of drugs for the topical treatment of cataracts contain medicinal substances that contribute to the activation energy and metabolic processes in the lens and cornea preservation electrolyte composition of the cytoplasm, the normalization of the function of cell membranes, providing antioxidant protection, enhancing the exchange of aqueous humor, which accelerates the leaching of toxic degradation products stimulate reparative and regenerative processes in cases involving violation of metabolism in tissues of the eye, reduces inflammation in the conjunctiva, cornea and other eye structures.

For our research we took a popular eye drops among the people of older age who suffer from cataract. The eye drops contain riboflavin, ascorbic acid and glucose.

In order to increase the shelf life of vitamin eye drops studies were conducted on the effect on the microbiological stability of antimicrobial preservatives, which are mainly used nipagin and nipasol, and their combination in a ratio of 1:3 in a total amount of 0,1%.

Eye drops were prepared by conventional techniques under aseptic conditions. For studies we have prepared a series of samples of 10 drops vials of 10 ml, which was sterilized at 120 °C in 8 minutes. Results of test "Efficacy of antimicrobial preservatives" in accordance with GFU showed that bacteria death occurs fast right after the test samples are contaminated. Logarithm of reduction in the number of viable cells S. aureus in the plated crop was 1,0 in a day and 3 when viable cells were not found during further platings. Logarithm reduction in viable cells in the C. albicans initial seeding was 0,43 after day – 1,021. After 7 days, viable cells C. albicans were not identified. To sum up, the eye drops that were stabilized with nipagin and nipasol stayed sterile and stable according to all factors that been researched during one week.

# TOPICAL TREATMENT OF ONYCHOMYCOSIS: CHALLENGES AND APPROACHES

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Introduction. Onychomycosis is a fungal nail infection and is thought to account for 40% of all nail disorder. One of the approaches for management of onychomycosis is topical treatment. However, topical treatment of nail disorders remains a challenge because of the difficulty encountered in achieving therapeutic concentrations of drugs at the site of infection.

Aim of the work was to justify use of keratolytic agents as penetration nail enhancers in topical treatment of onychomycosis.

Materials and methods. Pharmaceutical and medical data sources. Methods: search and systematization of information, logical analysis.

Results. The human nail forms a resistant barrier to the topical penetration of actives. To deliver the therapeutically sufficient quantity of antifungal drug to the fungus-infected sites of the nail, physical or chemical methods for penetration enhancement may need to be employed to overcome the nail barrier. Physically removing the entire diseased nail plate would be an effective way of eliminating the nail barrier, but it is painful and includes the risks of infection and abnormal nail growth. As opposed to the physical removal, chemical technique with using of keratolytic agents is almost always painless and provides partial removal of a diseased nail plate, or thinning of the diseased nail plate. Keratolytic agents enhance the drug permeation by breaking the physical and chemical bonds responsible for the stability of the nail keratin. The mechanism of nail penetration enhancers depends on the interaction with keratin bonds and may be quite different. Currently the following keratolytic enhancers have found their use in medicine: sulfhydryl compounds like acetylcysteine, salicylic and benzoic acids, thioglycolic and glycolic acids, urea etc.

Drug penetration through the nail plate is quite sensitive to the molecular weight of the penetrating compound and its solubility. The chemical composition of nail indicates that the aqueous pathway plays a dominant role in drug penetration into the nail. Consequently, an agent with lower molecular weight and strong hydrophilic characteristics will be the most effective.

Conclusion. The permeability of topically applied drugs through keratinized nail plate is highly poor and drug uptake into the nail apparatus is extremely low. Drug transport into/through the nail plate can be effectively assisted by the use of chemical enhancers like keratolytic agents. Effect of the keratolytic enhancers depends on the drug molecular mass and water solubility.

# USING NON-AQUEOUS SOLVENTS IN TECHNOLOGY OF OINTMENTS

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One of the common missions of the modern pharmaceutical sciences is to create a new and more effective medicines, as well as improving the well-known drugs proven to treat various diseases, based on their comprehensive (biopharmaceutical and technological) research.

The liniment of streptocide became an object of our attention due to its demand among the population for the treatment of inflammatory skin diseases. However, the existing structure of auxiliary substances which are coming along with the liniment itself does not provide stability, as well as the desired release of streptocide. Therefore, the aim of our research was to study the effect of some excipients on the structural and mechanical properties and release of streptocidum from emulsion bases. The most suitable hydrophilic co-solvents for semisolid dispersions are considered to be propyleneglycol, glycerol and polyethylenglycole. We studied the effect of the concentration of PEO-400 and PEO-1500 on how they obtained delay in growth of microorganisms.

The basis of liniment was obtained in the traditional way. The "Reotest 2" was used for mesuring the rheological parameters on given liniments. Rheological studies have shown that the introduction of polyethyleneoxides into the structure of liniment is effective. Flow curves of some samples are being seen to be within the rheological optimum for hydrophilic ointments. The presence of ”hysteresis loop" on the rheogram proves its thixotropy. Antimicrobial activity of the samples was determined by the method of diffusion in agar gel and further studying the rate of growth of test microbes. Further the rate of growth of our liniment was compared with the liniment of factory production. Obtained data shows that the presence of polyethyleneoxide in all cases affects the growth retardation of microorganisms, and thus the antimicrobial effect on a liniment. In respect to the concentration and molecular weight the rate changes differently. Diffusion of streptocide in agar gel increases in the presence of polyethyleneoxide based. Low molecular weight PEO-400 has a greater affect by the diameter of zones of microbial growth rate inhibition. Maximum diameter that was obtained is when adding 30% PEO-400. Further increase in concentration slightly increases the inhibition or keeps it on the same rate. Adding 5% PEO-1500 leads to a slight increase in the release of streptocide. The increase in its concentration affects very slightly. The highest release is obtained when there is 30% PEO-400 in the structure of the liniment.

# DEVELOPMENT OF TABLETS FOR TREATMENT OF MIND DISORDERS

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Over the past half century, biopharmaceutical research has helped transform mental illnesses from misunderstood causes of shame and fear into often highly treatable conditions. For example, medicines for treating depression are helping thousands of people live productive lives and breakthrough schizophrenia medicines have enabled patients to be treated in the community rather than being institutionalized.

One of the drugs that have led to a better way of life for mentally challenged people in recent years has been Piracetam. The drug influences neuronal and vascular functions and influences cognitive function without acting as a sedative or stimulant. Piracetam is a positive allosteric modulator of the AMPA receptor. In addition to Piracetam, vitamin B5 has been added to the drug, as a means of co-effection, in the indicated medical conditions. Pantothenic acid (Vitamin B5) is involved in the oxidation of fatty acids and carbohydrates. If people have enough Vitamin B5 in your system, it can result in the impairment of a process needed to synthesize acetylcholine. Vitamin $B_5$ is necessary for the metabolism of choline in order to make the acetylcholine neurotransmitter. When taking any sort of Choline supplement, it is recommended to use a multivitamin with $B_5$ in it to ensure that one has this nutrient to reap full benefits from the nootropic stack. Without sufficient levels of Vitamin $B_5$, one may not notice any changes when using acetylcholine precursors like Alpha GPC, Citicoline, Centrophenoxine or Acetyl L-Carnitine. This is particularly true if one is stacking with a Racetam (like Piracetam) in addition to a source of choline. In fact, insufficient levels of Vitamin $B_5$ may exacerbate the “Piracetam headache” that can occur when you do not have enough acetylcholine to keep up with the demands of your neurons.

In the university of our study, we carried out experiment and laboratory works on development of composition and technology tablets containing Piracetam and Vitamin $B_5$. Nowadays we have chosen composition of tablets and studied all technological properties of taken components. As method of tablet manufacturing we have proposed direct compression.

# DEVELOPMENT OF COMPOSITION OF MEDICINAL TEA FOR THE TREATMENT OF BRONCHITIS

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Bronchitis is an inflammation of the bronchial tubes, the airways that carry air to your lungs. It causes a cough that often brings up mucus, as well as shortness of breath, wheezing, and chest tightness. There are two main types of bronchitis: acute and chronic. Ability to combat respiratory infection, tend to have a viral etiology is largely limited to symptom relief.

In the acute phase of therapy should be directed at the elimination of the inflammatory process in the bronchi, the improvement of bronchial conductivity, restoration general and local immune reactivity. Phytomedications choice in chronic bronchitis is made taking into account the clinical symptoms and the possible morphological picture. Thus, appointed by the therapy is aimed at facilitating expectoration of thick mucus, reduce the frequency of attacks of coughing and improve overall health of the patient. Herbal medicines used in the treatment of bronchitis include expectorants and antitussives.

Bronchial and tracheal mucus covers and keeps the respiratory tract moist, and aids in warming and purifying inhaled air. However, in the case of respiratory tract inflammation or irritation, this secretion can be transformed into an exudates which impedes air circulation and induces coughing. Expectorants are therefore useful when it is desirable to reduce mucus viscosity. This will facilitate removal of the secretions through coughing (expectoration). Indications for reflex expectorants include cough linked to bronchial congestion and bronchitis.

Reflex expectorants. This class includes saponin-containing drugs and drug containing emetic, acid tasting or bitter compounds. These expectorants evoke a reflex stimulation of respiratory secretion by activating an afferent mechanism upon contact with the gastric or duodenal mucosa. These drugs can stimulate the emetic center and will induce vomiting unless administered in small quantities.

Direct-acting expectorants. This class includes essential oil-containing drugs. In contrast to reflex expectorants, the essential oils are well absorbed after oral administration and are partially excreted via the lung where they stimulate the serous glandular cells and ciliated epithelium.

Therefore, the development of tea for the treatment of bronchitis in the composition to be included as a medicinal plant containing saponins and essential natural oil.

# SECTION № 5

# MODERN BIOTECHNOLOGY

# REASEARCH OF ANTIBACTERIAL ACTION NEW TOPICAL GRUG

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One of the parameters that characterize the quality of medical means is resistant to microbial contamination. The level of microbial contamination depending from the majority of factors: the nature of the raw material, water contenting, the type of packaging materials or disorder drug manufacturing sanitary norms.

It is known that the conditions for the spread of microorganisms in mild topical means more favorable than solid. High level of microbial contamination of drugs is very dangerous for the stability of the drug and to human health.

Achievement the microbial purity of non-sterile means, which include soft means, carried out in two main directions: production according the full compliance with GMP requirements and/or the appending of antimicrobial substances, which, depending from the medical form, is added to kill microorganisms (bactericidal effect), or for the reproduction (bacteriostatic effect) preventing.

The GMP observance is guaranteed the high level cleanness of the prepared of the finished product will be always attained. Even with a threat of microbial contamination or other discrepancies at any stage of the production cycle of a procedure for all technological processes allows time to take appropriate action, so the risk of bad-quality drug release is virtually nonexistent.

It should be noted that conservation does not preclude observance of sanitary requirements of the production process and according to the State Pharmacopoeia of Ukraine 1 edition should not be used as an alternative to GMP. Long-term using of preserving agents is able to break the skin and microbiocenosis, to show allergenic, carcinogenic, mutagenic effect or embryotoxic effect.

During the development of medical forms' composition is obligatory to addressing issues related to adequate protection from the adverse effects preparation, which may be as results from its microbial contamination or reproduction of microorganisms in it during storing and using.

In a state institution "V. Danilevsky Institute for Endocrine Pathology Problems National Academy of Medical Sciences of Ukraine" being developed to create a topical treatment for skin lesions, which are caused by the abnormal various complications endocrinopathies.

Local drug therapy have a key role due to the relatively simplicity of using

available, and its selection depends from on the damage. Now gelatinous formulations for the treatment of damaged skin and tissue surface are preferring, because they have better absorptive capacity and the pasty consistence.

Most of soft drug using to treat skin diseases of various etiologies have antimicrobial activity to include in their composition solvents or other components of the framework, promoting a potentiation of the action.

Decide on the use of preserving agent in a new vehicle for topical treatment of skin lesions, which are caused by complications of different flow endocrinopathies, performed according to the method SPU 1 species (5.1.3. The effectiveness of antimicrobial preservatives).

Soft drugs inoculated test organisms: Pseudomonas aeruginosa - ATCC 9027; Staphylococcus aureus - ATCC 6538; Candida albicans - ATCC 10231; Aspergillus niger - ATCC 16404 and conducted research to study the number of viable microorganisms within 28 days.

Verification of the effectiveness of the antimicrobial preservative action is carried out on the second, seventh, eighth, fourteenth and twenty-eighth days. From each sample one gram sample is collected; calculate the number of microorganisms by seeding on plates or by membrane filtration.

Preservative effectiveness is evaluated by the reduction factor (RF) - the logarithm of the number of microorganisms included ($N_1$), to the remaining number ($N_2$). Reduction factor should be at least 3 for the bacteria and at least two of fungi. The preservative should reduce the number of bacteria and fungi at least 1000 and 100 times, respectively. At day 28, increase and growth of microorganisms in ointments should not be detected.

The effectiveness of the drug considered satisfactory if at the conditions of the test, at the storage of the inoculated samples at a setting the temperature during these periods the number of microorganisms significantly decrease or doesn’t increase, depending on the requirements of the finished product. Criteria of evaluation are showing reduce the number of microorganisms over time, depending on the desired degree of protection of medicines.

Today at the Department of Biotechnology of National University of Pharmacy together with the State institution "V. Danilevsky Institute for Endocrine Pathology Problems National Academy of Medical Sciences of Ukraine” research into the effectiveness of antimicrobial preservatives in soft dosage form with expected reparative activity is conducted.

# COMPARATIVE ANALYSIS OF METHODS FOR DETERMINATION OF ANTAGONIST ACTIVITY OF ACID LACTIC BACTERIA

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The in vintro methods allow you to check up quickly the big array of trains of the acid lactic bacteria and the test-cultures of undesirable microorganisms. You can include diffusion methods and methods of testing in liquid nutrient mediums to the given group. Diffusion methods (holes methods, blocks, perpendicular strokes, drops, etc.) are based on diffusion of antibiotic substances, formed by the test strains of lactobacilli, in thickness agar environment containing the test-culture, and suppression of growth by the last one. A method of perpendicular strokes is used the most. For an objective assessment of lactobacilli antagonistic action, detectable by this method, it is necessary to consider, that it gives advantage to strains which produce inhibitory connections of a small molecular mass, faster diffusing in thickness of agar layer and, consequently, giving more extensive zones of inhibition of the test-culture growth. This method has, however, essential deficiency: antibiotic substances producer and the test-organism are grown in the same environment, but not always the same environment is equally suitable for the producer and its formation of an antibiotic, and for growth of the test-organism. It is possible to define antagonistic activity of the pure and mixed dairy cultures of lactic bacteria by holes method, for example, to compare on this parameter various commercial dairy products. The disadvantage of the method is that there is a danger of leakage of liquids with lactic bacteria culture from hole in a crack between an agar and a bottom of a cup that causes the distortion of result. Unlike perpendicular strokes method, the blocks method gives an opportunity to compare a couple of (4-8) lactobacillus strains on one cup to the given test-culture. Besides, the method allows to use structurally various nutrient environment: one (block) is for the test lactobacilli, another is for the given strain test. Besides it is convenient for studying influence of a nutrient environment influence on inhibitory production connections studied by lactobacilli strains. Advantage of the agar layers method is the creation of a possibility to differentiate production of bacteriocins, and the disadvantage is the complexity of the process. As you can see, there are plenty of methods that help in defining of antimicrobial properties of studied microorganisms today, the choice of which depends on a predicted end result and research possibilities, but for reproducibility and unambiguity of results, in our opinion, it is necessary to conduct several methods.

# ANTIBIOTIC ACTIVITY OF ACTINOBACTERIA FROM THE RHIZOSPHERE OF PLANTS OF THE NIKITA BOTANICAL GARDENS

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In our world, and particularly in Ukraine, there is a complex problem of rapid spread of hospital infections that are mainly provoked by Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli, and others. The constant emergence of mutant strains of pathogens, resistant to the majority of known antibiotics, complicates the solution of the problem. Thus, the search for new biologically active compounds from natural sources, such as microorganisms, is topical now. Most of the *currently* available *antibiotics* are produced by microorganisms of the family Actinomycetaceae. Actinobacteria are soil microorganisms that have a wide range of biological activities; they produce enzymes, proteins, amino acids and antibiotic compounds.

The aim of our work is to outline and determine the properties of actinobacteria within the territory of the Nikita Botanical Gardens (NBG), located in the subtropical climate zone on a narrow section of the Black Sea coast of Crimea, what contributes to biodiversity of vegetation and, respectively, soil microorganisms, in comparison to other regions of Ukraine. In this study, the antibiotic activity of actinobacteria strains isolated from the root zone of plants from the upper (Phyllostachys viridi-glaucescens, Yucca aloifolia, Prunus domestica) and lower (Jubaea chilensis and Cedrus libani) parks was investigated. The soil samples were collected during 2008-2012.

Actinobacteria were isolated from the bulk samples of soil, treated with 1.5% solution of phenol, calcinated at 120°C during 60 min., by virtue of sowing of the diluted suspensions over seven agar medium with different composition. The antibiotic activity was studied by using strains of gram-negative bacteria Escherichia coli ATCC 25922, gram-positive bacteria Bacillus subtilis ATCC 31324 and Staphylococcus aureus ATCC 25923, yeast Saccharomyces cerevisiae D 67.S and fungi Aspergillus niger IBM 16706. Actinobacteria were sown over the agar medium by virtue of injection, grown at 28°C for 7 days and covered with 0,7% L-agar (bacteria) or Sabouraud medium (fungi) containing $10^9$ cells / ml of test cultures. After incubation in an incubator (at 37 ° C for 24 hours in the case of bacteria, at 25°C for 48 hours - yeast, 72 hours - fungi) the diameter of the zones of growth retardation of test cultures was measured. The activity level was determined by the ratio of the diameter of the zones of growth inhibition of test cultures to the diameter of the colony of actinobacteria and was designated as an activity index (AI).

524 isolates that attributed to the class of actinobacteria by morphological characteristics were allocated. About 50-70% of strains isolated from plants of the lower park (Jubaea chilensis and Cedrus libani), inhibited the growth of B. subtilis. Almost half of them (28-40%) delayed the growth of S. aureus. 9% of isolates from rhizosphere of the Cedrus libani and 17% from the root zone of the Jubaea chilensis respectively had AI 4.0-9.9 against B. subtilis. The same AI against S. aureus had only 4.7% of actinobacteria from the rhizosphere of the Cedrus libani. The remaining strains had lower AI against these test cultures. The growth of E. coli and S. cerevisiae was inhibited by 15.0 - 24.0% of strains isolated in the lower park. Only 1.75% of strains from the rhizosphere of Jubaea chilensis had the highest IA 4.0-6.9 against E. coli. The growth of A. niger was suppressed with about 40% of strains from the root zone of the Cedrus libani and only 9% from the rhizosphere of Jubaea chilensis. Their IA did not exceed 1.0-3.9.

Only about half the number of actinobacteria with antimicrobial properties against our test cultures were isolated from the root zone of Yucca aloifolia and Prunus domestica compared with strains from the lower park. At the same time, the number of strains from the rhizosphere of Phyllostachys viridi-glaucescens was about the same as in the group of strains from the lower park. Also it was found that the number of strains with AI higher than 4.0-6.9 in the samples from the upper park was significantly less.

Among the analyzed strains the isolates that inhibited the majority of used test cultures, including strain № 4-44 (from the rhizosphere of Phyllostachys viridi-glaucescens) and № 58-74 (the rhizosphere of Cedrus libani) were found. Only the last one - had the highest activity (IA 3.8) against A. niger.

We extracted strains that specifically inhibited the growth of only certain test cultures. Strains №58-8, №58-79 and №58-24 (from the rhizosphere of Cedrus libani), inhibited only growth of yeast and fungi. Strain № 4-236 (from the rhizosphere of Phyllostachys viridi-glaucescens) inhibited growth only of E. coli, and strain № 53-14 (from the rhizosphere of Prunus domestica) was active only against Staphylococcus aureus.

The results indicate that actinobacteria strains, isolated from different gardens of NBG, differ both in spectrum and level of antibiotic activity. It may be due to the composition of the soil, as well as features of species, from the root zones of which we isolated our strains. At the moment, a chemical analysis of metabolites synthesized by our strains is being studied. This will enable us to determine the structure of compounds that cause their antimicrobial activity. All strains of actinobacteria that were studied during our work are stored in the Culture Collection of Microorganisms – producers of antibiotics of Ivan Franko Lviv National University.

# PREPARATION OF PRACTICAL STUDIES IN RA-BOT WITH OBTAINING MONOLAYER CELLS

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We have considered the theoretical basis of the methods and systems of cultivation of cells in animals and humans, used in modern biotechnology. Special attention is paid to the cultivation of the cell monolayer.

Nowadays monolayer cultures have several advantages, JW-laudisa prerequisites for their use:

1. The possibility of in vivo observation of cells using a microscope.

2. The use of a small number of cells, i.e. one cell can replace the clinic patients.

3. The researcher may modify the terms of growing cells in a certain limited range, which allows to estimate the influence on the growth of cells by a variety of factors - pH, temperature, etc. Our research work is conducted in two directions:

1. Selection and training of laboratory equipment and the experimental conditions that are optimal for the chosen method of cultivation.

2. The development of cultivation technology of monolayer cells for effective for producing the desired product.

The first direction involves the appropriate equipment culture of Boxing, the selection of the culture dish, culture media and other solutions, providing optimal conditions to obtain a monolayer of cells, their transfer, and the choice of control methods: review and evaluation of the quality of the monolayer, cell counting, microscopy and photography. Indoor culture unit requires laminar, where we will perform all manipulations with cells, that is, it is actually working place, also need a $CO_2$-incubator, refrigerator, table with light and inverted light microscopes and a cupboard with kitchenware.

Monocline cultivation is carried out in bottles, probir quay, plastic plates, Petri dishes, flat-bottomed bottles, vessels Carrel. We have determined the feasibility of using Petri dishes or plastic tablets.

The creation of conditions of asepsis, the training of personnel and clothing: systematic treatment of the hands; strictly defined sequence dressing; the use of breathable bandages on his face, rubber gloves. Thus, based on the analysis of the theoretical foundations, requirements and conditions of cell cultivation, we have developed a cycle of preparatory work to obtain a monolayer of cells in the laboratory.

# QUALITATIVE AND QUANTITATIVE RESEARCH COMPOSITION BIOLOGICAL PRODUCT "BAIKAL EM"

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EM – technology – is one of the most promising directions of development agricultural production in the XXI century – application of effective microorganisms. Biological product "Baikal EM" – is a concentrate, created by a special technology in liquid form, which contains a large number of effective (useful) microorganisms living in the soil. The product includes microorganisms such as Saccharomyces, Lactobacillus, and Nitrogen-fixing photosynthetic bacteria; together they form a stable symbiosis. Interaction in the soil, microorganisms produce enzymes and physiologically active substances, amino acids, nucleic acids and other biologically active components that provide both direct and indirect positive effects on plant growth and development, accelerate the onset of flowering, increasing the number of ovaries and fruiting period, stimulating development of the root system, which restores soil fertility.

This biological product is also used as a supplement in food for animals and birds. Increasing the amount of essential amino acids by microorganisms which contains in this product improves the quality of forage. This forage is better digested and not only improves weight gain and other quality indicators animals, but also the prevention of gastro-intestinal diseases allergies, vitamin deficiency, intoxication and poisoning of animals, strengthen the immune system, the normalization of metabolism and others.

The objective of this study was to analyze the biological product "Baikal EM" on the presence of microorganisms specified by the manufacturer as part of the preparation, and their viability.

When conducting research on the qualitative composition, the product sample was plated on a special liquid and solid nutrient media. After isolation of pure cultures of microorganisms, was carried out to study the morphology of the colonies and microorganisms. As a result of microscopy it was established that in the biological product "Baikal EM" really includes microorganisms specified by the manufacturer, namely: Lactococcus, Lactobacillus, Saccharomyces.

Using the method of serial dilutions followed inoculation of each dilution on solid growth medium was set quantitative composition. The experimental results showed that the number of viable microorganisms' biological product "Baikal EM" is fully consistent with the established norms.

# HISTORY OF INSULIN

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Insulin - a hormone peptide nature formed in the beta-cells of the islets of Langerhans of the pancreas. It has a multifaceted effect on metabolic processes in virtually all tissues. The main effect of insulin is to reduce glucose concentration in the blood. Lack of insulin in the blood is a key factor in the development of diabetes person.

In 1921, Canadian doctors were able to isolate insulin from the pancreas of the dog. This medication they introduced to test the dog, which was called "experimental" diabetes. Shortly after injection sick dog woke up, got to her feet and walked. In 1922, seriously ill with diabetes boy was introduced drug derived from bovine pancreas. The result was not only save lives, but also to stop the progressive disease. The only source for industrial use of insulin in those days was the pancreas of pigs and cattle.

Unfortunately, the first animal insulin preparations cause a number of serious complications in patients, namely accumulation of antibodies to insulin, various allergic reactions, a decrease in insulin sensitivity, which forced to a constant regulation of the administered dose. This was due to the fact that the porcine and bovine insulin differs from human amino acid composition: bovine - three amino acids, and pig - one, leading to difficulty in treatment.

Only with the development of molecular biology towards the end of the 20th century it possible to determine the structure of human insulin. An active industrial production of insulin, human-identical hormone. One of the ways to get which were the biotechnology and semi-synthetic. Until now, the above methods are outdated. With semi-synthetic method feedstock passes many stages of purification. The disadvantage in this case is dependent on the supply of raw materials from livestock farms. The process for obtaining insulin via biosynthesis is: selected human insulin gene inserted into the genome of E. coli, which rapidly synthesize proinsulin. At the moment, relevant biotechnological method of producing insulin, it has a number of advantages: the lack of dependence on raw materials from cattle farms, simple scaling process. Production of insulin using genetically modified organisms is an important issue of modern biotechnology, since this method produces insulin preparation of high purity, most identical to human insulin, high efficiency, and minimize the cost of production, which will reduce the cost of the drug that is currently time is very important to the consumer market in Ukraine.

# STUDY OF BIOGENIC STIMULATORS BASED ON ALOE VERA

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The mankind has been worried about the maintenance of health and vital body functions for centuries. Biogenic stimulators mean biologically active substances produced in isolated animals and plant tissues in the process of adaptation to unfavorable conditions (cooling, being in the dark). In case of being administered in the body, they have a stimulating effect on the metabolism and regeneration processes. The chemical nature of biogenic stimulators has been sufficiently studied. As a rule, they represent a complex combination of substances. The qualitative and quantitative composition of biogenic stimulators in tissue preparations is unstable and partly depends on the specification of metabolism of the tissue itself. Dicarboxylic hydroxy acids of aliphatic series, aromatic acids of high molecular weight, vitamins, and minerals are the most biologically active. Their biological activity is evaluated according to their ability to enhance regenerative and metabolic processes in the body.

The mechanism of the effect of biogenic stimulators on the body is to change the activity of a range of enzymes, which in their turn leads to endocrine restructuring: secretion of hormones in the main endocrine glands in the body - in the pituitary gland is being increased. Pituitary hormones stimulate the production of other hormones: sex, thyroid hormones, adrenal glands, and so on, which contributes to enhance the metabolic processes in the body. It is known that aloe preparations contain biogenic stimulators.

Aloe preparations have anti-microbial, anti-inflammatory, and wound-healing properties. They improve appetite, enhance the secretion of digestive glands and bile secretion, they are mild laxatives, increase the protective properties of the body, and stimulate the regenerative processes in the damaged tissues. Aloe latex, extracted from fresh leaves, is used externally for the treatment of purulent wounds, burns, osteomyelitis, trophic ulcers, for rinsing in case of disease of the nasopharynx and gums. In gynecology fresh aloe is used in the treatment of cervical erosion. Aloe liniment, prepared from aloe leaves is used in the treatment of burns and radiation injuries of the skin. Aloe can also be used orally for improving the body's resistance to infectious diseases. Aloe syrup with iron is taken in case of diseases of the gastrointestinal tract, iron deficiency anemia, after infectious and other debilitating diseases and intoxications.

# DOMESTIC DAIRY PRODUCTS AS THE BASIS OF FUNCTIONAL FOOD

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Functional food - a special-purpose products of natural or synthetic origin with desired properties, which are designed for the systematic daily use and to replenish the lack of an organism, especially regulatory food substances. These products support physical health and reduce the risk of disease.

Products functionality contained in a large amount: lactic acid bacteria (probiotics and prebiotics), vitamins, oligosaccharides, cellulose, fiber, bioflavonoids, antioxidants, fatty acids, essential amino acids, proteins, and the like. Lactobacilli due to a wide range of physiological and biochemical properties have several advantages as components of functional foods.

Lactic acid bacteria has for several decades attracted increasing attention of researchers. Established their dominant role in the normal functioning microbiocenosis humans and animals, allowing the group to include lactobacilli GRAS (generally regarded as safe) microorganisms.

Lactobacilli have several advantages as part of functional food. They produce enzymes (including β-galactosidase), lactic acid (the presence of which inhibits the viability of many acid-sensitive pathogens), B vitamins, amino acids, lysozyme, biologically active L-amino acids. Lactobacillus strains have good adhesive properties. Due to this, lactobacilli colonize the intestines of animals active and stable in a wide range of pH values. Lactobacilli inhibit the growth and development of pathogenic organisms.

The aim of the study was to analyze the state of the domestic market of fermented probiotic products. Currently, there is a large enough range of probiotic fermented milk products on the basis of bifidobacteria and lactobacilli made in Ukraine. The consumption of these products decreased significantly in the period from 2011 until middle 2014. If in 2011 the market size of dairy products in kind was 549.9 thousand tons, in 2013 - 479.3 thousand tons, which is 2.8% less than in 2012.

Despite the general trends of the group of dairy products, yogurt consumption from 2013 increases. If in 2012 there was decline in the consumption of yogurt is almost 20%, possibly as a consequence of a decrease in income, in 2013 the market capacity increased by 4.8% to 79.2 thousand tons, and continued to grow in 2014. The market of dairy products Ukrainian producers are almost completely satisfy

consumer demand. While the share of domestic production in consumption is increasing every year.

Group "Lactalis", which consists of CJSC "Lactalis-Mykolaiv" and LLC "Milk House", are also increasing their share in the domestic market of dairy products, occupying 6.3% today. Trademarks are the «President», «Fanny", "Dolce from President», «Lactonia", "Bilosvit", "Immune +" and others.

Holding "Milk Alliance" brings together companies such as OJSC "Yagotinsky MF", JSC "Bashtansky CF", OJSC "Gorodenka CF", CJSC "Pyryatynsky CF", JSC "Trostyanetsky MF", CJSC "Zolotonisky MK". Share holding presence in the market of dairy products is increasing every year, and today it is 4.3%.The products of these plants produced under the trademarks "Slavia", "Milky Way", "Health" and "Yagotynske."

The share of "Rainford" in the market has considerably decreased over the past three years. Now the company occupies a 4.3% market share in the segment of dairy products and introduced to the market under the trade mark "Bravo".

Holding company "Terra Food" closes the top ten markets, including share of 3.4%. As part of such companies as LLC "Belotserkovsky MF", LLC "Tulchinsky BCF", LLC "Mogilev-Podolsky MF", Novoodesskaya branch "Inter-Food". The most well-known trademarks are holdings "Tulchinka», «Premialle» (in the premium segment), "White Line".

Conclusions. In contrast to the rational or balanced diet advocated by nutritionists past years, functional food takes into account not only (or even mainly) the nutritional value of the products (the presence of fats, proteins and carbohydrates), but their functionality (utility) or biological value.

The lack or excess of appropriate food substrates can serve as a signal to the base, and immune and neuroendocrine regulation of homeostasis of the human body. By varying the quantitative value and value coming from probiotics and functional food products for certain food substrates can be controlled virtually all life processes.

Fundamental research in lactic acid bacteria strains and search with a strong antimutagenic, immunogenic activity and explore possible mechanisms of action in the future will create a comprehensive probiotic multystrains drugs and food of a new generation whose use in functional foods will improve the quality of life, provide resistance to harmful environmental influences and various infectious diseases.

In general, the consumption of functional foods (including yogurt) will remain stable in Ukraine. The consumption per capita output is still far from the recommended rational norm. Therefore, the Ukrainian market has the potential for further development.

# A STUDY OF THE MORPHOLOGY AND GROWTH OF CANDIDA GLABRATA

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Candida glabrata is the yeast-like fungus from the genus Candida, formerly known as Torulopsis glabrata. Until recently, Candida glabrata was considered to be a non-pathogenic saprophyte presents in the normal flora of healthy people. It can be found on the skin, in the urine. This species is the second pathogen in the genus Candida prevalence after Candida albicans. Candida glabrata infections are difficult to treat - 20% of fungi are resistant to antifungal azole series, which is the gold standard in the candidiasis treatment. This is especially true of fluconazole and ketoconazole. Candida glabrata is associated with diseases of the oral mucosa and esophageal - about 20% of mucosal yeast infections are caused by this pathogen. Urinary candidiasis caused by Candida glabrata, attributes to nosocomial infections. Bloodstream systemic infection – candidemia, caused by this microorganism, is a serious disease with mortality rates of 50% in patients suffering from malignant diseases, and 100% in recipients with bone marrow pathology. Symptoms of Candida glabrata to detect the initial evaluation is not always easy. Most often asymptomatic urogenital candidiasis. In complicated forms of candidiasis observed edema, extensive erythema, there may be minor release. They have kroshkoobraznuyu fairly thick consistency. Due to the lack of symptoms in patients with kandodemiey often observed deaths, especially if patients are oncology. For the Candida glabrata cultivation liquid and solid nutrient medium were used: Sabouraud agar and Sabouraud broth, some of them were enriched with 10% serum of cattle. On the solid nutrient medium to obtain isolated colonies growth the fungus was inoculated by debilitating culture technique. Cultures were incubated at 37˚C. Accounting for culture growth was carried out every 24 hours. The fungus morphology was studied in preparations for microscopic examination: "Crushed drops" and smear preparations stained with a solution of methylene blue. In the course of this research the nature of Candida glabrata growth in liquid media and the morphology of colonies on solid media was studied and evaluated. We have studied the colonies structure, texture, shape, color, size and shape as well as cell morphology in stained preparations.

As a result of this experiment we can conclude that Candida glabrata is an excellent model object. It can be used in antifungal effects of known and novel agents studying. Knowing the Candida glabrata characteristics is important because it is an essential part of human microflora.

# PECULARITIES OF MICROBIAL EXOPOLYSACCHARIDE ETHAPOLAN SYNTHESIS ON VARIOUS OIL-CONTAINING SUBSTRATES

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Microbial exopolysaccharides (EPS) due to the ability of their solutions to gelation, emulsification, suspending and changing rheological properties of aqueous systems are widely used in various industries, agriculture and medicine. The vast majority of known microbial EPS are obtained from carbohydrate substrates. Last years the researches of using industrial waste have been activated to obtain a practically valuable microbial metabolites. Oil-containing waste are promising for using in microbial technologies. Previously, we have established the possibility to use sunflower oil as a source of carbon and energy for the synthesis of microbial polysaccharide ethapolan by *Acinetobacter* sp. IMV B-7005. The purpose of this work − to research refined oil replacing on waste (fried) one for the strain IMV B-7005 cultivation.

*Acinetobacter* sp. IMV B-7005 was carried out in a liquid mineral medium of such composition (g/l): $KH_2PO_4$ − 6.8; KOH − 0.9; $MgSO_4 \times 7H_2O$ – 0.4; $CaCl_2 \times 2H_2O$ – 0.1; $NH_4NO_3$ – 0.4; $FeSO_4 \times 7H_2O$ – 0.001. Refined, unrefined sunflower oil and waste oil after frying meat or potato (5%, v/v) were used as a sources of carbon and energy. In additionally yeast autolysate (0.5%, v/v) and multivitamin complex "Complevit" (0.00095%) were added to the medium as growth promoter and source of pantothenate, respectively. In additionally yeast autolysate (0.5 %, v/v) and multivitamin complex "Complevit" (0.00095 % ) were added to the medium as growth promoter and source of pantothenate, respectively.

Culture from the exponential phase, grown in the medium with 0.5 % of sunflower oil was used as the inoculum. Quantity of inoculum was 10 % from the volume of the medium. Cultivation of *Acinetobacter* sp. IMV B-7005 was carried out in flasks (750 ml) with 100 ml of medium in shacker (320 rpm) at 30 ºC for 120 hours.

We have established that amount of synthesized EPS in the medium which contained unrefined sunflower oil and waste oil after frying meat was 15.5 and 14.4 g/l respectively, that is in 1.2 times higher under *Acinetobacter* sp. IMV B-7005 cultivation on refined sunflower oil. At the same time parameters of ethapolan synthesis on waste oil after frying potato were the lowest: the concentration of EPS and EPS- synthesizing ability didn't exceed 4.2 g/l and 2.8-3.3 g EPS/g biomass, respectively. In these studies, inoculum was grown on refined oil regardless of the oil type used for cultivation, as it gave better results. And only indices of ethapolan synthesis in the medium containing waste oil after frying potato were increased to 8.1 g/l with using inoculum grown on the same substrate.

Thus, this work shows the possibility of replacing refined sunflower oil in a medium on unrefined and waste oil after frying meat or potato to produce exopolysaccharide ethapolan. The synthesis dependence on the method of inoculum preparation were also shown.

# PROMISING TO STUDY THE ADHESIVE PROPERTIES PROBIOTIC FERMENTS

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In recent years, probiotic products and functional food products prepared on the basis of live bacteria ferments culture have been increasingly used in complex therapy of a number of pathological conditions occurring against the backdrop of the broken normal microflora of the human body.

A number of authors demonstrated that probiotics for humanmust meet the following requirements: save the necessary concept in the process of production; have the potential colonization, to adhere well to the relevant mucosal epithelium; antibiotic substances produce anti -E. coli factor, etc.

Special attention should be paid to the study of the adhesive properties of probiotic cultures as a fundamental factor in their competition with the conditionally pathogenic microflora or infectious agents.

Adhesion - a complex multi-component process, which provides the colonization of microorganisms any solid substrates including human and animal tissues.

Commonly known method for determining fixing properties of microorganisms to epitheliumusing the cell line - Caco-2 based on the relationship with the bacteria wall colorectal epithelial cells in human colon carcinoma monolayer.Its advantage is that it allows to study investigated the properties directly on human cells, but unfortunately, is the expensive and time consuming.Known method of simultaneous determination of microbial colonies primary adhesiveness seeding erythrocytes. There is also a photometric method for determining the activity of bacteriafixingto erythrocytes, which allows you to accurately and objectively sufficient to simulate the process of attachment of bacteria to the epithelial cells.

The most common by far the study of adhesion of bacterial microflora ferments used detailed Brilis' method.As cells in this method is proposed to use the native human erythrocytes O / I Rh (+) - groups which contain on their surface glikoferin - a substance identical glycocalyx of epithelial cells. Adhesion is assessed by the following parameters: average adhesion and the index of adhesion of microorganisms.To date, at the Department of Biotechnology of the National University of Pharmacy adhesive properties of probiotic fermented sourdough cultures such as: "Bifivit Vivo", "Simbilakt Vivo", "Yogurt Vivo", "Yogurt", "Lactobacterin"have been studied.

# STUDY OF COSMETIC WITH PROBIOTICS

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At present, the actual direction of modern pharmaceutical science is the study of cosmetic products with probiotics. Probiotics - a class of microorganisms and microbial agents and other origin used for therapeutic purposes, as well as food and dietary supplements containing live microculture. Probiotics - mainly bifidobacteria and lactobacilli, but may also be other organisms such as yeast.

Probiotics restore the natural microflora of the human body, helps to improve digestion, detoxification, a beneficial effect on the immune system, lower cholesterol, etc.

The main objective of probiotics in the composition of cosmetic beauty products - affect the state of the microflora of the skin, thereby improving its protective function and prevent moisture loss, reduce the manifestations of inflammation, remove redness, dryness cope with and activate fibroblasts, stimulate the production of structural components of the skin - collagen and elastin. Data from numerous studies have shown that probiotics can exert a pronounced tightening effect, increase the skin's ability to regenerate and repair processes, reduce the number and depth of wrinkles, restore its vitality and help eliminate toxins. In addition, recent results were obtained: application to the skin means with probiotics reduce unsightly defects acne.

As a rule, administered in creams fragments lactobacilli and bifidobacteria. They have a positive effect on the skin

Means with probiotics are presented in cosmetic products Lancome, Clinique, Burts'nBees, Amala, Christina, Payot, Decleor, Dr.PierreRicaud

Clinical trials have confirmed that probiotic technology helps transform your skin at a deep level. Probiotic technology eliminates up to 50% of skin lesions, and can activate cell regeneration to 70%. Probiotics also stimulate the immune system of the skin and restore its natural defenses, prevent the destruction of collagen and moisturize, slowing the aging process.

However, some dermatologists are not yet ready to call probiotics anti-aging means the new generation and believe that their anti-aging effect yet has little scientific evidence. In addition, you need to be careful to select probiotics: incorrectly selected bacteria can cause acne eruptions.

But in general, researchers agree that cosmetics based on probiotics is really useful if you use the right bacteria.

# THE REVIEW OF DOMESTIC AND INDUSTRIALLY PRODUSED YOGHURTS BY CUSTOMER PREFERENCES

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At present, the major problem is the lack of supply of vitamins and separate trace elements, which causes metabolic disorders and as a consequence, the development of pathologies. Recently, one of the important directions is expanding the range of dairy products, especially yoghurts, improvement of production technology, production of innovative packaging for the retail trade, expansion and development of new types with different physical and chemical indicators based on consumer preferences, such as acidity and viscosity, containing various additives, enriched with vitamins, trace elements and dietary fibers that promote and enhance immunity, is one of the important directions.

Given work bears the objective to consider the relevance of expanding the range of dairy products, as well as to consider the modern technologies in this area. Yogurt can be produced by a thermostat and reservoir methods. The raw material for yoghurt is whole cow's milk with acidity less than 19 °T; cream with a fat content of less than 30% and less than 18 °T acidity (plasma acidity lower than 26 °T); dried whole milk and spray dried skimmed milk powder, beet sugar, fruit syrups made from natural fruits and berries made especially for milk beverages. The concentration of nonfat milk solids is increased by adding milk powder. When formulating yogurt by reservoir method the following operations are made: reception and preparation of raw materials, thermal processing, homogenization, cooling, fermentation, ripening; cooling, blending, bottling and in the thermostat mode of production after fermentation are made the following operations: bottling and capping fermented milk; souring in an incubator; cooling the finished product; storage. The digestibility of fermented products in the human body is higher than that of milk, so they are the most common. In recent years scientists in our country and around the world are working to create milk drinks for patients of all ages with food allergies and disorders of the digestive system, accompanied by food intolerance, such as lactose intolerance milk. Due to the extremely wide use of antibiotics by our population, the environmental degradation that has resulted in violations of human microbiocenosis, fermented milk drinks are becoming more and more popular. Especially popular among the population are yogurts - fermented milk products with high mass fraction of solids. Therefore, it is topical is to expand the range of dairy products functionality, including products with high mass fraction of solids.

# BACTERIOPHAGES USED IN COSMETOLOGY

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For treatment of become inflamed illnesses of microbial nature historically adopted to use preparations of antibacterial action: disinfectants and antibiotic. But despite on undoubtedly effectiveness of these means, their using provoke simultaneous uppression of whole microflora: as pathogenic, also and normoflora – up to full destruction of her symbiotical population. The most safety and «ecologically clear» method of contest against microbial infections is using of natural ways of regulations of number of populations – biological limitations. Natural biological limiter for bacterium is bacteriophages. Using of bacteriophages with narrowly specifically lytic action on couter - inflaming and antibacterial therapy allows not only to destroy population of pathogenic microorganisms (also and antibioticaly resistant strains), but and enrich conditions for development«usefull» bacterium of normoflora. Undeniably advantages of protobes are narrow spectrum of antimicrobial action, capability to accumulation, long time of acting and harmlessly for patient.

Actual problems of phagotherapy are in the center of attention. Generalization accumulated information by results of protobe consisted means and narrow cooperation virologists, bacteriologist, practical doctors, biotechnologist and veterinary allows to create means, which do not have analogues in the world of microorganism and use them for precaution of illnesses of microbial ethiology by the way clearing from conditionally-pathogenically bacterium. One of such means is gel-spray for hand – biological gloves.

Purpose of work is showing the perspective of using cosmological means based on bacteriophages also explanation of need passing biotechnical researches of cosmological means on activity of said bacteriophages. It is going to make researches of bacteriophages which are used by operation cosmetics «Sengara» on specificity. For studying we will be use gel-spray for hands – biological gloves made by "NEC Agrovetzaschita S.-P.," Russia, commissioned by LLC "Sengar" for JSC "Faberlic". Specify is characterized by occurrence or nonoccurrence acritical activity of bacteriophages in a ratio of heterolytic bacterium. and studying for occurrence announced bacteriophages (Wolinella Spp., Actinovyces Spp., Actinobacillus actinomycetemcomitans, Porfiromonas gingivalis, Campylobacter Spp., Bacteroides Spp., Staphylococcus aureus, Streptococcus pyogenes, Streptococcus mutans, Pstudomonas aeruginosa, Proteus vulgaris, Klebsiella).

# ANTIFUNGALS MEDICINE

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In recent decades, there has been substantial growth of fungal diseases. This is due to many factors, with wide application in medical practice, broad-spectrum antibiotics, immunosuppressive drugs and other groups.

Due to the rising trend of fungal diseases (both surface and severe visceral fungal infections associated with HIV infection, hematologic malignancies), the development of bacterial resistance to existing drugs, the identification of fungal species previously considered non-pathogenic (currently considered to be potential agents of mycoses about 400 species of fungi), has increased the need for effective anti-fungal agent.

Currently are 4 groups of fungal diseases:

1) Keratomikozy (pityriasis versicolor, etc.) Under which the fungi are located in the stratum corneum and not cause inflammation and sensations;

2) Tinea in which mushrooms are localized in the epidermis, expressed inflammatory cause skin reactions, affect skin appendages. This group includes trichophytosis, microsporia favus and others;

3) Candidiasis (candidiasis), and that can affect the mucous membrane of the mouth, skin, nails and internal organs;

4) Deep mycoses, where the process involved the mucous membranes, skin, muscles, bones, internal organs and the nervous system.

Fungal diseases are known for a long time, since the days of antiquity. However, agents of ringworm, candidiasis were detected only in the middle of the XIX century.

At the beginning of XX century pathogens have been described many of visceral mycosis. Before the advent of medical practice for the treatment of fungal infections antifungals used antiseptics and potassium iodide. Antimycotics began to develop and apply at the beginning of the XX century.

Antifungal agents (antimycotics) - drugs having fungicidal or fungistatic activity and used for the prevention and treatment of fungal infections.

For the treatment of fungal diseases using a number of drugs of different origin (natural or synthetic) spectrum and mechanism of action, antifungal effect (fungicidal or fungistatic), indications for use (local or systemic infection), a method of assigning (oral, parenteral, externally).

# STUDY OF ANTIMICROBIAL PROPERTIES OF "NON-TRADITIONAL" DAIRY BEVERAGE TYPE KUMYS

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Nowadays fermented milk drinks, i.e. milk, fermented by various lactic acid bacteria enjoy well-deserved popularity among millions of people of different countries. The growth of consumer interest in fermented milk products (FMP) is caused by bringing their positive effects on the human body. In addition, because of the relevance of a healthy diet unconventional for our regions dairy products appear in retail. It is worth noting that the emergence of new products shows that although the market and formed, there is a need for new kinds of products, which are healthy and of high quality. This explains the growing popularity of functional FMP.

The above encourages domestic producers to expand its product range. New products for our market include ayran, tan, kumys, etc. Despite the fact that the history of these drinks has 15 centuries, for many consumers, this product remains unknown, and is in low demand.

The Department of biotechnology of NUPh in the laboratory developed manufacturing technology of such a product as Kumys. The study of the qualitative and quantitative composition of the product manufactured by us showed the presence of a large amount of Lactobacillus and yeast microflora, which is responsible for the manifestation of antimicrobial properties.

This paper presents the results of the study of antimicrobial properties of Kumys which was made by us and its comparison with the product of trademarks LLC "NEO Product".

The study of antimicrobial properties of unconventional FMP was performed with method of co-culture with conditionally pathogenic microorganisms (E. coli, St. aureus) followed by inoculation of the corresponding dense environment. The principle of the method consists in counting the number of colonies of conditionally pathogenic microorganisms that grew up after cultivation in liquid medium with FMP and compared with the control (test microorganisms without FMP).

The results of the experiments showed that both types of non-traditional FMP have antimicrobial properties against of the most common pathogens - St. aureus and E. coli. But, it should be noted that the products manufactured by us had a more pronounced antimicrobial effect, which is associated, primarily, with a large number of microorganisms in the microflora of our product and, secondly, using the "correct" controlpane raw materials.

# STUDY OF ANTIMICROBIAL ACTIVITY OF ESSENTIAL OILS

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In present tense in the whole world there is a tendency to the use of preparations of phytogenous that is explained by content in them by a complex biologically active substances, more soft operating on an organism and less at their application. In medicine all more often at various infections and diseases appoint antimicrobial therapy, however her application results in negative consequences. With every year the amount of proof and not sensitive forms of microorganisms grows substantially. The necessity of search of new anti-infectives that does not assist forming of stability appeared in this connection. For the last twenty years many experimental researches that confirmed the antimicrobial action of essential oils in the relation of different types of bacteria and mushrooms were executed. Considerable interest in that behalf is medicinal preparations that have essential oils. From literary sources it is known that microorganisms at the protracted contact with essential oils practically do not have signs of getting used to them, that is them by ponderable advantage before antibiotics. Essential oils and medical plants bring over to itself attention foremost as not exhausted sources of medical raw material for creation of preparations with antimicrobial, antiinflammatory and restores immunity. Essential oil is liquid volatile mixture of organic substances, that is produced by plants and gives to them to the smell. Most essential oils well dissolve in petrol, ether, chloroform, lipids, in oils and other substances of lipophil, and badly - in water. In addition, comparisons of antimicrobial activity of the same oil are related to that on composition of essential oils influence as ground-climatic and ecological terms of increase of plants with essential oils, and also technology of receipt of oil and condition of his storage. The aim of this research was a study of antimicrobial activity of next essential oils : eucalyptus, orange, lavender and to crumple перечної. As organisms of tests Escherichia of coli were used - (ATCC) 25922, Staphylococcus of aureus - (ATCC) 25923, Bacillus of subtilis - (DICK) 1313, Proteus of vulgaris - (ATCC) 4636, Candida of albicans - (ATCC) 885\653.

In quality of nourishing environments used a nutrient agar and agar of Sabouraud. As a result of research mildly-active bacterial activity was educed in relation to the organisms of tests used by us. In future works will proceed on the study of antimicrobial properties of various essential oils on the base of department of biotechnology of the National University of Pharmacy.

# THE STUDY OF STRUCTURE AND PROPERTIES OF KOMBUCHA MEDUSOMYCES GISEVI

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Kombucha (Medusomyces gisevi), also in the household is “mushroom”, is a symbiosis of yeast and acetic acid bacteria. In this work, we had studied the microbiological structure, physico-chemical, microbial and therapeutic properties of this object. Therapeutic effect of Kombucha Medusomyces gisevi is shown in improving of digestion, strengthening of the Central nervous system, reduction of blood pressure in patients with hypertension, and the drink has a tonic and calming effect, helps with diabetes, diseases of the prostate and kidney problems.

The study was conducted in two stages: the first is the cooking of the drink Kombucha (cultivation); the second is the study of its properties: determination of pH of a solution (active acidity), organoleptic, chemical and microbiological structure.

As a result of studying of organoleptic properties it was found that during the time of cultivation of the mushroom they was changing: the color of the drink from the light changed to light brown; the taste was fickle; primary sugar solution during cooking of the beverage acquired a sour taste, which eventually became richer; also observed the separation of carbon dioxide, the drink was acquired a slightly carbonated taste.

The study of the microbiological structure of Kombucha showed the presence of cultures of microorganisms is in a symbiotic relationship: yeast-like fungi (Saccharomyces ludwigii, Saccharomyces cerevisiae, Candida stellata, Schizosaccharomyces pombe, Torulaspora delbrueckii, Zygosaccharomyces bailii etc.) and bacteria (Acetobacter xylinum and other species of the genus of Acetobacter).

Due to the accumulation in the drink different organic acids (gluconic, citric, lactic, acetic, malic), in the process of vital activity of microorganisms, the pH of the beverage decreases over time, it has become a high acidity.

When Kombucha is culturing is formed natural antibiotic Medusan, which is perfectly cope with the infection and doesn’t weakens the human immune system. Medusan affects the bacteria that are not able to develop resistance to it. So drink of Kombucha can be used in the fight against organisms such as Staphylococcus, Streptococcus, Pneumococcus etc. The Department of biotechnology of NUPh conducts experimental research on the cultivation conditions of Kombucha Medusomyces gisevi, properties of the drink and antimicrobial action.

# THE USE OF GLUCOSE OXIDASE IN BIOFUEL CELLS

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Microbial enzymes are known to play a crucial role in various industrial processes. In the last few years glucose oxidase (GOD) produced mostly by microscopic fungi *Aspergillus* and *Penicillium* has gained great commercial importance due to its multitude of applications in the chemical, food, beverage, pharmaceutical, clinical and other industries. The purpose of this work is to analyze the possibility of the GOD using in biofuel cells.

Enzymatic biofuel cells are devices that convert chemical energy into electrical one through the enzyme-catalyzed oxidation of renewable fuels such as sugars or organic compounds. Because of their ability to operate under physiological conditions biofuel cells are suitable for in vivo applications. Theoretically, they can use fuel withdrawn virtually without limit from the flow of blood to provide a long-term power supply for such devices as pacemakers, glucose sensors for diabetics, small valves for bladder control or even for an artificial heart.

Biofuel cells consist of a two electrode set modified by biocatalytic enzymes to specifically oxidize/reduce substrates. One approach towards the design of an implantable, membraneless and biocompatible biofuel cell consists in catalyzing the oxidation of glucose at the anode using highly specific GOD. This enzyme is coupled to the reduction of oxygen at the cathode by an oxygen-reducing enzyme such as laccase, bilirubin oxidase or cytochrome oxidase. Both fuel molecules (glucose and oxygen) are present and continuously replenished in physiological fluids by the metabolism. Moreover, at the electrodes these molecules are converted into naturally occurring degradation molecules in low concentration - gluconolactone and water. The maximum theoretical electromotiveforce allowed by the thermodynamics of glucose oxidation and oxygen reduction at physiological pH is approximately 1 V. It should be noted that glucose biofuel cells are still not ready for applications outside the laboratory. Two main problems are the limited lifetime and power output of the cells. The major way to increase enzymatic electrodes lifetime and efficiency is to improve the enzyme connection with the electrode surface.

Therefore, nowadays it is necessary to explore various producers of GOD with higher stability and catalytic rate and to develop new methods of enzyme immobilization. Improved glucose biofuel cells can become a real alternative to lithium-ion batteries for the power supply of implanted medical devices.

# SITUATION WITH PREPARATIONS OF BLOOD AT THE MARKETOF UKRAINE

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Preparations of blood are the remedies got from blood. There are preparations of complex, immunological, hemostatic, antianaemic and stimulant action.

Until recently, the production of blood products and their quality remained virtually unchanged both in Ukraine and the former Soviet Union. The function of harvesting and processing of blood in the country was given to the numerically small network of centers and blood transfusion stations, and a few plants for processing plasma. All of them were owned by the state. Equipment and testing standards are not kept even the most basic requirements for the safety of donated blood and blood components. There was a need to reorganize blood services in the country and, above all, the introduction of strict requirements of quality assurance harvested blood.

In developed countries, manufacturers use modern tests for the analysis of raw materials. The test is based on the polymerase chain reaction is used along with the known enzyme immunoassay, feels much more-flax. It is obligatory to use specific procedures to inactivate viruses. The manufacturer must prove (validate) the effectiveness and completeness of the inactivation of the pathogen in the production process.

Today in Ukraine manufacturers of blood products are private enterprises "Pharmstandard - Biolik" and "Biopharma". Thanks to foreign investment they reconstructed and launched production of products conforming to international standards. However, in production, they fully use the plasma from the European Union, in particular from Slovakia. These raw materials meet the requirements of the European Pharmacopoeia, passed the registration on the territory of Ukraine.

Only "Biopharma" is a producer of blood products in the territory of the former Soviet Union and Eastern Europe, where the production of immunoglobulin implemented global standards viral safety of blood products.

Ukraine has also recorded blood products of foreign production, for example, drugs Swiss pharmaceutical company "Genfa Medica SA", Belarusian-Dutch joint venture "Farmland".

Several years ago, Ukraine has a policy of import substitution of high-tech foreign lifesaving drugs. Experience and practice show that the cost of medicines domestic production is several times lower than foreign counterparts - it allows receiving quality care to more patients.

# DEVELOPMENT OF METHODS FOR DETERMINING THE MICROBIOLOGICAL PURITY OF ORAL AGENTS BASED ON DERIVATIVES OF CAMPHOR ACID

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It is known that natural carboxylic acids play an important role in the human body. But nowadays there is no treatment for male infertility based on their properties. In a public institution "V. Danilevsky Institute for Endocrine Pathology Problems National Academy of Medical Sciences of Ukraine". There was a development based on an original non-hormonal compound - a derivative of camphor acid, which is a low toxicity in experimental models in rats leads to restoration of male hypofertile. For practical application in medicine have been proposed to develop formulations containing these substances which are in different stages of learning. When the developing an oral dosage form based on camphor acid derivative started. There was a question of studying its microbiological characteristics, primarily microbiological purity characterizing the final product. High levels of microbial contamination significantly affects the quality indicators preparation shows great danger to its stability, may be cause of severe infectious diseases or lead to the loss of therapeutic activity. In this connection, the test "Microbiological purity" is an integral part of the analytical documentation to the drug. Microbiological purity samples freshly oral dosage form based on the derivative of camphor acid, which does not exhibit antimicrobial activity in the conditions of the test was carried out by direct seeding method for State Pharmacopoeia (SP) of Ukraine 1.4 (1:10 dilution). It was established that all samples tested do not contain bacteria of the genus Enterobacteriaceae - Escherichia coli, wherein the total number of aerobic microorganisms bacteria not more than 10 Colony Forming Unit per g (CFU/g), and the content of yeasts and molds was significantly less than 10 CFU/g. Thus, regulation of the microbiological purity of the oral dosage forms based on camphor acid derivative showed that it meets the quality criteria of acceptability nonsterile SP of Ukraine 1.4 - non-aqueous medicines for oral administration. It was performed by direct sowing in accordance with the requirements of SP of Ukraine 1 (2.6.12, 2.6.13). Today at the Department of Biotechnology of National University of Pharmacy together with the State institution "V. Danilevsky Institute for Endocrine Pathology Problems National Academy of Medical Sciences of Ukraine" determining the microbiological purity of new oral agents based on derivatives of camphor acid is conducted.

# BACTERIA AND YEAST ADHESION TO ABIOTIC SURFACES TREATED BY PREPARATIONS OF MICROBIAL SURFACTANTS

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Formation of microbial biofilms on various equipment surfaces of food industry and medicine is undesirable. The danger of biofilms formation is associated with the resistant forms of bacteria emergence, materials' surface destruction and the spread of humans infectious diseases. One of the ways cleaning and disinfection such surfaces is using of surface-active substances (SAS) of microbial origin as antyadhesive agents that can prevent the biofilm formation or stimulat the destruction of existing structures.

The producers of microbial surfactants *Nocardia vaccinii* IMB B-7404 was grown in liquid mineral medium with sunflower oil (2%, v/v). The cultivation duration was 5 and 7 days. The following preparations wereused for researches: preparation 1 – supernatant of culture fluid; preparation 2 – solution of surfactant, dedicated by Folch mixture extraction (chloroform and methanol, 2: 1) from the supernatant of culture fluid (preparation 1). Bacteria (*Bacillus subtilis* BT-2, *Escherichia coli* IEM-1) and yeast *(Candida albicans* D-6) were used as test culture. The adhesion degree of test-cultures to plastic, polyvinylchloride, tile and steel was determined by spectrophotometric method.

Results have shown that surfactant preparations synthesized on 7th day of cultivation are more efficient antiadhasive agents than similar one received during 5 days of cultivation. Thus, *B. subtilis* BT-2 vegetative cells adhesion on all investigated surfaces was 21-48% after treatment by preparations 1 and 2 (0.01 mg / ml), synthesized on 7th day of cultivation. Similar preparations synthesized on 5th day showed antiadhasive properties at 0.02 mg/ml concentration. Related results were obtained in *C. albicans* D-6 adhesion studies. Materials processing by solution of surfactants (0.01 mg/ml) synthesized during 7 days, accompanied by decrease in yeast adhesion on 70% and synthesized during 5 days - 50-60%. Other patterns were observed during *E.coli* IEM-1adhesion study. In this case, more effective antiadhasive agent was solution of surfactants synthesized on 5th day of cultivation.

However, irrespective of cultivation duration, test-culture type and abiotic surfaces natura, surfactants solutions (preparation 2) reduced bacteria and yeast adhesion more effectively compared with supernatant in similar concentrations of surfactants.

These data shows the dependence of surfactants biological properties on producer's cultivation conditions, and the possibility to use *N. vaccinii* IMB-7404 surfactants as antiadhasive preparation component.

# INFLUENCE OF CULTURE MEDIA COMPOSITION ON THE MORPHOLOGY AND GROWTH OF CANDIDA ALBICANS

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Fungi of the genus Candida, as causative agents of nosocomial infections in the last 10-15 years took 4-th place in the United States and Russia and 5-th place in Europe. C. albicans is a typical member of the yeasts that live in the small intestines, genital tract, mouth, esophagus, larynx. Under certain conditions it is possible the rapid multiplication of the pathogen and the development of infection called candidiasis. Candidiasis often occurs in people with weakened immune systems - both men and women, newborns can become infected with C. albicans by sick mother during childbirth. According to the WHO incidence for different types of fungal infections has increased more than two times and tends to further increase.

For the detection of C. albicans direct microscopy and culture of pathological material for nutrient media are used. For this purpose Sabouraud agar and Sabouraud broth are used. On solid nutrient media C. albicans grows as smooth cheesy colonies, wet or matt with gray, with yellow or pink pigment on the surface. In liquid media they can form a pellicle or a homogeneous precipitate, which is sometimes consists of pellicles layers. The consistency of the pellicle can be different: grain-like, dry, mucoid. It is known that this species is characterized by filamentous-yeast dimorphism - the ability to form hyphal or yeast-like growth.

Sabouraud agar and Sabouraud broth, unenriched and enriched with 10% serum of cattle were used for studying the culture media composition effect on cultural and morphological characteristics of C. albicans. Cultures were incubated at 37 ° C for 7 days. For microscopic examination of the cultures grown native preparations (crushed drop) and stained preparations (smear preparations stained with a solution of methylene blue and Romanovsky-Giemsa solution).

After 24 h of growth on solid nutrient media the colonies of yeasts consisting of oval budding cells was observed. On liquid nutrient media the turbidity and precipitation in the broth were observed. After 48 hours and 7 days, no change of culture morphology was observed. In microscopic preparations from 7-day-old cultures the yeast cells and elements of hyphal growth were seen.

The results of these studies confirm the importance of yeasts C. albicans as a model object in medicine and biotechnology, for studying of the influence of culture media, the development of new culture media for a more effective of candidiasis diagnostics.

# BACTERIAL TOXIN DETECTION BY USE OF BOMBYX MORI HAEMOLYMPH

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Modern aspects of application of various vital forms of silkworm in medical practice are studied and the basic directions of their further use are deter-mined. The object has chosen for the future scientific researches – the caterpillar of silkworm and the complex application model has developed for medicines for prophylaxis, diagnostic and treatment.

Host cells stimulation by excessive amount of bacteria and their fragments in the blood is considered nowadays are starting mechanism of bacterial meningitis. Lypopolysaccharid is the most active and studied fragment for Gram negative bacteria's, peptidoglycane – for Gram positive bacteria's.

These compounds are fractions of cell walls of respective bacteria's; peptidoglycane is common component for both Gram negative and Gram positive bacteria's. Unfortunately, clinical practice today does not have available methods of laboratory diagnostics of bacterial modulines. Highly sensitive reaction with amoebocyte lysate of Limulus genus crabs is not only expensive, but insufficiently specific (interacts only with lypopolysaccharid).

The method of bacterial toxin detection using Bombyx mori haemolymph suggested by Japanese scientists in 2003 is known in world practice. The test is based on the cascade of reactions in Bombyx mori haemolymph caused by peptidoglycanes or (1, 3)-β-D-glucane, which are the components of Gram negative and Gram positive bacteria's cell wall.

The basic ferment of this cascade – prophenol – oxidase catalyzes the reaction of conversion exogenic substrate 3,4- dihydroxyphenylalanine into melanine. Ferment activity is proportional to the concentration of bacterial endotoxines. We have tested this method in patients with generalized form of meningococcal infection.

The patients were divided into two groups: 1 group (10 patients) – meningococcal meningitis with severe course confirmed bacteriologically and molecularly-genetically; 2 group (10 people) – patients with intact liquor (group of control). Liquor samples (0,5 ml) were taken from patients on admission to the hospital by routine diagnostic spinal puncture. Disposable puncture needles and sterile apyrogenic disposable test tubes were used in order to prevent false-positive results.

The obtained results of the study have shown that peptidoglycane level in cerebrospinal liquor in patients with meningococcal meningitis at the height of disease was significantly higher than in control group ($p < 0,05$). Further, during convalescence the indices dropped to the normal. Consequently, the test can be used for intoxication level evaluation.

# BIOLOGICAL PROPERTIES OF SURFACTANTS SYNTHESIZED IN DIFFERENT CONDITION OF *NOCARDIA VACCINII* IMB B-7405 CULTIVATION

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During last decades the increasing resistance of pathogenic microorganisms to well-known biocides can be seen. This situation led to the search of new alternative antimicrobial drugs. From literature it is known that such drugs are microbial surface-active substances (surfactants).

It can be noted that microbial surfactants are secondary metabolites and, as a rule, are synthesized in the form of a complex of similar compounds (amino-, glyco-, phospho - and neutral lipids). In different conditions of producers cultivation the ratio of complex secondary metabolites components may changes that can influence on their biological properties. In this regard, the purpose was to investigate the influence of carbon source nature in the medium of *Nocardia vaccinii* IMB B-7405 on the antimicrobial properties of surfactants.

As a source of carbon and energy glycerin in a concentration of 1% (by volume) was used, as well as refined, processed after frying of potatoes and meat, sunflower oil at a concentration of 2% (by volume). Duration of cultivation was 5 and 7 days.

In the experiments phytopathogenic bacteria of *Pectobacterium carotovorum* УКМ B-1095, *Pseudomonas syringae* pv. *atrofaciens* УКМ B-1015, *Pseudomonas. syringae* pv. *coronafaciens* – УКМ B-1154, *Xanthomonas campestris* pv. *campestris* УКМ B-1049 genera from Ukranian collection of microorganisms were used.

It was shown that not depending on the nature of oil-containing substrate (refined or wasted oil) and degree of surfactants purification (supernatant, the surfactant solution) the increase of the *N. vaccinii* IMB B-7405 cultivation up to 7 days was accompanied by the synthesis of surfactants with more pronounced antimicrobial properties against phytopathogenic bacteria compared with surfactants formed within 5 days of the producer cultivation. Note that regardless of the duration of cultivation, the surfactant solutions were more potent antimicrobial agents compared with the corresponding supernatants.

It was established that the most effective antimicrobial agent were surfactants synthesized under the *N. vaccinii* IMB B-7405 cultivation in the medium with the wasted after frying potatoes sunflower oil for 7 days: minimum inhibitory concentration in relation to the studied phytopathogenic bacteria was 7-20 μg/ml, which is significantly lower compared with minimum inhibitory concentration of the known from the literature surfactants.

Thus, results that were obtained during experiments show the prospect of microbial surfactants *N. vaccinii* IMB B-7405 use for the development of highly effective and environmentally safe products for the control of phytopathogenic bacteria number.

# SYNTHESIS OF SURFACTANTS UNDER *ACINETOBACTER CALCOACETICUS* IMV B-7241 CULTIVATION ON FRYING SUNFLOWER OIL

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Surface-active substances (SAS) were and are the main component of most detergents. The environmentally friendly and biodegradable surfactants of microbial origin are alternative to chemical SAS. As the chemical nature of microbial surfactants is lipids (neutral hliko- and phospholipids), the oil and oil-containing substances may be the most favorable substrates for their biosynthesis. So, using wastes of oil-fatty industry will allow solving the problem of waste utilization and reducing the cost of the product in several times.

Previously, it was found that during *Acinetobacter calcoaceticus* IMV-7241 cultivation on refined sunflower oil maximum concentration of synthesized surfactants was observed at 4-6% of oil. The purpose of this study – to research the possibility of replacing refined oil on the waste oil after meat and potato frying for biosynthesis of SAS.

Strain IMV B-7241 was grown in liquid mineral medium (g/l): $(NH_2)_2CO$ – 0.35; $MgSO_4 \times 7H_2O$ – 0.1; NaCl – 1.0; $Na_2HPO_4$ – 0.6; $KH_2PO_4$ – 0.14. In additionally yeast autolysate (0.5%, v/v) and solution of microelements (0.1%, v/v) were added to the medium.

The composition of the solution of microelements (g/100 ml): $ZnSO_4 \times 7H_2O$ – 1.1; $MnSO_4 \times H_2O$ – 0.6; $FeSO_4 \times 7H_2O$ – 0.1; $CuSO_4 \times 5H_2O$ – 0.004; $CoSO_4 \times 7H_2O$ – 0.03; $H_3BO_3$ – 0.006; KI – 0.0001; EDTA (Trylon B) – 0.5.

Waste sunflower oil after potato and meat frying (4–6%, v/v) was used as a source of carbon. The inoculum was grown in described above medium composition, which contained 0.5% molasses. Quantity of inoculum was 10 % from the volume of the medium. Cultivation of *A. calcoaceticus* IMV-7241 was carried out in flasks (750 ml) with 100 ml of medium in shacker (320 rpm) at 28-30ºC for 120 hours.

Concentration of extracellular surfactants was determined gravimetrically after extraction with a Folch mixture (chloroform and methanol, 2:1) from the supernatant culture fluid.

Experiments have shown that irrespective of the waste oil after meat and potato frying concentration in the *A. calcoaceticus* IMV-7241 medium, amount of synthesized surfactants was in 40–50% lower compared with the results in the medium which contain the same refined oil content. This phenomenon can be caused by the presence of growth and SAS biosynthesis inhibitors in waste oil.

One approach that will help to improve the effectiveness of fryed oil bioconversion into the *A. calcoaceticus* IMV-7241 SAS can be using of inoculum grown on the refined substrate or reducing of the waste oil amount in a medium, which will be the subject of our further researches.

# FERMENTED MILK PRODUCT – RYAZHENKA, THE STUDY OF FERMENTS

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Dairy industry is one of the most important industries in the Ukraine. It has deep historical roots. Nowadays ryazhenka is one of the national Ukrainian fermented milk products. History of ryazhenka started from time immemorial in Ukraine. It was made by stewing milk and cream at high temperature, without making it boiled, in special low clay pots "glechiks" until it got a nice creamy colour. Then ryazhenka was made sour by adding some sour cream and putting it into a warm place. In this way ryazhenka gots homogeneous dense structure. Nowadays making ryazhenka takes much less time. The technology of making ryazhenka starts when milk is poured into a tank in which it is heated up to 50 °C, then it is heated by steam up to 98 °C and maintained at this temperature. As a result baked milk is received. Then it is cooled down to 40 °C, special lactic acid bacteria (ferments) are added and ryazhenka is left to get fermented until product acidity reaches a definite indicator. After that the product is cooled down, stirred very well and transferred into the dispensing machine.

The main ryazhenka properties are rather thick consistency, creamy colour and a delicate sweetish flavour. It can be drunk as it is or used in different recipes. Ryazhenka improves digestion and boosts immunity. If drunk regularly ryazhenka strengthens bones and teeth, due to the high content of phosphorus and calcium.

A large number of ryazhenka of different trade marks is represented in Ukraine. The main leaders are: TM "Zarechye", TM "Voloshkove Pole", TM "Hutorok", TM "Lukavytsia", TM "Dobryana", TM "Lubimchik".

The choice of ferments is rather important for making quality ryazhenka. Ferments produced by trademarks «VIVO», «Good Food», «SACCO» can be purchased in the Ukrainian market nowadays.

The quality of ferments can be identified by their activity, which is controlled by souring duration and acidity, ferment cleanliness and the relation between cultures (qualitative and quantitative composition), as well as by the presence of foreign microflora and organoleptic characteristics of a clod. Experimental works in researching culture milk product fermentation are done at the Department of Biotechnology. One of such researches is the research of ryazhenka, making ryazhenka in laboratories, conducting ryazhenka comparative analysis with ryazhenka of popular Ukrainian trademarks.

# HISTORY OF CHEESE MAKING

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Cheese has been one of the favourite food for all times and people. Having high taste qualities cheese is a unique product from the diet point of view as cheese concentrates in itself the medicinal force of milk. Cheese contains the same milk constituents but in much higher concentrations: thus, milk contains only 3,2% protein but cheese – not less than 20-25%.

The food value of cheese is also determined by high content of essential amino acids (tryptophan, lysine, methionin), fat (up to 30%), mineral salts (especially calcium), vitamins (A, E, $B_1$, $B_2$, $B_{12}$) that are necessary for both children and adults.

The aim of the work was to study educational and entertaining history of cheese making, the classification of cheese and the description of the most common types of cheese.

During the experiment it has been found out that cheese has been used for 7000 years, some interesting facts have been given from the history of cheese making.

The analysis of the rennet and sour milk cheese has been done; the composition, description, recommendations as for the consumption of fresh cheese (Mascarpone, Rhiccotta), unboiled pressed cheese (Edam, Gauda, Pecorhino); boiled pressed (Emmental, Parmijano, Grana Padano, Gruier), soft cheese with mould made with the use of Penicillium camemberti ( Camamber, Bri, Coulomie); soft cheese with blue mould Penicillium roqueforti (Roquefor, Danablue, Gorgonzola), cheese made from goat and ewe's milk (brynza, Feta, Sent-Moor, Shevr), processed cheese have been given. The secrets of the special attitude of people to cheese have been discovered, the benefit from the consumption of the above product has been proved, the necessity of some types of cheese in the ration of the child and teens' age, in the period of pregnancy as well as to prevent and treat some diseases including oncological ones has been proved.

The main conclusion of the article can be cited by the famous Salvador Dali's words " If there are no fifty types of cheese and good wine in the country it means that the country has failed …".

# PROSPECTS FOR PRODUCTION AND USING OF PURIFIED DEXTRANASE

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Microbial production of enzymes is one of the most important line in development of biotechnology. Every year volume of enzyme production is growing, while assortment of enzymes and field of their application are expanding. For a long time enzymes depolymerizing dextran with microorganisms that produce it are being researched.

The purposes of this work are to analyze the prospects for production and using of purified dextranase; to determine the main enzyme producers and the features of its production.

After detailed studying of catalytic properties of different dextranases they have been divided into dextranase (EC 3.2.1.11), exo-1,6-α-glucosidase (EC 3.2.1.70), glucan-1,6-α-isomaltosidase (EC 3.2.1.94), dextran-1,6-α-isomaltotriosidase (EC 3.2.1.95) and dextran-α-1,2 debranching enzyme (EC 3.2.1.115).

Dextranase or α-1,6-glucan-6-glucanohydrolase (EC 3.2.1.11) has a high specificity for the types of links between glucose residues. Enzymes of this group do not catalyze the cleavage of mannose and α-1,6-linkages in amylopectin and glycogen branching points.

Dextranase specificity plays a very important role in dentistry where dextranase pharmaceuticals are successfully used. In microbiological industry α-1,6-glucan-6-glucanohydrolase is used to obtain medical dextran. Native dextran is not suitable for using as plasma substituting agent because it has a very high molecular weight, considerable viscosity, toxic effects and change immunoreactive properties of the organism. Therefore, it is partial hydrolyzed with dextranase (enzymatic or specific hydrolysis).

The main dextranase producers are filamentous fungi of genera *Penicillium, Aspergillus, Spicaria, Humicola, Sporotrichum, Amixiella* and others. The ability of yeast to synthesize dextranase is mainly observed in species of *Lypomices*. Among actinomycetes 240 cultures of *Chromogenes* were investigated for the ability to synthesize dextranase. Bacteria of the genera *Bacteroides, Lactobacillus* and *Bacillus subtilis* are used as producers of exo- and endo-dextranase. It should be noted that the

dextran-hydrolyzing enzymes are genetically different structures. This is evidenced by the new classification system of enzymes, based on a comparison of the amino acid sequence.

There are attempts to obtain industrial dextranase producers using genetic engineering techniques in addition to the traditional methods of selection and breeding. For the last 10-15 years, works on cloning of exo- and endo-dextranase genes have become widespread. Currently, there are about 11 nucleotide sequences of dextranase genes from *Streptococcus, Arthrobacter, Penicillium, Paenibacillus*.

Industrial dextranase enzymes are produced by cultivation of microorganisms using dextran and/or ketodexstran as a source of carbon and energy. To increase dextranase yield it is better to use ketodextran medium. Ketodextran is a derivative of dextran in which aldehyde groups converted into ketone groups. Ketodextran can be obtained using dimethyl sulfoxide and acetic anhydride. Its content must be from 0.1 to 10%. If other sources of carbon are used, enzyme synthesis is significantly reduced due to inhibition of its induction. The source of nitrogen and nutritional minerals are also important. It should be noted that mineral nitrogen in the form of ammonium salts (especially ammonium citrate) is more effective than organic.

In the case of submerged cultivation an enzyme purification begins with the previously concentrated filtrate of culture liquid. A well-known method of dextranase purification is based on the enzyme precipitation from the culture liquid with ammonium sulfate, followed by fractionation with PEG solutions and extraction in terms of a two-phase system. An enzyme yield from the culture fluid is 33% at 49-fold purification degree (for *Paenibacillus illinoisensis*). The specific activity of dextranase from *Paenibacillus illinoisensis* IB-101D increases 733-fold with the 19% activity after chromatography on DEAE-Sepharose. Highly purified dextranase from *Paenibacillus illinoisensis* IB-101D shows high activity in a wide range of pH 6,0-7,6, keeps 35% and 53% activity at pH 5.5 and pH 7.8, respectively. The maximum activity of purified dextranase is observed at 50°C. The enzyme remains stable at temperatures below 50°C after 1 h heating at pH 6.8. Thermal inactivation begins at temperatures more than 60°C.

In view of the beneficial properties, absence of side effect, economic feasibility of production, purified dextranase are in demand on the world market of enzyme preparations for pharmaceutical industry. Therefore, it is proposed to register dextranase as an active pharmaceutical ingredient allowed for use in Ukraine. That will allow producing not only dextrans substitutes, but also finished medicinal products for the prevention and treatment of dental caries.

# COMBINED INACTIVATED CELLS OF FUNGI C. ALBICANS AND C. TROPICALIS IN THE PREVENTION CANDIDIASIS

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As in developed countries and in Ukraine there are difficulties of diagnosis and treatment of candidiasis. Among patients with a fatal outcome, have not received adequate treatment is one of the first places are candidiasis. Many researchers believe that the use of drugs that can stimulate protective immune responses against Candida infection, whatever vaccine is a promising direction in the fight against candida and an alternative antifungal drugs.

The purpose of this study to investigate the ability of inactivated cells fungi C. albicans and C. tropicalis together to form immunity against Candida infections.

Comprehensive inactivation associated cell suspension fungi C. albicans and C. tropicalis performed consistently using first physical processing, and chemical, inactivated at 50 ± 2 ° C for 1 hour. Then the suspension mushrooms added 0.5% formalin and left overnight at 25 ± 2 ° C. To study the optimal composition associated inactivated cell suspension fungi C. albicans and C. tropicalis were produced several variants with different suspensions containing cells of these strains (mln.kl. / ml): 2.5 + 2.5; 5 + 5; 4 + 6; 6 + 4; 10 + 10; 8 + 12; 12 + 8 (mln.kl./ml). The study was conducted in white mice. Mice were intramuscularly in the upper part of the back paws injected twice inactivated cells of fungi C. albicans and C. tropicalis in a volume of 0.2 ml. After 1 month of a group of test animals and 3 months for the second group of test animals after administration of inactivated cells was performed intraperitoneally hybiv Candida infection.

As a result of studies found associated inactivated cell suspension fungi C. albicans and C. tropicalis, comprising (mln.kl./ml) 10 + 10; 8 + 12 and 12 + 8 at 1 and 3 months after re-entering protected from infection 84% of the animals. At the time when 16% of the animals were observed minor manifestations of the disease, unkempt appearance, refusal of food, weight loss body dysfunction excretory organs. Given the fact that the associated suspension cells inactivated fungi C. albicans and C. tropicalis, containing 10 + 10 (mln.kl./ml) is preparing a little easier than other relationships and further simplifies the calculations, it is more appropriate for further research This dose was chosen.

Thus suspension cells of fungi can be used to create a vaccine-associated candidiasis.

# INFLUENCE OF CARBON SOURCE NATURE IN CULTIVATION MEDIUM OF *ACINETOBACTER CALCOACETICUS* IMV B-7241 ON ANTIADHESIVE PROPERTIES OF BIOSURFACTANTS

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The problem of food and medical branches is formation of microbial biofilms which contain bacteria resistant to antibiotics and disinfectants on different surfaces. The current direction of the researches is the using of microbial surface-active substances (SAS, surfactants) to prevent cell adhesion on surfaces.

The producer of SAS *Acinetobacter calcoaceticus* IMB B-7241 was grown in liquid mineral medium containing ethanol (2%, v/v) and glycerol (1%, v/v).

Such preparations of surfactants were used in studies: preparation 1 – supernatant of culture liquid, to obtain which the culture broth was centrifuged (5000 g, 45 min); the surfactant-containing supernatant was subjected to extraction with the 2:1 chloroform/methanol (Folch) mixture to isolate the surfactant (preparation 2).

The strains of bacteria (*Bacillus subtilis* БТ-2, *Escherichia coli* IEM-1) and fungi (*Candida albicans* Д-6) were used as test-cultures in researches. Spectrophotometric method was used to determine the degree of test-cultures adhesion to plastic, polyvinylchloride, tile and steel.

The experiments showed that the supernatant and surfactant solution (3-18 mg/ml), synthesized as on ethanol so on glycerol, reduced the degree of test-cultures adhesion on all investigated abiotic surfaces.

It was established that adhesion depended on the material's type, the concentration of SAS in the preparations and the degree of their purification. From the preparations received on ethanol preparation 1 (supernatant) was more effective than surfactant solution (preparation 2): after the treatment of the abiotic materials with supernatant the amount of attached cells of bacteria decreased on 48–88%.

The adhesion of yeast *C. albicans* Д-6 on all materials treated either preparation 1 or preparation 2 was almost the same and amounted 25-36%.

Biosurfactants, received on glycerol, were more effective antiadhesive agents than the corresponding supernatants and preparation 2, synthesized on ethanol. Thus, the amount of vegetative cells of *B. subtilis* BT-2 and *E. coli* IEM-1 attached to abiotic surfaces decreased by 65-80% after the treatment with preparation 2. The maximum reducing of *B. subtilis* BT-2 spores and yeast *C. albicans* Д-6 adhesion was 55-78 and 65-85%, respectively.

Thus, the preparations of *A. calcoaceticus* IMV B-7241 SAS of different purification degrees (either supernatant or surfactant solution) can be used for producing highly effective preparations reducing the microorganisms' adhesion on surfaces of different materials.

It must be noted that it is more appropriate to use preparation 1 (supernatant), from the economic point of view, because the technology of its receiving does not imply the additional steps of isolation and purification.

# OPTIMIZATION OF THE ENZYMES PRODUCTION DURING MALT FABRICATION

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There are three stages of the preparation of malt: soaking, germination and drying. The first two steps are carried out in a single unit, the third - in the heating oven.

The glass with 220 mm of diameter was used to perform the initial steps. The netting was stretched on top of glass and covered by cloth. The grain layer of 20-30 mm was poured on the cloth. A glass filled with water up to 30% of its volume. The grain was disinfected by potassium permanganate with concentration of 0.02 mg / l. The bubbler was placed on the bottom of the glass and supplied with air to the grain airing. The grain was irrigated by drinking water with a total density of 5.3 mmol / $dm^3$ periodically. The soaking was performed at ambient temperature of 12-15℃. The grain was mixed twice a day and its samples were taken to determine its humidity.

Thus, grain irrigation and purging completely wet air passed through the water layer created the optimum conditions of the process of accumulation of the enzymes in the grain. Maintaining regular breathing conditions grains can reduce the time it soaking and germination. Such a method of processing of grain allows to create a maximum humidity of the environment while maximizing the flow of oxygen and remove carbon dioxide. Air flow was reduced or completely stopped when appearing germinal leaf. Thereby inhibits the development of the embryo and increases the rate of accumulation of the enzymes. The fresh malt quality was controlled by its organoleptic properties and the length of germinal leaf and spine.

Malt drying was conducted in the heating oven with a gradual temperature rise up to 60℃ and the humidity reducing to 3-5%. Then the malt sprouts was breaking and crushed in a mortar.

Malt amylolytic activity was determined by starch-iodine. The starch slurry and 1-2 drops of iodine solution was added in portions to the aqueous malt extract. Contents of the beaker was stirred with magnetic stirrer until the bleaching solution. Amylolytic activity expressed in grams of malt starch amount (g), which was hydrolyzed for one hour.

# STUDY BIOGENIK STIMYLATORS CONTAINED JUICE KALANHOE

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The problem of preserving human health has never lost its relevance. At the same time an important role in her decision belongs to the medicinal plants. In various countries, a quarter used therapeutic agents are drugs on the basis of biogenic stimulant plant origin.

Biogenic stimulators - a substance produced in isolated tissues of animals and plants that are in conditions unfavorable for their existence: for animal tissues - a reduced temperature for the plant - reduced temperature and darkness. In the process of the thinking biostimulants was found that these substances can not only occur in isolated tissues, but also in vivo during adaptation to unfavorable conditions such as irradiation, trauma, inflammatory processes and intense muscular activity, etc. Biostimulyators is a complex in which the main role is played carboxylic acids: succinic, oxalic, malic, citric, tartaric, cinnamic, cinnamic, as well as high aromatic acids.

The greatest number of biogenic stimulators accumulate plant family Crassulaceae: aloe drug, kalanchoe, sedum and other large. One of the widely used plants for biogenic stimulators is Kalanchoe. Kalanchoe belong to the family Crassulaceae and genus kalanchoe. During a large number of pharmacological studies have found that the juice has many Kalanchoe therapeutic properties, including bactericidal, bacteriostatic, anti-inflammatory action, wound healing action and a pronounced biostimulating effect. Each of the members of the kalanchoe components plays an important role, and together they reinforce each other's action. The juice kalanchoe contain anthracene derivatives, essential oils, tar substances, vitamins, polysaccharides, succinic acid, and enzymes. Over the past three or four decades interest in kalanchoe increased markedly. Formulations plants virtually non-toxic and is rapidly cleared from the wound and ulcer necrotic tissue. Application of kalanchoe in medicine is different: it is part of the set of ointments and cosmetics skin care products, used as the basis for some solutions and tinctures. The main drugs kalanchoe, widely used in medical practice, are syrup, ointment, tincture of alcohol; kalanchoe is also used in medicine in the form of fresh products and condensed juice (Sabur). They exert anti-inflammatory effects, and save from necrosis. But more often than juice kalanchoe is used as an external agent. The pharmaceutical industry produces medical kalanchoe as alcohol tincture or juice in vials or ampoules.

# MODERN ASPECTS OF EXTRACTION ESSENTIAL OILS FROM PLANTS MATERIAL

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Traditional technology of extraction essential oils from plant material are based on pressing, extraction with organic solvents, or steam stripping. The quality of the final product is influenced by many undesirable processes - the impact of vapor, oxygen, high temperature, difficulty distillation of residual solvents. It leads to appreciable loss of volatile aromatic substances, upsetting the natural balance of the components in the composition of essential oils in an undesirable decrease in their quality.

A more effective extraction is carbon dioxide extraction. In fact it is variant liquid extraction (similar to the water-alcohol, etc.), but with a more elegant solvent. Carbon dioxide is used in the liquid state in the subcritical region (pressure below 73.8 atm). Subcritical $CO_2$-extraction, well-known in our country, was developed in the form of a supercritical extraction.

Exactly supercritical (73.8 atm pressure over almost any temperature range) parameters sharply change the selectivity of carbon dioxide as a solvent that allows small changes in temperature and pressure to regulate the extraction process. It provides the most complete extraction of the complex fragrances from natural raw materials of plant origin, preserve their natural balance and high concentration. In the world, according to the European database of organizations DASFAF, engaged in supercritical fluids, it is common supercritical $CO_2$-extraction. This process is cost-effective, more technological, and produces lot of products. Subcritical $CO_2$-extraction, where the process is uncontrollable, it turns $CO_2$-extract with the amount of substances, not reflecting the true composition. Moreover, subcritical $CO_2$-extraction suffers the same disadvantages as the conventional extraction process, which is active during the process of oxidation, hydration, condensation, etc. Carbon dioxide as a raw material is available, cheap, relatively safe for the environment, as it is removed from the extract by simple evaporation in the latter stages of the technological cycle. This means that the final extract does not contain any traces of solvent, and together this ensures a very good ecological production process. The incorporation of supercritical fluid technology in the practice of producing essential oils provides a range of features to significantly improve the production of process. Solutions based on the use of the special properties of supercritical fluids are modern, knowledge-based, innovative, environmentally friendly and commercially attractive.

# PROMISING OF USING BACCILUS BACTERIA AS PRODUCERS OF ENZYMES

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The Bacillus genus is one of the most varied and commercially useful group of microorganisms. An aptitude of some strains to adapt to high or low temperatures and high or low pH makes them an important source for producing of commercial enzyme preparations. The aim of our research was to select the genus Bacillus bacteria from natural sources, identificate them and analysis the enzymes functions of their metabolites. As the source for Bacillus bacteria selection was chosen different kind of hay: oats, thyme, hypericum. To isolate the Bacillus bacteria, we created the conditions under which the growth and reproduction of micro-organisms other genera is suppressed. Boiling is the factor to the death of vegetative forms, but Bacillus bacteria create spores and survive in such conditions. After boiling each type of hay for 30 min and filtration, hay extract was kept in a warm place for about 5 days to get the bacterial pellicle extract at the surface. Micro scoping of this pellicle proved the presence of bacteria of the genus Bacillus in the sample. The pellicle from the surface of hay extract was inoculated in a solid substratum in the Petri dishes to the formation of isolated colonies. Analysis of colonies morphology proved the presence of several different by shape, size and texture type of Bacillus bacteria. After accumulating a pure culture we identified Bacillus bacteria by traditional microbiological methods (by morphology of spores, cells mobility, oxygen sensibility), most likely, we got B.subtilis, B.thuringiensis and B.lisheniformis. Through inoculation in starch agar and solution iodine impregnation we studied amilolytic activity. The area with starch was painted in dark blue color, but the hydrolysis area didn't change color or painted in reddish brown. Starch hydrolysis area was measured in millimeters. Proteolytic activity was studied through inoculation in a gelatin column; proteolytic activity was determined visually by dilution around injection of culture. Analysis of enzymatic function of isolated bacteria demonstrate amilolytic and proteolytic activity for all kinds of bacteria of the genus Bacillus. As a result of this research, from the few types of hay we got the mixture of bacteria of the genus Bacillus, accumulated pure culture, identificated Bacillus bacteria by cultural and morphological characteristics, determined species belonging by physiological and biochemical characteristics and studied enzymatic functions of isolated bacteria of the genus Bacillus. The presence of enzymatic activity of the samples had demonstrated valuable perspective of using Bacillus bacteria as producers of enzymes.

# MODERN ASPECTS OF BEER PRODUCTION

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For a long time beer is a valuable product, third most popular in the world (after water and tea), and the most popular among alcoholic beverages. Beer - low alcoholic drink obtained by an alcohol fermentation of the malt worth (usually based on barley) using brewer's yeast with the addition of hops. Beer is common in many countries of the world and is popular because of its taste and aroma. There are about a a thousand species of beer. Taste characteristics of different types may be radically different.

One of the most important components of beer, which affects the formation of taste and odor, is hop. Brewery hops are produced from only unpollinated female inflorescences, which are soft lumps. It is in these cones substances needed to beer are concentrated in the largest number. Hops contain bitter resinous substance – lupulin wich includes aromatic resins, essential oils, tannins, alkaloids, etc. Person consuming beer, to a significant extent replaces in his own body male hormone to female. The female body works more difficult and more elegant than male in it every month a hormonal background changing substantially, and invasion in the delicate mechanism of by introducing of phytoestrogens or other hormonal drugs would have serious consequences, including infertility. In connection with this, have a goal to explore the possibility of replacing it by a similar hop product properties in order to prevent pernicious influence on the body of hop. Therefore proposed to replace hops on needles. After studying the history of beer brewing, found out that the first recipe coniferous beer invented a few centuries ago, the people of Northern Europe. The fir essential oil has long been used as an expectorant for inhalation with the inflammation of the upper respiratory tract in medicine. So, modern Europeans have lost the tradition of cooking beer from the needles completely in vain. Conifer is a large, ancient group of gymnosperms. The cedar, cypress, fir, juniper, larch, spruce, pine, redwood, yew and cowries are belong to the coniferous trees. Two kinds of conifers are spruce and pine mentioned in the history of brewing. We consider them as a replacement hop. Comparing hops and pine needles on the main brewing components, we can conclude: 1) the tanning agents in the needles of 1.5% - 2% more than hops 2) bitter substances in hop more than in the needles in 4 times 3) contents of essential oil - approximately equal to (1.5%). Thus, based on literature data it can be concluded about the prospects of use for replacement of the needles in the production of beer hops.

# THE STUDY OF THE MORPHOLOGY AND GROWTH OF FUNGI OF THE SPECIES CANDIDA TROPICALIS

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Candida tropicalis is a unicellular yeast-like fungus, oval or round shape with a size of 6-10 microns, is a new major causative agent of human infections.

Candidiasis - diseases of the mucous membranes, skin, and internal organs. Candidamikids - secondary allergic rashes, indicating a significant degree of sensitization to the pathogen and the products of its life. C. tropicalis is considered the third most isolated from cultures. The composition of the cell wall of the fungus provides good protection from the effects of adverse environmental factors, including medicines. Fungi C. tropicalis are ubiquitous and the common members of the human microbiota. However, they are also important opportunistic microorganisms for people with weakened immune systems. The fungi of this genus can be found in almost everywhere: from soil, vegetables and fruits to household items and its own body, where the fungi are part of the normal microflora, they are even found on the mucous membranes of the oral cavity in 14-50 % of healthy individuals.

Opportunities C. tropicalis: a strain of yeast of the genus C. tropicalis demonstrates that it has the potential for use in bioremediation (purification of polluted water from high-strength oil-containing compounds). Also C. tropicalis can be used to produce biodiesel from olive wood. For the cultivation of the fungus of the species Candida tropicalis were used liquid and dense nutrient medium: Sabouraud agar, Sabouraud broth, some of them was enriched with 10% serum of cattle. On a dense nutrient medium to obtain growth of isolated colonies the culture was inoculated method debilitating sowing. The inoculations were incubated at 37 °C. The growth of the culture was carried out every 24 hours.

The morphology of the fungus was studied in preparations for microscopy - "crushed by the drop" and the smears stained with methylene blue solution. During these studies it was assessed, the growth in liquid nutrient media and colony morphology on solid media (their structure, texture, shape, color, size and shape), as well as the morphology of the cells in stained preparations.

The results of the experiment it can be concluded that this type of fungus Candida tropicalis well-cultivated on nutrient dense environments. Form a bi-zonal colony of white or gray in color, with smooth edges, with smooth or slightly wrinkled surface. The first two days creamy, then medullar form, smoothed edges ragged. In liquid media there was only observed benthic growth, usually visible surface film, high parietal ring.

# BACTERIOPHAGES IN PHARMACEUTICAL AND FOOD INDUSTRIES

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Bacteriophages - viruses that selectively affects the bacterial cells. Most often, bacteriophages multiply within bacteria and cause them lysis.1896 - opening bacteriophages British bacteriologist Ernest Hankin.

Bacteriophage consists of a protein coat and genetic material - single-stranded or double-stranded RNA. The particle size – of from about 20 to 200 nm.

Due to its destructive effect on bacteria phages can be used with curative - prophylactic in various diseases (dysentery, cholera and so on.), As well as in the food industry: in the production of meat, poultry, cheese, vegetable products, etc. Improving the quality requirements of raw materials and products of animal origin requires the development of reliable and safe methods of protection from various hazards. One solution to this problem is to use a food production bacteriophages.

Bacteriophage applied for controlling various pests technical bacterial fermentations in the production of enzymes produced by bacterial cultures.

At the same time bacteriophage infecting bacteria culture is a dangerous pest - degenerate industrial strains of microorganisms (vaccines, agents of lactic acid, atsetonobutilovogo and some other fermentations, producers of antibiotics), causing serious violations of the process.

Bacteriophage - one of the most powerful factors in the variability of bacteria and actinomycetes. It plays a role in the self-purification of water and soil. Sets the standard phage, including international, are used for phage typing of pathogens number of diseases (cholera, typhoid, salmonella, staph and other. Diseases). Bacteriophages are also used in genetic engineering as vectors carrying DNA segments, it is also possible the natural gene transfer between bacteria through some phage (transduction). Typically, such patients with antibiotics. But due to the fact that constantly mutating the bacteria have become resistant to antibiotics, their effectiveness is diminished in the recent years. Unlike antibiotics, which kill both harmful and healthy microflora of the organism, bacteriophages selective, fall under their effect only pathogenic bacteria. They penetrate only in certain cells and interact with their DNA, creating a lysogenic or lytic effect. Acting on microbes during lytic type, bacteriophages destroy them, allowing them to multiply rapidly.

In practice, the liquid used as bacteriophages and dry.

# PRODUCTION TECHNOLOGY OF CHILDREN CURDS

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Currently, no one could doubt that rational nutrition from birth largely determines the health of a person throughout life. It is especially important in the first three years of a child's life because this is a period of normal physical and mental development, there is produced by the body's resistance to adverse external factors. A list of the beneficial nutrients is needed for proper growth and development of each child. The first 6 months, these substances enter the body of the child with mother's milk. As for nutrition after 6 months in the child's diet, in addition to mamma milk, introduce complementary foods. The best source of protein for young children is the cheese. Cottage cheese is recommended for children of all ages. It is a structured protein milk product, its use is valuable, and it strengthens bones, and healthy teeth and correct formation of the whole organism. The cheese sold in the store is not recommended for children under one year of age. He grainy, which is good for an adult, but a child with a weak chewing reflex it will be difficult to chew. Also store the curd contains coarse protein, which may lead not a health benefit and harm. The children's cheese has a more low acidity (not exceeding 150 Tons) high content of moisture (not more 75%) and higher requirements for sanitary indicators then the usual. Increased acidity of the curd may cause irritation of the mucosa of the intestine of the child. The production of useful and dough curd is associated with the need to comply with stringent process, temperature and hygiene requirements. Technology of production of cheese is based on the leaven fermenting milk for the purpose of receiving curd and its further processing. There are three ways of obtaining curd: 1) acid coagulation in milk during ripening make sourdough prepared on pure cultures milk souring Streptococcus; 2) acid - rennet coagulation - in this method the production of the cheese curd is formed not only as a result of lactic acid fermentation, but also via the insertion of rennet; 3) thermo-calcium coagulation - provides for the introduction of calcium chloride . It is used in industry for the deposition of milk proteins from skimmed milk. This way of production of curds allows to get a product with low acidity and in a short time, with a high content of calcium. Today in the Ukrainian market a small selection of children's curds domestic production. Therefore, the study and improvement of this technology is a pressing issue today. At the Department of Biotechnology of the National University of Pharmacy development the technology of production of curds for children has carried out.

# MICROBIAL ASSOCIATIONS PROPERTIES STUDY - INDIAN RICE

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The microbial association of the Indian (sea) rice's existence has historical roots from the times most ancient civilizations of the world existed. The earliest societies of China and India were aware of the sea mushroom's infusion medical properties.

Indian sea rice is a zooglea, symbiont organism, combining properties of mushrooms and bacteria. The microbial association looks like rice. There two types of the Indian sea rice: large and fine.

Amylase, protease, glucosides, lipase, enzymes that split uric salt and other harmful acids. It also contains coenzyme Q is a part of the organism's cell, promoting adenosine triphosphate (ATP) synthesis, which provides energy supply in alive cells. Lipase fully provides disintegration or formation of fats. In the patients suffering obesity, this enzyme shows low activity, and the patients suffering an atherosclerosis in general, the enzyme shows deficiency. Therefore sea salt infusion is good when you experience these diseases. Amylase is the enzyme which is responsible for splitting of starch, preventing increase of sugar in blood. Availability amylase in sea rice infusion allows to use it to treat patients suffering diabetes. Protease splits proteins into amino acids, meaning that it helps an organism to digest animal protein better.

The sea rice has various effects on human organism: decrease in arterial pressure, stimulation of immunity, antimicrobial, metabolic processes improvement, easy diuretic effect and so forth. Furthermore, the Indian rice drink provides antibacterial effect on arbitrarily-pathogenic microorganisms. It is important to remember that the Indian rice drink has contradictions: it is not recommended to take it for diabetic patient with insulin intake, children under age three and pregnant women. It is also not recommended to take it if you suffer a gastro enteric disease with the high level acidity, and stomach ulcers. The Indian (sea) rice cultivation comes from a nutrient environment change. You should not allow direct contact of Culture and sugar crystals. The ideal version is the preparation of a sweet solution, and then its addition to culture of sea rice. The sea rice infusion should be made at a room temperature, out of direct solar beams within 5-7 days. These timeframes can change depending on various factors, basically it depends on temperature. Nowadays, researches on studying nutritious solutions, conditions of cultivation and properties of microbial association of the Indian rice have been conducted at biotechnology faculty.

# THE STUDY OF THE TECHNOLOGICAL CHARACTERISTICS OF POWDER MIXTURES ON THE BASIS OF THE DERIVED CAMPHORIC ACID

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Natural carboxylic acids play a critical role in the biochemical processes that ensure the functioning of the body. On their basis a significant number of pharmacological agents and obtained biologically active substances (carbenoxolone, decamp).

In a State institution "V. Danilevsky Institute for Endocrine Pathology Problems National Academy of Medical Sciences of Ukraine" derived camphoric acid had been synthesized studied, which in experimental models of disturbed spermatogenesis improves its functions in the absence of hormonal and antihormonal action. Despite the widespread use and potential usefulness for the functioning of the reproductive system, there are medicines based on natural carboxylic acids that is designed for the treatment of its disorders in men.

A rational approach to the selection of the components of the dosage forms based on different technological tests provides a high level of therapeutic action and minimum unwanted side effects.

In this regard, the aim of our work was the rationale for the composition of the oral dosage form of the original drug derived on the basis of camphoric acid.

The objects of study were the substance derived camphoric acid, excipients, which are recommended for use by Ministry of health of Ukraine, and experimental powder mixture.

The definition of pharmaco-technological parameters of powders and powder compositions based on a derivative of camphoric acid (flow rate, angle of repose, coefficient Carr, bulk density, moisture content, moisture absorption) were performed according to standard techniques and tests the State Pharmacopoeia of Ukraine 1 edition.

Each formulation of the drug is necessary to choose a pharmaceutical factors based on their immediate effect on the activity and side effects of the drug. Selection and study of pharmaceutical factors is achieved by a complex pharmaco-technological tests at various stages of pharmaceutical drug development, registration, confirmation of the quality and the production technology.

Research for the purpose of selection of the composition of the oral dosage form of the original drug based on a derivative of camphor acid, primarily carried out

taking into account the physico-chemical and technological parameters of the powder substance, and a synthesis of literature data regarding the components of the most popular drugs in this pharmacological groups represented in the modern pharmaceutical market of Ukraine.

Testing of the active substance showed that derivative of camphor acid is a fine powder with crystals of irregular shape in the form of spheres, prisms and their fragments (predominant fraction with a particle size 6,01-12 micron), characterized by complete non-moisten, lack of moisture-absorbing properties and relates to free flowing materials. Also, it was determined that due to the complicated surface of the particles, the powder tends to accumulate statistics of electric charge, which can create potential difficulties at the stage of screening or mixing and heterogeneity in particle size can affect the time of the dissolution processes.

Thus, the technological characteristics of the substance of derivative of camphor acid allow to predict the use of conventional fillers, as well as their composition and quantity.

Bulk density of solids is an important factor that defines the parameters and constructive solutions to technological stages of production, namely the speed of loading, the use of special, standard or optional equipment. Powders differ in the bulk of the mass values from very heavy (> 2.0 g/cm$^3$) to light (< 0.6 g/cm$^3$).

The ability of the powder to leak out during overload or downloads characterized by means of such process parameters as fluidity (flowability) and the relative mass flow (angle of repose) and is described respectively from very good (8,6-12 g/sec; 25-30 degrees) to very bad (0.3 to 1 g/sec; >66 degrees).

Simple, fast and popular methods for predicting the flow properties of powders are the definition of the indicator of packing or coefficient of Hausner carried out by measuring the bulk volume and the volume of the powder after shrinkage.

Cellulose derivatives or copolymers of acrylic acid, varieties of starch, talc, salts of stearic acid, aerosil, sucrose, lactose, sugar alcohols (polyols) were requested as components of the dosage form. At first individual auxiliary substances in the experimental mixtures were studied with pharmaco-technological tests and then in various combinations for prediction of their behavior in dosage form. It was found that bulk density of the investigated powders was in the range of values of the middle class (of 1.1 to 0.6 g/cm$^3$). Parameters angle of repose allowed to take them to fluid materials 35-45 degrees. The value of pressing also meets satisfactory requirements of this technological indicator.

It can be concluded that the required ingredients allow to get technologically suitable mixture for the manufacture of oral dosage forms.

## PROBLEMS OF PRODUCTION OF GLASED CURD BARS

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Production of glazed curds is the one of the fastest growing segments on the date of the dairy industry over the past 10 years. This is not surprising, because more and more people realize the need of introducing into their diet products which provide normal functioning of the body. Glazed curd this is a product which made from cottage cheese weight and glazed. According to the State standard, glazed curd – is molded cottage cheese weight obtained from pre-molded cheese covered food glaze, weighing not more than 75 g. Glazed curds have a high nutritional value due to its high content of protein and carbohydrates. Curd protein better absorbed by the body than fresh milk proteins. At the moment, our goal is to highlight modern production of glazed curds in Ukraine, and justify the need for verification of the product with the relevant requirements. According to the results, it is necessary to find promising in creating not only tasty but also healthy food. Most often the major components of glazed curds are: cheese, sugar, vegetable fat, modified starch, sodium alginate, guar gum, vanilla flavoring, potassium sorbate, palm oil, cocoa powder, and lecithin. It should be noted that the glazed curds, on the market today contain the minimum amount of nutrients and their base – vegetable fat and sugar. Experts often found in the composition of curds harmful ingredients not listed on the package. Also there are a large quantity of harmful sugars and cheap fats, as well as starch, colorings and flavorings and emulsifiers in the composition of the glazed curds. Examination of the program «Test purchase», revealed that in the curds of brand «Rostagroexport» were found preservatives that are not listed on the packaging, and in the curds of brand «Danon» yeast is 7 times higher than normal, which is dangerous to the consumer. In addition, glazed curds of brand «Dmitrov Dairy Plant» and «Karat» contained coliform bacteria, and in glazed curds of brand «Dmitrov Dairy Plant» was discovered a mold. In addition, the harm of these curds is a high rate of cholesterol, which allows us to completely eliminate a product from the ration of certain groups of people, for example, people with diabetes, overweight and suffering from cardio-vascular system disease. E. coli was detected in a half of the samples which studied in the program. E. coli, causes an accumulation of toxic substances, malfunctions of the gastrointestinal tract, and affects the function of the kidneys, liver and immune system. These studies show the need to create not only delicious, but also useful products, so work on the development and technology of glazed curds, which takes place at the Department of Biotechnology, is promising.

## SECTION № 6

# PHYSIOLOGICAL AND BIOCHEMICAL FUNDAMENTALS OF THE ACTION OF BIOLOGICALLY ACTIVE COMPOUNDS

# BENFOTIAMINE IS PROMISING FOR THE INTEGRATED TREATMENT OF DIABETES MELLITUS

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Benfotiamine (Sbenzoylthiamine O-monophoshate) is a synthetic S-acyl derivative of thiamine. Once absorbed, benfotiamine is dephosphorylated by ecto-alkaline phosphatase to lipid-soluble S-benzoylthiamine. Transketolase is an enzyme that directs the precursors of advanced glycation end products (AGEs) to pentose phosphate pathway. Benfotiamine administration increases the levels of intracellular thiamine diphosphate, a cofactor necessary for the activation transketolase, resulting in the reduction of tissue level of AGEs. The elevated level of AGEs has been implicated in the induction and progression of diabetesassociated complications. Chronic hyperglycemia accelerates the reaction between glucose and proteins leading to the formation of AGEs, which form irreversible cross-links with many macromolecules such as collagen. In diabetes, AGEs accumulate in tissues at an accelerated rate. Experimental studies have elucidated that binding of AGEs to their specific receptors (RAGE) activates mainly monocytes and endothelial cells and consequently induces various inflammatory events. Moreover, AGEs exaggerate the status of oxidative stress in diabetes that may additionally contribute to functional changes in vascular tone control observed in diabetes. The anti-AGE property of benfotiamine certainly makes it effective for the treatment of diabetic neuropathy, nephropathy and retinopathy. Interestingly, few recent studies demonstrated additional non-AGE-dependent pharmacological actions of benfotiamine. The present review critically analyzed the multifaceted therapeutic potential of benfotiamine.

Benfotiamine has ability to halt the progression of many serious complications of prolonged hyperglycemia that certainly supports its therapeutic applications in diabetic patients. In fact, any bodily function improved by a therapeutic level of thiamine would most likely be enhanced by benfotiamine. The exaggerated benfotiamine consumption as a dietary supplement could over-stimulate the enzyme transketolase, whichmay account for some serious adverse drug reactions; however, the clear scientific data are missing in this regard. Growing body of evidence suggests that benfotiamine alleviates diabetes-associated neuropathy, kidney diseases, cardiac impairment, peripheral vascular diseases and retinopathy.

Hence, benfotiamine may be considered as an adjuvant nutritional therapeutic agent against the devastating consequences of hyperglycemia due to its inherent ability to confer functional support for blood vessel, nerve, kidney, eye and the heart.

# THE STUDY OF EXTRACT OF BLUEBERRIES LEAVES ON INDICATORS OF TYPE 2 DIABETES

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**Introduction.** Diabetes mellitus – is a complex systemic disease caused by absolute or relative deficiency of the hormone insulin, because of which a violation of carbohydrate metabolism develops in the body, in particular glucose utilization of tissues is inhibited. In addition to this the metabolic processes of fat, protein, water and salt balance are broken.

The purpose of this study has been to investigate the effect of a dry extract from the leaves of blueberry on the development of metabolic disorders in rats with experimental insulin resistance.

**Materials and methods.** The experiment has been conducted on a 18-month-old white male randombreeds rats weighing 350-370 g. Insulin resistance has been modeled by keeping the animal on a diet enriched with fructose (60.3% fructose, 18.3% protein, 5.2% fat), which is accompanied with obesity, impaired carbohydrate and lipid metabolism. We have used the glycosylated hemoglobin level (HbA1c), fructosamine, ss a marker of the degree of compensation of carbohydrate metabolism.

**The Results.** As it can be seen from the results of the studies, the maintenance of the rats on the diet enriched with fructose causes an increase in blood glucose concentration, which leads to an increase in the concentration of 20% HbA1c, fructosamine and 84%. The decrease of the α-cholesterol level and elevated levels of β-cholesterol are associated with increased transfer of cholesterol esters from HDL to atherogenic apoB-LP and due to the accumulation of TAG. The injection of the dry blueberry extract has expressed a normalizing effect on all studied parameters: significantly reduced the concentration of glucose, insulin, glycated hemoglobin, fructosamine, TAG, as well as improving the ratio of α-cholesterol levels to β-cholesterol.

**Conclusion.** Therapeutic and prophylactic application of the dry extract of blueberry leaves has a normalizing effect on glycosylation, as well as glucose and lipid metabolism in the serum of the studied animals that proves the further feasibility study of this extract with the aim of creating on its basis the means for correcting sugar type 2 diabetes.

# STUDY OF ANTICOAGULANT ACTIVITY OF LIQUID EXTRACT FROM THE LEAVES CORYLUS AVELLANA

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Introduction. Varicose veins of the lower extremities is the most common peripheral vascular disease. According to epidemiological studies in developed countries more than 20% of adults have a pronounced signs of this disease. Incorrect or untimely treatment can bring to complications such as deep vein thrombosis, thrombophlebitis, thromboembolism.

The main direction of pharmacotherapy thrombosis and prevention of thromboembolic complications is using the direct anticoagulants. A classic representative of direct anticoagulants is heparin. However, for the manifestation of heparin should be enough antithrombin - III, which dramatically decreases with disseminated intravascular blood clotting. In addition, the use of injectable heparin limited and short duration of effect. Therefore, search for new anticoagulant drugs is the actual problems of modern pharmacology, particularly among of plant materials.

In this regard as perspective materials for the study of anticoagulant properties was selected liquid extract from the leaves of Corylus avellana, which according to the literature, is used in folk medicine for varicose ulcers, capillary hemorrhage and contains in its structure, tannins, alkaloids, flavonoids ( myrytsetyn, kvertsitin, kaempferol, afzelin), minerals (iron, potassium, magnesium, iodine), amino acids, organic acids, carotenoids, vitamins (nicotinic and ascorbic acid, tocopherol, riboflavin, thiamin), polysaccharides, fatty acids.

The purpose of the research. To study anticoagulant activity of liquid extract from the leaves of Corylus avellana.

Materials and methods. Initially, the research of anticoagulant activity conducted in vitro experiments by the method Sukharev. The principle of the method is to determine the time when the first spontaneous fibrin strands appeared in whole blood for this we took 2-3 drops of blood from the tail of white non-linear rats and placed in the hour glass, which warmed the palm to body temperature. The initial liquid extract at a concentration of 136 mg/ml and in dilutions of 1:2, 1:4, 1:8 was added to hour glass. Every thirty seconds carried by the blood lancet until the needle is not pulled by the first thread of fibrin. Clotting time compared with the control.

Results. The study was determined pronounced anticoagulant activity of the initial liquid extract from the leaves of Corylus avellana, as evidenced no coagulation after 16 minutes of the beginning of experiment. Extract in a dilution of 1:2 also showed anticoagulant activity, as evidenced by time dilation of blood clotting 1.6 times in comparison with the control.

Conclusions. According to the results of research it was found that a liquid extract from the leaves of Corylus avellana showed anticoagulant activity that is cause for further research anticoagulant properties in experiments in vivo.

# EFFECTS OF LOW AND ULTRA DOSES ON HETEROSIDES BONE MARROW CELL CULTURE

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The real effect and the lack of explanation of the low and ultra-low doses (**LaULD**) action mechanism on biological objects remains an urgent problem for chemists, biochemists, pharmacologists and clinicians. The establishment and management of these mechanisms opens up new opportunities to reduce doses of drugs and therefore their toxicity, side effects, the environmental load of chemical and pharmaceutical industries, explains the mechanisms of adaptation of living organisms and homeopathy, expand the understanding of the origin and functioning of biological systems.

The aim of our research is the search and development of informative research of **LaULD** model. Heterosides with a broad spectrum of biological activities and culture of bone marrow cells (**CBMC**) were chosen as the objects of study, since this tissue has a fundamental mission in hematopoietic system and protective (immune) properties of the organism. Studies of **LaULD** on the **CBMC** allow more effectively fix their "direct" expression at the molecular and morpho-functional levels as organismic level compensatory factors are excluded. The **CBMC** was prepared by a special technology. Heterosides were studied in the concentration range of $10^{-4}$M to $10^{-18}$M. It was determined experimentally that hetrosides can increase cell concentration in **CBMC**, do not influence this process and inhibit the heteroside proliferative activity that depends on their concentration and exposure. The inhibitory activity had an expressed temporal character: if on the day 1, culture growth stimulation was observed, on the 2nd - inhibition of growth, increasing by the day 4. Further reduction of heteroside concentration in the culture medium also stimulated an increase in the amount of bone marrow cells in culture as compared to controls, although to a lesser degree. On the days 2-3 the number of cells did not change, and to the day 4 their number had decreased. The concentration reducing the concentration to $1 \cdot 10^{-18}$M caused the greatest inhibition of the proliferative process and the decrease in the cells number in culture. This effect was observed on day 1 and up to the day 4 the number cells was 4-times lower compared with the control. Calculations of the ratio of **BMC** and heterosides molecules in the culture at a concentration of $1 \cdot 10^{-18}$M is 4/1, which contradicts the molecular-kinetic mechanism of inhibition and suggests its signal (wave) nature.

Such a pronounced effect of suppression of cell proliferation in low doses suggests that heterosides can be considered as potential anticancer and spermicidal substance.

# CORRECTION OF EXPERIMENTAL INSULIN RESISTANCE BY ADMINISTRATION THE EXTRACTS FROM BLUEBERRY AND COWBERRY LEAVES WITH THE ADDITION OF ARGININE

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Insulin resistance - insensitivity of tissues to insulin - is one of the factors of type 2 diabetes and its consequences development. Diabetes is characterized by a disturbance of all types of metabolism and high risk of cardio-vascular complications.

Antidiabetic properties of blueberries and normalizing effect of cowberry on metabolism are well known. Arginine - a natural precursor of the vasodilator nitric oxide - is used for the treatment of vascular pathologies.

The aim of present work was to investigate the effect of the extracts from blueberry and cowberry leaves with the addition of arginine (EBA and ECA respectively) on metabolic disorders under experimental insulin resistance.

Experimental insulin resistance was modulated by fructose-rich diet (18.3% protein, 60.3% fructose and 5.2% fat). Experimental rats were divided into 4 groups: 1) the control group received regular rat chow, 2) the study group received fructose-rich diet, 3) and 4) the study groups received fructose-rich diet with EBA or ECA in dose 2.5 mg/100 g b.w. Plasma glucose, insulin concentration, levels of triacylglycerols (TAG), free fatty acid (FFA), α- and β-cholesterol (ChS) were determined after 6 weeks of experiment.

Fructose-rich diet provoked hyperglycemia, hyperinsulinemia, increase of TAG, FFA and β-ChS level and decrease of α-ChS content. These data demonstrate the development of insulin resistance and atherogenic dyslipidemia. Upon both extracts administration decrease of glucose and insulin levels was observed. The latter is due to the ability of polyphenols to increase tissue insulin sensitivity and enhance glucose uptake by them. EBA and ECA treatment also normalized plasma levels of the indices of lipid metabolism. This is due both to the effect of hypoglycemic properties as well as to hypolipidemic and antioxidant properties of extracts components. It is known that the leaves of investigated plants are rich in phenolic compounds, hydroxycinnamatic compounds, flavonoids and unsaturated fatty acids. EBA had a more pronounced protective effect than ECA, obviously, due to the different composition of anthocyanins.

Studied extracts provided a normalizing effect so they are perspective raw materials for the development of new drugs for the treatment and prevention of diabetes.

# CORRECTION BY PLANT POLYPHENOLS THE ACUTE STRESS NEGATIVE CONSEQUENCES

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Excess of stress situations in modern life increases the interest of researchers to acute effects of stressors on the metabolism. The influence of stress damaging factors on the endothelial cells ability to synthesize vasodilators is harmful and can lead to endothelial dysfunction (ED) development. So it is of interest to find ways of ED correction, especially using natural substances that have antioxidative and phytoestrogenic activity. Therefore, the study and use of therapeutic and prophylactic activity of grape products can be perspective.

Acute stress was caused in rats by subcutaneous injection of epinephrine (2 mg on 100 g body weight). The correction of stress consequences was done by grape seed polyphenol concentrate from grape "Cabernet" (PC) administration during 14 days (9 mg of polyphenols on 100 g body weight). There were determined: arginase activity and content of total protein, urea, citrulline, arginine, creatine, and creatinine. Epinephrine injection caused the significant decrease of arginine content in blood serum and liver tissue (by 15% and 20% respectively), moreover, arginase activity in liver increased in 2.25 times in stressed animals. However, citrulline content was decreased by 51%. Arginine deficiency that reduced NO formation and led to ED development can be caused by decrease of synthesis as well as by activation of its degradation or using for creatinine synthesis. Therefore, epinephrine injection not only causes ED development but provokes energy shortage under stress because of energy metabolism activation. The lack of arginine in these conditions causes deficiency of creatine required to form a source of metabolic energy – creatine phosphate. As a consequence creatinine was increased in the blood and liver of animals (by 98% and 29% respectively). Catabolism activation was also observed in rat liver tissue under adrenaline injection. Thereby total protein was decreased in liver by 24% that is the evidence of increased use of amino acids in the process of catabolism.Administration of PC increased arginine content in blood and liver and decreased arginse activity in stressed animals. PC administration completely normalized the arginine and citrulline levels in the liver tissue. PC administration obviously influences the muscle energy supply that is proved by increased creatine and decreased creatinine level in stressed animals.

Thus, our studies revealed the significant protective activity of polyphenol concentrate under the epinephrine injection.

# PHARMACOLOGICAL ACTIVITY OF OINTMENT “ALLERGOLIC” ON THE MODEL OF CONTACT ALLERGIC DERMATITIS

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Dermatitis is one of the most common and frequent skin disease presenting as inflammatory skin reactions in response to various environmental factors. In medicine contact dermatitis is classified into two types: a simple (non-allergic) and allergic. During the last decade increased the proportion of allergic dermatitis in general morbidity of man, first of all, because of medicinal toxicodermatosis and other skin lesions of an allergic ethiology. The pathogenesis of allergic dermatoses is largely determined by the inadequate mechanisms of immune reactivity caused by hypersensitivity of immediate and delayed types. For effective treatment of allergic dermatological diseases need medicine with a wide spectrum of action. Drugs of plant origin are seemed to be very perspective one. The aim of our study was to investigate the effect of the ointment codenamed "Allergolik", which was developed by scientists of NuPH, at the Department of Drug Technology under the guidance of prof. Yarnykh T.G., on the course of allergic inflammation of the skin on the experimental model of allergic contact dermatitis caused by 2,4-dinitrochlorobenzene (DNCB). As a reference drug was used ointment "Fladeks" – 2% ointment for external use (LLC "Pharmaceutical company"Zdorovie", Kharkov, Ukraine). In the experiment were used 24 guinea pigs with the weight 370-410 g. Experimental animals were divided into 4 groups of 6 animals each: group 1 – intact control, group 2 – positive control, group 3 – animals treated with the ointment "Allergolik", group 4 – animals treated with the ointment "Fladeks". Antiallergic action of study drugs were investigated in conditions of therapeutic and prophylactic regime, which began with the first day of sensitization. Modeling of allergic contact dermatitis was performed on groups of guinea pigs № 2-4, which were sensitized by the method of Zalkan P.M. and Ievleva E.A. In the group №3 with the treatment of ointment "Allergolik" on the 1-5-th day of the experiment we observed a significant, relative to the control pathology, decreasing of skinfold thickness in 2,3 times, as well as reducing the intensity of the inflammation of the skin that was characterized by a decreasing of edema and hyperemia. In the group of animals treated with the comparison preparation "Fladeks" significant decrease in skinfold thickness was observed only on the 5th day of the experiment. In addition, studied ointment with the extract of licorice root was significantly more effective than comparator "Fladeks". All things consider, ointment "Allergolik" is perspective for further use as a medicament for the treatment of allergic contact dermatitis.

# RESEARCH ON THERAPEUTIC EFFECTS OF SIBUTRAMINE ON HUMORAL FACTORS OF OBESITY UNDER CONDITIONS OF EXPERIMENTAL METABOLIC SYNDROME.

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Metabolic syndrome (MS) is a multisystem complex of metabolic and hormonal disorders developing under obesity. An imbalance of humoral regulators of appetite plays an important role in the obesity development: leptin (anorexigenic hormone of adipose tissue) and the orexigenic mediators group of ghrelin and anandamid. Disorders of secretion and reduce sensitivity to their actions lead to excessive eating. For expedient of MS correction is the use of pharmacological agents that restore the balance between humoral feeding behavior regulators and normalize appetite.

The aim of this work was the study of indicators dynamics of appetite humoral regulation under the sibutramine influence (anorectic drugs) in experimental MS. Pathology in rats was modeled by the dexamethasone introduction at a low doses and the keeping of animals on hypercaloric diet during 5 weeks.

Against the background of the metabolic syndrome there was a significant increase of leptin content at 1.09 times compared to intact, which confirms the widening of adipose tissue producing excessive amounts of leptin. Hyperleptinemia did not exert anorexigenic effects, probably due to the lowest throughput of blood-brain barrier (BBB) for this hormone. However, the ghrelin and anandamid levels were significantly increased in 1.11 and 1.30 times respectively, which was accompanied by abnormal increased appetite and, as a result, overeating.

The introduction of the investigational drug was accompanied by a significant decrease in the ghrelin level in the blood on 1.07 times, and anandamid in the hypothalamus in 1.33 times, which indicated the hunger feelings suppression. The blood concentration of leptin was significantly increased in 1.11 times, which was manifested by a severity increase of anorexigen sibutramine action.

According to the literature sibutramine normalizes the indices of lipid metabolism in the blood, suppresses the synthesis of proinflammatory cytokines and stimulates the production of adiponectin, which eliminates the metabolism disorders. Such mechanism makes it possible to assume that anorexigenic effect is achieved by a throughput increasing of the BBB for leptin under the lipotoxicity correction background of fatty tissue metabolites.

# MESO THEADS - A NEW WORD IN AESTHETIC COSMETOLOGY

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Modern cosmetology doesn't stand still. Women didn't have time to try on a classic strand facelift as beauticians are ready to offer women a new technique – meso threads. Meso thread lifting is a qualitative breakthrough in a face reinforcing, productive injection facial rejuvenation technique which has no analogues.

The purpose of this article is to inform the consumer that this procedure is more effective and less traumatic than conventional facelift.

In itself, a facelift procedure is new, it was started practicing in the beginning of 2013. The idea belongs to the Korean cosmetologists who developed a technique based on the physiological characteristics of the skin.

Meso threads is recognized as the most effective and not traumatic way of the filament face and body liftings. The system consists of an injection needle and a very thin filament, which is attached to the tip of the needle. After passing the needle and thread through the fabric, the needle thread is separated from the conductor on its way back and stays where it is fixed. The needle is made of the stainless steel and has a special ability that allows the doctor to level it, depending on the skin surface features or specifics of the tightening.

The implantable thread is covered with a polyglycolic acid based on polydioxanone (synthetic absorbable suture material). It is completely splits in the water and carbon dioxide in 180-200 days which eliminates the risk of rejection and allergy. The rapid absorption of threads is an important condition for ensuring the formation of young collagen without damage to the microcirculation in the tissues in the area of the meso threads installation.

This treatment is used for smoothing unwanted wrinkles. This method is less painful than a normal strand lifting as the skin after the procedure restores within 7-10 days. Some patients don't even ask for the anesthesia except for the area of the

forehead which requires local anesthesia. The duration of the procedure varies from 30 to 40 minutes.

Meso threads is a procedure that is done at the initial stage of ptosis (sagging of the facial soft tissues). That is why it is more effective at a young age when the tissues are lighter, without extra fat. The age at which you can start using meso threads is from 36-38 years (when small omission of the malar area begins) till 50 years, but it all depends on the client because each has its own particular skin.

However, there are contraindications: pregnancy, cancer, acute infections (SARS, ARI), fever.

Compared with the rejuvenation method by the gold threads, thread lifting (meso threads) is made of completely decomposed material. Meso rejuvenation effect is provided by forming the new collagen in the skin, whereas the gold threads use its permanent presence in the tissues, which excludes the further use of any hardware rejuvenation techniques. Meso threads is a more gentle and progressive method. It does not require anesthesia, does not involve incisions and also it's 100% biocompatible with the skin as it is hypoallergenic.

The leading companies of the production (used in Ukraine): KARSE, IQ - COSMETIC.

Based on the words of the practicing cosmetologist it can be concluded that the procedure is in demand and satisfies all customer needs. Hence the procedure is popular and in demand in the market of cosmetic services.

But, unfortunately, there is no methodology which can solve all the problems and thread lifting procedure is not a monomethod. In practice it is usually combined with other methods such as contouring or botulinum toxin injections. Complementing each other, these techniques give excellent results. Doctor creates a framework with the threads, adds the necessary bulk by fillers and botulinum toxin removes wrinkles.

On the assumption of all parameters it can be concluded that this procedure helps to obtain a lifting effect in a natural way without surgery. Meso threads helps the skin to stay supple, smooth and soft.

# SOME EFFECTS OF MELATONIN ACTION AND POSSIBILITIES OF ITS APPLICATION

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Melatonin (MT) –is a hormone that is synthesized from tryptophan mainly by the epiphysis. The last one together with suprachiasmatic nuclei (SCN) of the hypothalamus is a part of the so-called biological clock of the body that plays a key role in the mechanisms of "internal time accounts" and aging. The main biological effects of MT are: hypnotic, hypothermic, antioxidant, antitumor, adaptogenic, synchronization, anti-stress, antidepressant, immunomodulatory effects.

The hormone is produced in the epiphysis cells and then secreted into the blood predominantly in the dark at night. In the light, in the morning and afternoon hours, hormone production is drastically suppressed. Epiphysis of a healthy adult releases about 30 mg of MT into the blood per night. Easily penetrating into the brain from blood, MT influences a number of cerebral functions. This justifies its use in the treatment of some organic disorders of the brain such as stroke. This neuropeptide provokes some mild sedative and gipnogennye effects. Thus, the MT drug Melaxen has a positive impact on the quality of sleep when it breaches that is caused by stroke. The studies on the animal have shown that MT reduces cerebral edema in the rats with experimental stroke and increases neuroplasticity in these animals under stress, which also can be observed in the elderly ones.

MT is also used in the case of neurodegenerative diseases ( The Parkinson's disease and Alzheimer's disease). During the Parkinson's disease there is a significant reduction in nocturnal melatonin secretion. The application of neuropeptide leads to better night's sleep, a certain increase in motor abilities and reduce depression. The sharp decline of hormone secretion is also shown in the Alzheimer's disease.

A sufficient number of studies show a lower level of MT in the patients with frequent attacks of epilepsy, which explains the need for its use in case of this disease. The hormone is necessary to add to the basic anticonvulsant therapy due to the presence of a neuroprotective properties as an inhibitor of glutamate receptors and the activator of GABA-receptor.

MT is one of the most potent endogenous antioxidants. It is able to bind free radicals at the same time launching a natural antioxidant defense system through the activation of its enzymes (superoxide dismutase, glutathione peroxidase, glutathione reductase and catalase). As an antioxidant, MT acts everywhere, permeating through all biological barriers. In in vitro studies it has been found that the MT has a significantly greater antioxidant activity in terms of interruption of lipid peroxidation processes and inactivation of free radicals than the known antioxidants.

The hormone also plays a significant role in immune regulation. It has a dual effect on the function of the immune system: on the background of pre-immunosuppression we can observe its distinct stimulation by the hormone and increase of antiviral sustainability; under the same initial conditions of the immune system hyperactivity MT inhibits the formation of cytokines, reduces the function of activated macrophages and T helper cells.

Neuropeptide has a positive effect on lipid and carbohydrate metabolism, reduces the amount of cholesterol in the blood. It can normalize lipid oxidation process, thereby reducing the risk of atherosclerosis involved in the hormonal regulation of blood pressure, reducing emissions of ACTH, the production of noradrenaline, vasopressin and renin.

MT blocks the development of malignant tumors. It has been found that its use has an inhibitory effect on the origination and development of tumors in various organs of animals, which agrees well with the results of clinical observations. It is shown that the use of MT for the treatment of cancer patients reduces the relative risk of mortality. It has been established that the TM has an effect on the system as well as on the tissue, cellular and subcellular levels. In particular, at the system level MT reduces the production of hormones that contribute to these processes, and stimulates the immune defense system. It inhibits the proliferative activity of the cells and increases the level of apoptosis, preventing the emergence and development of cancer. At the genetic level, the hormone inhibits the effect of mutagens, and also suppresses the expression of oncogenes.

Based on the biological effects of TM, it can be concluded that it has very important role in the therapy of many diseases.

# ADIPONECTIN AS A MAJOR LINK IN THE PATHOGENESIS AND THERAPEUTIC TARGET IN CHRONIC HEART FAILURE

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**Background.** The observed links between chronic heart failure (CHF) and obesity increase the risk of cardiovascular events and mortality. Survival rates of CHF haven't significantly changed in the recent 30 years.

**The aim.** To analyze the results of researches that demonstrate the role of adiponectin in the pathophysiological mechanisms of CHF and potential ways of pathogenetic therapy.

**Materials and methods.** An extensive literature search was conducted on the Cochrane Library, PubMed, Web of Science and Embase, published before March 1, 2015. We used the following keywords and terms: "chronic heart failure", "heart failure", "CHF", "HF" and "adiponectin".

**Results.** Adiponectin is a hormone synthesized predominantly by adipose tissue. This protein mediates its actions via three receptors: AdipoR1, AdipoR2 and T-cadherin. The inverse correlation was found between serum levels of adiponectin and body mass index. Overweight across the life course has a cumulative influence on adipokines, inflammatory and endothelial markers. Avoidance of overweight from adolescence onwards is important for cardiovascular disease prevention. Adiponectin exhibits anti-atherogenic and anti-inflammatory effects by suppression the binding of monocytes to endothelial cells by inhibiting the expression of adhesion molecules VCAM-1, ICAM-1 and E-selectin through inhibition of activation NF-kB. This hormone reduces the growth factor induced proliferation of smooth muscle cells of the vascular wall by inhibiting the processing of the MAP kinase. Adiponectin suppresses the formation of foam cells and reduces oxidation of low density lipoprotein. Chronic adiponectin overexpression protects against the progression of CHF in a murine model by improving diastolic dysfunction and modulating left ventricular hypertrophy. Cardiac hypertrophy is decreased by stimulation of the signaling pathway dependent AMP kinase in cardiomyocytes.

**Conclusions.** Treatment with recombinant adiponectin has already demonstrated positive results in experimental models with animals. The weight reduction and lipid-lowering drugs partially realize their effects through the regulation of products and secretion of adiponectin. Further investigations of the adiponectin biological effects are perspective direction in the development of prevention and treatment of CHF.

# THE BIOLOGICAL ACTIVITY OF REPRESENTATIVES OF HEATH FAMILY (ERICACEAE)

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Heather in the broadest sense of the taxon is represented on the globe with 3000 species belonging to 100 genera. The list of indications for a clinical use of extracts from these plants is very limited. At the same time, in the folk medicine plants of this family have been widely and successfully used for the treatment of many diseases for a long time. Available information obout the chemical composition of the plant heath family indicates the presence of different classes of biologically active substances (BAS): flavonoids, phenol carbonic acids, coumarins, essential oils, triterpene compounds, and some others. Finally, the experimental pharmacological studies of the biological activity of the extracts from plants of the family Ericaceae indicate a wide range of their effects on the body. These data substantiate the prospects of using some representatives of the heath family to develop new high-performance low-toxic drugs, which is the topical problem of the modern pharmacy and pharmacology. The most promising one among the studied species of the heath family is Ledum palustre, which is characterized by a combination of a wide spectrum of biological activity, low toxicity, significant, renewable, operational stocks of raw materials.

The aim of this experimentation is to investigate the antioxidant properties of the Rhododendron tomentosum Extract.

The study has been conducted on the antioxidant activity of the experimental hepatitis model, which has been caused by an intragastric administration of carbon tetrachloride (CCl4). The state of the antioxidant system has been determined in serum and liver tissues in the level of TBA-reactive substances (TBA-AP) and reduced glutathione (WG). The experimental data suggest the presence of the antioxidant activity in the studied extracts made of Rhododendron tomentosum. This is confirmed by the normalization of the level of TBA-PA to the level of the intact animals and increased in comparison with the untreated pathology, the number of SH.

Thus, BAR (mainly polyphenolic compounds) that are the parts of the extracts made of Rhododendron tomentosum, are able to normalize the processes of free radical oxidation and antioxidant system to stabilize the hepatocytes.

# MECHANISMS OF ATHEROGENIC DYSLIPIDEMIA UNDER THE METABOLIC SYNDROME IN HAMSTERS OF DIFFERENT AGE

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Metabolic syndrome is the complex of hormonal and metabolic disorders that increase the risk of type 2 diabetes mellitus and cardiovascular system diseases. It's known the prevalence of metabolic syndrome in the population increases with age and is highest among the elderly. However mechanisms of atherogenic dyslipidemia and age-related differences in lipid metabolism changes under metabolic syndrome are not fully understood.

**The goal:** to investigate the mechanisms of atherogenic dyslipidemia under the metabolic syndrome in hamsters of different age.

**Material and methods**

Experiments were planned to develop a diet-induced MS in Golden Syrian hamsters of different age (4 weeks and 20 weeks at the beginning of the experiment), which were kept in a standard vivarium conditions. Animals were fed a standard normal diet (intact group), and during 5 weeks high-calorie diet that contained 29% of fats (predominantly saturated) with fructose addition – 1 g daily per 100 g body weight (metabolic syndrome groups). Blood samples were taken after decapitation in necessary terms and prepared according to individual procedures.

Experiments were carried out according to the “European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes” (Strasbourg, 1985). Statistical analysis were performed using nonparametric van der Waerden criterion.

Triacylglycerol (TAG) content was determined by enzymatic assay (“KONE”, Finland). Free and esterified cholesterol (CE) were determined by the help of enzymatic assays (“Boehringer Mannheim GmbH diagnostica”, Germany). Lipoprotein fractions (very low density lipoproteins (VLDL); low density lipoproteins (LDL) and high density lipoproteins (HDL)) were determined by the help of electroforesis. Total LDL and apoB-containing lipoproteins (apoB-LP) in blood serum were determined by by gradient gel electrophoresis.

**Results**

Changes in blood hormone levels observed under the MS led to a shift in the lipolysis/lipogenesis balance and were accompanied by the excessive production of the free fatty acid. Indeed, the free fatty acid level was increased by approximately 40% in male experimental animals independently of age (table 1).

Atherogenic dyslipidemia develops independently of age in males fed high-calorie diet (table 1). As it can be seen from the data presented, increased serum total lipids level in animals is mediated by the increase of apoB-LP level because the HDL content did not change. Herewith, serum TAG level rose by 47% and 30% relative to intact groups, in young and adult animals respectively (table 1).

Table 1.

Some lipid metabolism parameters in blood serum of male Syrian hamsters with the experimental metabolic syndrome

| Age | Group | Parameter | | |
|---|---|---|---|---|
| | | Triacylglycerols, g/L | ApoB-containing lipoproteins, g/L | Free fatty acid, |
| 4 weeks | Intact | 1.06±0.07 | 4.72±0.23 | 1.02±0.07 |
| | Metabolic syndrome | 1.56±0.09* | 6.68±0.15* | 1.44±0.29* |
| 20 weeks | Intact | 1.57±0.22 | 5.66±0.34 | 1.64±0.16 |
| | Metabolic syndrome | 2.00±0.13* | 6.68±0.21* | 2.29±0.25* |

Each group was composed of six animals. Mean±S.D. * – p□0.05 vs the same age intact group.

**Conclusion**

The blood TAG content increase under metabolic syndrome is considered as the key factor in the atherogenic dyslipidemia formation. A clear correlation between hypertriacylglycerolemia and ApoB-containing lipoproteins accumulation in the blood plasma demonstrated in numerous experimental and clinical studies.

Based on these data, we can suppose that lipolysis activation and free fatty acids accumulation in the blood leads to morphological changes of lipoproteins that secreted by the liver under the metabolic syndrome development.

# MITOCHONDRIAL DISEASES: PHARMACOLOGICAL APPROACHES

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Mitochondrial diseases are a heterogeneous group of disorders affecting energy production in the human body. The diagnosis of mitochondrial diseases represents a challenge to clinicians, especially for pediatric cases, which show enormous variation in clinical presentations, as well as biochemical and genetic complexity. The lack of standardized diagnostic criteria poses difficulties in evaluating diagnostic methodologies. The current approach to diagnosing and classifying mitochondrial diseases incorporates clinical, biochemical, neuroradiological findings, and histological criteria, as well as DNA-based molecular diagnostic testing.

There are several diseases that have a mitochondrial origin such as chronic progressive external ophthalmoplegia and the Kearns- Sayre syndrome, myoclonic epilepsy with ragged-red fibers, mitochondrial encephalomyopathy, lactic acidosis and strokelike episodes, Leber's hereditary optic neuropathy, the syndrome of neurogenic muscle weakness, ataxia and retinitis pigmentosa, and Leigh's syndrome. Likewise, other diseases in which mitochondrial dysfunction plays a very important role include neurodegenerative diseases, diabetes or cancer.

Generally, in mitochondrial diseases a mutation in the mitochondrial DNA leads to a loss of functionality of the antioxidant system and and a violation of the energy balance thus to a depletion of ATP and overproduction of reactive oxygen species, which can, in turn, induce further DNA mutations.

The basic pharmacological apprache in treatment mitochondrial diseases may be activated to the compensatory mechanisms that prompt mitochondria to produce more energy even under mitochondrial defect-conditions. These compensatory mechanisms include the overexpression of antioxidant enzymes, mitochondrial biogenesis and overexpression of respiratory complex subunits, as well as metabolic shift to glycolysis.

Several pharmacological strategies are the use of quercetin or resveratrol and addition of antioxidant supplements to the diet (dietary supplementation with antioxidants) such as L-carnitine, coenzyme Q10, MitoQ10 and other mitochondria-targeted antioxidants, N-acetylcysteine, vitamin C, vitamin E, vitamin K1, vitamin B, sodium pyruvate or lipoic acid.

Thus, accurate diagnosis and appropriate treatment of mitochondrial diseases is the actual direction of modern biochemistry, pharmacology and medicine.**THE**

# INVESTIGATION OF TOXIC PROPERTIES OF THE CREAM MADE OF POLYPHENOL CONCENTRATE FROM CULTURAL GRAPE "ENOPSOR" DESIGNED FOR THE TREATMENT OF PSORIASIS

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A topical problem of pharmacological correction is a high incidence of severe adverse reactions. One promising approach to solve the problem of anti-inflammatory drugs security may be the usage of some drugs based on biologically active substances of various herbs.

The cream used in the experiment with the polyphenolic concentrate made of grape cultural "Enopsor" is intended to treat a damaged skin so it is necessary to study the possible action of locally irritating and sensitizing properties.

The study of possible locally irritating actions of the studied drug has been carried out using a test " conjunctiva sample", which is a sensitive test and in some cases reveals the reaction of animals to possible irritant properties of the drug. The hyperemia of conjunctiva and cornea has been evaluated with the help of the point scale. The experiments have been carried out on rabbits. To study the sensitizing properties of the substance "Enopsor" we have used the method of skin applications. The experiment has been conducted on guinea pigs.

The experiments to determine an irritating effect of the drug to mucous membranes have been performed on guinea pigs. When applying the cream in a conjunctiva bag of the animals in 5 minutes, 24 hours and 48 hours we have not observed red coloring of conjunctiva and leakage of fluid infiltration of lacrimal ducts, mucous membrane and sclera in the guinea pigs. Cornea is transparent, smooth, without ulceration and turbidity. The conducted experiments have shown that daily applications of the studied cream has not had the any affects to the overall condition of the animals. The guinea pigs have been active, skin has been corresponded to normal, any changes in the form of congestion, infiltration, edema have not been observed. In addition, after applying the cream we have determined the skinfold thickness. During the palpation the pain areas have not been observed, the skinfold thickness has remained unchanged.

Thus, the cream made of polyphenolic concentrate with the cultural grape "Enopsor" does not have any locally irritating effects. The obtained results have also shown that there are no sensitizing actions of "Enopsor».

# NEGATIVE INFLUENCE OF SMOKING ON THE HUMAN ORGANISM

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Nowadays it is known that tobacco products contain approximately 4000 chemical compounds, and tobacco smoke – nearly 5000 compounds, 60 from which are capable to provoke cancer. Besides, a man smoking one pack of cigarettes a day gets a dose of irradiation about 500 roentgens per year.

Nicotine is a natural component of tobacco products, a narcotic and strong poison for humans. It easily enters the bloodstream, accumulates in vitally important organs causing their dysfunction. It is 3 times more toxic than arsenic. Nicotine poisoning is characterized by headache, dizziness, nausea, vomiting; in heavy cases – loss of consciousness and cramps; chronic poisoning – memory weakness, loss of efficiency as well. A lethal dose equals to just 60 mg of nicotine; a smoker inhales 0.533 mg of it from one cigarette.

Other toxic compounds in tobacco smoke are tar, nitrosamines, carbon monoxide, hydrocyanic acid, acrolein, nitrogen oxides, free radicals, various metals (including nickel, cadmium, chrome, lead etc.), radioactive components (e.g. polonium-210). Many of them are carcinogens negatively influencing on lungs, liver, brain, blood vessels and other organs and tissues.

Smoking increases level of creatinine, urea and uric acid (key nitrogen end products) in blood. Glucose level may also be elevated right after smoking. This process is a very serious cause of higher LDL cholesterol content in the blood (in contrast – lowering positive HDL), thus leading to atherosclerosis development.

Nicotine stimulates increased synthesis of corticosteroids in adrenal cortex, that (cortisol) in turn causes destruction of bone tissue.

Smoking significantly affects sex hormone content in blood of both males and females. Testosterone level in blood plasma was shown to be lowered in men smoking on regular basis. That decrease had been caused by low concentration of gonadotropic hormone as well as negative influence of smoking on the testes. In smoking women a constant and noticeable decline in estrogen content in the luteal phase of menstrual cycle was observed.

Smoking leads to vitamin D metabolism abnormality, low Ca level in blood and bones. Vitamin C content in smokers' blood is twice as less than in non-smokers.

Carbon monoxide that is present in tobacco smoke forms a steady compound with hemoglobin – carboxyhemoglobin – resulting in hypoxia (oxygen starvation).

Hemorheological changes in smokers are realized in increasing of blood viscosity, high hematocrit and fibrinogen.

# SECTION № 7

# PRECLINICAL PHARMACOLOGICAL STUDY OF NEW MEDICINES

# INFLUENCE OF RALEUKIN ON THE ACTIVITY OF GLUTATHIONE-DEPENDENT ENZYMES ON THE MODEL OF DIABETES

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Diabetes mellitus (DM) is one of the first places in the structure of endocrine diseases. High medical and social significance of diabetes requires effective and safe treatment. Therefore, optimization of treatment of diabetes is one of the pressing health and social issues of our time. Is constantly looking for new treatment regimens and drugs capable of detecting both normalizing impact on several pathogenic disease links. Particularly noteworthy anti-diabetic drugs, which along with hypoglycemic action have antioxidant properties.

The aim was to investigate the influence of recombinant receptor antagonist IL-1 ralerkin on the activity of glutathione-dependent link of antioxidant system on the model of low-dosed streptozotocine diabetes in rats. Model pathology reproduced by intraperitoneal administration of streptozotocine at a dose of 40 mg / kg for 5 days, to white males rats. For reference drugs were selected metformin and anakinra. Study drug was administered in the treatment mode for 14 days after the last injection streptozotocine: raleykin and anakinra - subcutaneously in doses of 7 and 8 mg/kg, respectively, metformin, 30 mg/kg - intragastrically. In liver homogenate was determined activity of glutathione peroxidase (GPO), glutathione reductase (GR) and glutathione-S-transferase (G-S-T) in the pancreas homogenate - activity GPO and GR. Under the action of raleukin GPO activity in liver homogenate was significantly increased in 1.7 times, GR – in 1.4 times, the activity of G-S-T fell in 1.7 times, content GPO in pancreas homogenate grew in 2.1 times, content GR – in 1.9 times compared to the group of animals of control pathology. Introduction of anakinra contributed to a significant increase activity GPO liver homogenate in 1.7 times, while the content of G-S-T fell in 1.7. Level of GPO in pancreas homogenate under the of anakinra was significantly increased in 2.1 times, GR – in 1.8 times. The use of metformin significant decrease the activity of G-S-T in liver homogenate in 1.4 time, increase glutathione-dependent enzymes in pancreas homogenate, namely, GPO activity - in 1.9, GR – in 1.6 times. Other changes in the background metformin were not significant.

Thus, on the model of diabetes raleukin contributed to the restoration activity of glutathione-dependent components of antioxidant system of animals. By normalizing effect on the above indicators raleukin wasn`t inferior anakinra and exceeded metformin.

# THE EXPERIMENTAL STUDY OF THYROID-STIMULATING PROPERTIES OF AQUEOUS EXTRACT FROM FEIJOA LEAVES

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Treatment and prevention of thyroid diseases are important medical and social problems of healthcare. Today it is recognized as the most common endocrine abnormality in the world. Pharmacological correction of hypothyroid state aimed mainly at restoring the level of thyroid hormones through the use of hormone replacement therapy. However, despite the existing arsenal of drugs with thyroid-stimulating action, the need for effective and safe means is stored. Recently prevention and comprehensive treatment of thyroid diseases, more attention is paid to the use of herbal medicine that is safer and with proper combination no side effects. Medicinal plants are the most promising source of biologically active substances with thyroid-stimulating action. One of the herbs used in unconventional medicine to treat and prevent diseases of the thyroid gland is Feijoa.

The aim of our research was to study the thyroid-stimulating properties of aqueous extract from Feijoa leaves.

The pharmacological screening of the effects of aqueous extract from Feijoa leaves on functional activity of the thyroid gland was performed in healthy rats at doses of 0.5, 1.0, 1.5, 2.0 and 2.5 ml. It was determined the level of thyroid hormones –triiodothyronine ($T_3$) and thyroxine ($T_4$) in blood plasma by enzyme multiplied immunoassay after the experimental period. Increasing of the concentration of the hormones in the blood serum of experimental animals compared with the control group indicatesabout thyroid-stimulatingeffect of researched substance.

The results of experimental studies demonstrate the stimulating effect of aqueous extract from Feijoa leaves. All studied doses observed a significant increase of $T_3$ hormone in the serum of experimental animals compared with control group. Accordingly, a dose of 0.5 ml - 65%, 1.0 ml - 71%, 1.5 ml - 31%, 2.0 ml - 34%, 2.5 ml - 31%. Analyzing the results on the concentration of thyroxin ewe may note similar to the dynamics of changes in the concentration of $T_3$ hormone effect, but less expressive. Increasing of $T_4$ levels in serum takes place in doses of 0.5 ml and 1.0 ml.

So, the result of experimental studies showsa thyroid-stimulating effect of aqueous extract from Feijoa leaves, which leads to conclusion about the viability and feasibility of further research.

# THE RIBES NIGRUM INFLUENCE ON VASCULAR PENETRATION

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Herbal medicines are being used as a tonic, hemostatic, antiphlogistic, diuretic and other preparations. Low toxicity and possibility of the durable using without significant side effects are the advantage of the herbal medicines. Herbs demonstrate its therapeutic effect because of availability of different chemical composition and different structure of the components that have pharmacological actions. The chemical nature of the most of the plants-based drugs is much closer to human body than synthetical. Herbal medicines that demonstrate an antiphlogistic action make the special interest because of the high frequency of the inflammatory diseases. They've got a wide distribution in the scientific and peoples' medicine because of the treatment of the inflammatory diseases in the form of decoction, infusion and tincture. The Ribes nigrum is a plant that have these activities. The increase of the vascular permeability is one of the mechanism of an inflammatory edema's development. So it represented a significant interest to explore the effect of the 40% tincture of the Ribes's nigrum leaves on vascular permeability.

The tincture's influence on the vascular penetration was seen by the difference of coloration of the papules in time that were induced by histamine, kaolin, carrageenin, formalin and protein. An assessment of the vessel-strengthening effect was conducted by the difference of coloration of the animals' papules of the control and experimental groups.

In the result of exploring it was found that preliminary injection of the leaves of the black currant's tincture slows the coloration of the histamine papule in 4 times, kaolin in 1.6 times, carrageenin and protein in 3 times and formalin papules in 2.3 times in contrast with control.

So, we can make a conclusion that an infusion of the Ribes's nigrum leaves has vasodilatative effect and reduces permeability of the vascular wall in a period of inflammation.

# THE MECHANISMS OF NEUROPROTECTIVE ACTION OF NEW OLIGOPEPTIDES-HOMOLOGOUS OF PRIMARY $ACTH_{15-18}$ SEQUENCE

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The ischemic stroke is undoubted leader among neurological disease, it's prevalent cause of high disability and mortality of working-age population. For the treatment and prevention of it use cerebroprotective agents.

Ideas of peptidergic cerebroprotection have been developing since the 70s of the 20th century. They originated from the work of de Wied [de Wied D., 1977], who has showed protective effect of different sequences of adrenocorticotropic hormone (ACTH) at various brain diseases. Cerebroprotective drugs have created in particular analogue of $ACTH_{4-7}$ semax. The peptidergic mechanism of cerebroprotective effect has established for classical nootropic drug piracetam later [Гудашева, 1985], the most important metabolite of which is native factor of neuronal protect cycloprolylglycine.

The works on the creating of more effective peptidergic cerebroprotectors continue. At State Research Institute of Highly Pure Biopreparations have created number of primary sequence of $ACTH_{15-18}$ analogues by Sc.D. A.A. Kolobov, that include D- and N-methylated forms of lysine and arginine. The low toxicity, long-term effect, absence of hormonal and antihormonal action have discovered at the conditions in vitro [Ковалицкая, 2009; Патент RU №2356573 C1, 2012]. The presence of neurotropic properties have suggested for these oligopeptides.

The hypothesis of the presence of such properties was confirmed. The antiischemic and nootropic activity of the peptides Acetyl-(D-Lys)-Lys-Arg-Arg-amide (КК-1), Acetyl-Lys-(D-Lys)-Arg-Arg-amide (КК-2), Acetyl-Lys-Lys-(D-Arg)-Arg-amide (КК-3), Acetyl-(D-Lys)-Lys-(D-Arg)-Arg-amide (КК-5) was established; the improvement of integral mental activity, antihypoxic, actoprotective and antialcoholic activity of tetrapeptides KK-1 and KK-5 was established; elements of sedative and tranquilizing effects of neuropeptides KK-2 and KK-3 was established [Патент RU №2537560 C2, 2015]. Furthermore the investigated

neuropeptides don't influence on the depressive behavior of mice and don't potentiate the exciting action of neuronal toxin penthylentetrazole under the experimental conditions. The resulting factual material have been leaving unclear mechanisms of neuronal protect of studied neuropeptides.

Leaders of investigate in terms of neuroprotective and psychotropic action are tetrapeptides KK-1 and KK-5. They have demonstrated synergism of antiischemic and antihypoxic activity among 10 homologous compounds (and too identical in the presence D-lysine in the first position of hydrocarbon chain peptide Acetyl-(D-Lys)-(D-Lys)-(D-Arg)-(D-Arg)-amide (KK-9)). They increase the time of mouse life at hermetic chamber under conditions of normobaric hypoxia with hypercapnia. The results of pulse oximetry and flowmetry have confirmed they beneficial effect on hemoglobin oxygenation (not less than 95 per cent) and hemodynamic parameters: the volume velocity of blood flow in the internal carotid artery, arterial and central venous blood pressure, that on the background of cerebral ischemia restored to physiological level.

Neuropeptides KK-1 and KK-5 correct deferred mechanisms of neuronal death at penumbra (inflammation and apoptosis) beside restore of adequate brain blood perfusion (primary neuroprotection). The ability of peptides KK-1 and KK-5 to normalize the balance of pro- (IL-1β, TNF-α) and anti-inflammatory (IL-4) cytokines at ischemic brain was detected with the help of immunoferment analysis. The ability of peptide KK-1 to reduce to 5.34 and 2.25 times ($p<0.05$) the expression of neuron specific enolase and protein S-100 (markers of brain injury) have ascertained.

Anti-apoptotic action of KK-1 have confirmed by decrease of 90 per cent of DNA fragmentation level on the background of cerebral ischemia compered to control pathology ($p<0.05$).

At last, neurotrophic mechanism of protective action of tetrapeptides KK-1 and KK-5 have confirmed. It consists in normalization of nerve growth factor overexpression, which arises on the background of cerebral ischemia.

According investigated indices oligopeptides KK-1 and KK-5 exceed the comparator drug, chemical and pharmacological analog, known peptidergic cerebroprotector semax.

In this way, further experimental and clinical research of oligopeptides KK-1 and KK-5 is perspective.

# DECAMETOXIN ACUTE TOXICITY STUDY AND ITS MEDICINAL FORM "DECASAN" FOR THE TREATMENT OF INTESTINAL INFECTIONS

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The search of effective and safe drugs for the treatment of intestinal infections is topical problem. One of the ways of this problem solution is the possibility of decametoxin using for oral administration. Decametoxin is cationic active surface detergent with a broad spectrum of antibacterial, antiviral, antifungal activity. It has the ability to degrade the microbial toxins, causes anti-inflammatory and anticholinesterase effects. 0.02% isotonic solution of decametoxine is called "Decasan" ("YURiA-PHARM ", Ukraine), which is widely used for the treatment of septic surgical diseases in neurosurgery, stomatology, otorhinolaryngology, urology, gynecology, pulmonologiy in the form of washing, irrigation, rinsing, inhalations. It is known that the decametoxin solution has been effectively used for a long drop irrigation of digestive anastomosis zone for prevention of complications associated with seams failure. There is a question about the possible acute toxic effects on the macro-organism within the complex of preclinical studies of decametoxin by new indication (intestinal infection).

**The purpose** of the research is to determine the acute toxicity of decametoxin and "Decasan" when administered orally.

**Materials and methods**. $LD_{50}$ of decametoxin substance (by the Pastushenko method) and the "Decasan" was determined according to the guidelines on pre-clinical study of drugs in rats of both sexes with body weight 180-200 g after single intragastric administration. The "Decasan" was administered in a dose of 20 ml/kg because decametoxin concentration is low (0.02%) and according to the guidelines for pre-clinical study drugs limiting volume of liquid for intragastric administration in rats with such body weight is 5 ml. The substance of decametoxin was administered in a maximum tolerated single dose of 400 mg/kg intragastrically. The general

condition and dynamics of body weight was evaluated. Animals were euthanized on the 3$^{th}$ and 15$^{th}$ day after drug administration. The coefficients of internal organs mass were determined. The condition of the liver, kidneys, heart, lungs, adrenal glands, spleen, thymus, stomach, intestine in all parts, gonads was evaluated macroscopically and by light microscopy with hematoxylin-eosin staining.

**The Results.** It was impossible to determine $LD_{50}$ of "Decasan" after single administration intragastricaly because the maximum dose for its administration 20 ml/kg has no toxic effect in animals and does not cause their death. The $LD_{50}$ of decametoxin substance is 586 (484÷588) mg/kg, which corresponds to the IV$^{th}$ class of toxicity – low-toxic substances (500 mg/kg<$LD_{50}$<5000 mg/kg). The decametoxin substance toxic dose (400 mg/kg) did not cause the death or disturb the dynamics of body weight during a two-week observation. Mass coefficients of internal organs had no differences with the control. In 2 days there are signs of the mucous membrane irritation in the gastric fundus and pyloric part microscopically. Epithelial cells were flatter with increased exfoliation. Somewhere it was found the initial stages of superficial erosions formation, subepithelial capillary network is full-blooded. The single extended glandular tubes which are same to cyst, submucosal edema, full-blooded vessels and somewhere subepithelial stromal edema were observed in the stomach. The reactive changes in the thymus, some stress of adrenocortical zona fasciculata and the chromaffin cells of the adrenal medulla, slight decrease in the protective effect of small intestinal mucosa were observed. These changes were transient and in 14 days after intragastric administration of decametoxin substance in a dose of 400 mg/kg were absent. There were no pathological changes in other organs.

**Conclusion.** "Decasan" that is 0.02% decametoxin solution, has acceptable parameters of acute toxicity and a high level of safety. The $LD_{50}$ value for the "Decasan" in rats can not be established because the administration of the drug in a dose more than 20 ml/kg is not possible. $LD_{50}$ of decametoxin substance is 586 mg/kg, which corresponds to the IV$^{th}$ class of toxicity – low-toxic substances. Slight irritation of the gastric mucous membrane after decametoxin substance administration is temporal.

# CHRONORHYTMS OF CARRAGENIN AND ARCOXIA ACTION

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The interest in the study of chronobiology, chronopatology and chronopharmacology has substantially increased in the last 30-40 years and it puts the task of studying the temporal characteristics of the action of medicines and agents that are used to model a particular pathology.

The aim of the study was to establish seasonal and circadian (daily) rhythms of action of carrageenan and arcoxia. Carrageenan edema over the years is one of the classical models for the study of antiexudative activity of nonsteroidal antiinflammatory drugs (NSAIDs). Carrageenan was introducted to rats as 1% solution in autumn and winter at 7 and 22 o'clock, as rats have night life chronotype. Measuring the size of edema in conventional units (c. u.) was carried out mechanically. The obtained data show that after the introduction of 1% solution of carrageenin into female rats at 22 o'clock in autumn the acrophase (maximum value) of the inflammatory edema was observed at the fifth hour after administration and amounted 55,6±1,25 c. u.

After administration at 7 o'clock in the morning acrophase was observed on the fourth hour and amounted 57,67±1,66 c. u.. In winter carrageenan was administered at 22 o'clock also, but acrophase shifted and was observed on the fourth hour 51,5±0,33 c. u. After administration of carrageenin at 7 o'clock, acrophase of inflammatory edema was observed at third hour and amounted 46,83±0,54 c. u.

Also, we investigated the activity of Arcoxia 10 mg / kg administered 1 hour before the time of inflammatory edema acrophase. Effectiveness of the drug at the peak of the inflammatory process amounted as follows: the introduction of carrageenan at 7 o'clock in the autumn – 47,26±5,47%, at 22 o'clock – 61,09±2,66%, and in the winter – 48,89±1,46% and 56,58±2,85%, respectively.

These data confirm the facts that the inflammatory processes are most pronounced in the autumn, and the dosing of NSAIDs especially in autumn and winter are similar what is confirmed by the comparable activity of the drug in these seasons.

The findings suggest the need to study the temporal features of the proinflammatory agents' action as well as the development of the most rational appointment of NSAIDs.

# MECHANISMS OF ACTION CARBOXYTHERAPY

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2012 was declared the European Year carboxytherapy, the mechanism of action is associated with the physiological properties of carbon dioxide ($CO_2$). There are two major mechanisms of action in the body of $CO_2$. The first mechanism of action is direct and reflex stimulation of $CO_2$ respiratory and vasomotor centers of the medulla oblongata. And also, at the expense of local action on the cells of arterioles $CO_2$:$CO_2$ injection body perceives as hypoxia and reacts to the increased blood circulation and the generation of new blood cells. As a result of the introduction of $CO_2$ per area of the body more oxygen and nutrients, and the process of restoration and renewal of cells. Also, by reflex, by chemical action of $CO_2$ receptors, promoting formation of bioactive substances.

The second mechanism of $CO_2$ action is called effect Verigo Bora, it is associated with lung function. Its essence is that, without the presence of $CO_2$, oxygen cannot be released from the bound state of the hemoglobin, which leads to oxygen deficiency in an organism even at a high concentration of oxygen in the blood. But the greater the amount of $CO_2$ in arterial blood, the easier it is done separation of oxygen from hemoglobin and its transition into tissues and organs is rapid elimination of hypoxia - the main component of the pathogenesis of most diseases. In these mechanisms of action of $CO_2$ based carboxytherapy.

Cellulite also involved three mechanisms carboxytherapy. By increasing the local concentration of carbon dioxide increases oxygenation defective site, it promotes "burning" of fat cells actively pumped into the tissues with oxygen. Increased lipolysis - fat reduction process, eliminating stagnation of lymph tissue and improve the elimination of toxins and fluid from the tissues. Increased sensitivity of beta-adrenergic receptors responsible for the process of lipolysis.

Carboxytherapy also widely used in orthopedics. Firstly, the introduction of carbon dioxide along the spine and joints to improve local blood circulation, increasing oxygenation. Second, the reflex irritation of carbon dioxide nociceptors, and trigger points, causes vasodilation and thus easing pain, eliminates functional disorders of the musculoskeletal system.

# INFLUENCE OF GYALURONIC ACID ON THE STATE OF SKIN

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A skin is an integrument of organism. In a skin there is a number of processes : synthesis of the special proteins - collogen, elastin, melanin, synthesis of vitamin of D, and such process, as aging. Aging of skin is inalienably related to the general process of aging. Distinguish a few reasons of aging of skin, but one of leading mechanisms is a loss of moisture skin cells.

Water balance of skin holds out 2 passive processes: by diffusion of water in a derma through the walls of vessels and evaporation of her through a horny layer.

Water balance of skin holds out 2 passive processes: by diffusion of water in a derma through the walls of vessels and evaporation of her through a horny layer.

Gyaluronic acid (GA) is in our organism, mainly in a skin, she is the inspector of moisture in our skin, that helps to save elasticity, resiliency, tone, and helps the squirrel of skin (to the collogen and elastin) to support the form. One molecule of GA links about 1000 molecules of water and creates the effect " of pampers".

GC creates the internal volume of fabrics, providing optimal terms for functioning of skin cells. GA helps to bring down the process of evaporation of moisture from a skin; to influence on activity of cages; to assist neutralization of free radicals (they are main culprits of aging of skin); to perform the protective duty of the cutaneous covering (from infections); to assist more rapid cicatrisation of wounds; gel- and tape to form with an anti-inflammatory action.

There are 2 types of GA : high molecular to GA and low-molecular to GA. High molecular to GA impenetrate skins in less degree, her function is the superficial moistening, she creates microtape allowing to retain moisture, there is an instantaneous effect of lifting and smoothing out of skin at her application, and she is used for the contour plastic arts. Low-molecular to GC does not smooth out a skin, in a much less degree is a humectants, her basic function is adjusting of formation of enzymes, supporting integrity of skin barrier, providing of natural UF- protective, and is used for biorevitalithation .

GA enters in the complement of cosmetics, including fitocream, that gives an opportunity longer to save youth of skin.

# SCREENING RESEARCHES OF INFLUENCE OF GEL WITH THE GLYCOSAMINE ON WOUND PROCESS

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Wound process in response to any damage of integrity of an organism develops. Considering that skin bears big functional loading it's exposed to influence of the damaging factors more than other parts of our body. Soft dosage forms of preparations are a traditional method of treatment of wound process which reduce terms of healing of wounds. That's why development of preparations for local treatment of wound process is actual.

The analysis of the market showed that for second phase of wound process in the market of Ukraine there are 5 preparations: 3 of them - ointments prepared on a fatty basis, 1 - gel and 1 - ointment prepared on a hydrophilic basis. Medicines for local treatment of wounds on a hydrophobic basis create "greenhouse effect" that interferes with formation of granulated tissue. The hydrophilic basis of gel doesn't interfere oxygenisation of the skin cells, absorbs quickly, doesn't leave fat spots. Besides this gel provides uniform distribution of particles, increasing efficiency of treatment, and promotes preservation of humidity in wound tissues, interfering with a tissue hypertrophy.

One of the modern approaches increasing efficiency of wounds healing is development of the preparations containing plastic material. Glycosamine is one such materials.

Glycosamine is the polysaccharide which is taking part in formation of granulated tissue. It is synthesized by fibroblasts and is the plastic material that necessary for biosynthesis of mucopolysaccharides which make a basis of interweft substance of connecting tissue. Surrounding collagen molecules, mucopolysaccharides take part in formation of collagenic fibers, providing stabilization and cementation of fibrous structures.

In the 2nd phase of wound process there is a normalization of a metabolism, especially carbohydrate and protein, process of healing of a wound becomes more active. The glycosamine as a component of connecting tissue accelerates this process.

In this regard the glycosamine was entered into composition of the gel received under the leadership of the department of Industrial technology the prof. Ruban E.A.

Work purpose. To conduct screening research of influence of gels with a glycosamine in concentration of 0,5%, 1%, 1,5% for the course of wound process for models of a linear wound at rats.

Materials and methods. Experiment is made on white rats by weight 180-220 g. For creation of a linear wound to rats under a ksilazin anesthesia on a site of skin of a back a section long 5 sm, immediately imposed seams and processed leather by 5% iodine solution. Animals were divided into 4 groups: the control pathology (CP) - uncured animals, the 2nd, 3rd and 4th groups – animals who were treated by 0,5%, 1%, 1,5% gel with a glycosamine respectively. 7 days of treatment later skin sites with wounds were cut out and hem durability on a tenziometra was investigated.

Results. In group of animal CP durability of cicatricial tissue corresponded to an indicator of a tenziometry of 660,83 g. When drawing on a wound gel with a glycosamine of 0,5% reparative activity in comparison with CP increased by 1,15 times; with 1% - by 1,36 times ($p<0/05$); with 1,5% - by 1,24 times. Therefore, on model of linear wounds expressiveness of reparative effect of gel with 0,5% of a glycosamine made 14,88%; with 1% - 36,19%; with 1,5% - 24,34%.

Conclusion. Thus, gel with the maintenance of a glycosamine of 1% authentically increases durability of cicatricial fabric that is experimental justification of optimum concentration of a glycosamine in wound healing gel.

# THE INFLUENCE OF N,N'-(ETHANE-1,2-DYYIL)BIS(QUINOLINE-2-CARBOXAMIDE) ON GLUCOSE BLOOD LEVEL IN NORMOGLYCAEMIC RATS

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The search of effective and safe drugs for the treatment of diabetes mellitus (DM) is topical problem. One of the ways of this problem solution is using of N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide), a compound containing the fragments of the chemical structure of imidazoline receptors type $I_2$ blocker – (2-(4,5-dyhidroimidazol-2-yl) quinoline hydrochloride). N,N'-(ethane-1,2-dyyil)bis (quinoline-2-carboxamide) is known as antitumor agent in a dose of 1.5 mg/kg intraperitoneally (i.p.).

On the model of alloxan-induced DM in rats in our previous experiments was shown the pronounced hypoglycemic effect of N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) in intraperitoneal (1.5 mg/kg) and intragastrical administration at wide dose diapason (7.92-31.67 mg/kg). This compound reduced the level of glucose in the blood by 57.2% and by 27.3-63.1%, respectively, with nonlinear relationship "dose-effect". $LD_{50}$ of N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) is 10.005 mg/g i.p. and 633,45 mg/kg intragastrically (i.g.). $ED_{50}$ is 11.64 mg/kg, the therapeutic index is 54.42, indicating a sufficient level of the substance safety.

The purpose of research is to determine the N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) influence on blood glucose level during normoglycaemia.

Materials and Methods. Hypoglycaemic effect was investigated on the white random-bred male rats with the body weight equal to 0.20±0.02 kg. Plasma glucose content was determined by glucose oxidase method in the blood samples which were taken from the vessels of tip of the tail before and 90 min after drug administration. N,N'-(ethane-1,2-dyyil)bis (quinoline-2-carboxamide) was administered as an aqueous suspension, stabilized by polysorbate 80 at a dose of 1.5 mg/kg i.p. and 7.92 mg/kg (1/80 $LD_{50}$), 15.84 mg/kg (1/40 $LD_{50}$) i.g.

The Results. In normoglycemic rats N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) in a dose of 1.5 mg/kg i.p. the hypoglycaemic effect is moderate (blood glucose decrease by 16.2% vs 57,2% in DM model). After intragastrical administration in a dose of 7.92 mg/kg there was no hypoglycaemic action (blood glucose decrease by 3%), in a dose of 15.84 mg/kg it was more marked (by 24,9% vs 63,1% in DM model).

Conclusion. The hypoglycemic effect of N,N'-(ethane-1,2-dyyil)bis(quinoline-2-carboxamide) in normoglycaemic animals is significantly less than in diabetic ones.

# CIRCADIAN RHYTHM OF ALBUMIN AND TOTAL PROTEIN CONTENT IN BLOOD SERUM OF INTACT RATS AND ON THE BACKGROUND OF PARACETAMOL HEPATITIS

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The aim of our work was to study the circadian rhythm of albumin and total protein content in intact rats and in the conditions of paracetamol hepatitis.

**Materials and methods.** The study was conducted on mature male and female rats weighing 150-200 g in the spring (March 2015). The albumin and total protein level were made in intact rats and on the background of one-day paracetamol hepatitis. In order to establish circadian dynamics of albumin and total protein level in blood serum of animals in defined hours: 09 a.m., 03 p.m., 09 p.m., 03 a.m. they were decapitated, the blood was taken and blood serum obtained. The results were calculated with the help of mathematical statistics methods Cosinor-Analisis 2.4 for Excel 2000/XP followed by chronogramm obtaining and their detailed analysis. The analysis determined hronohram akrofazu and batyfazu.

**Results and Discussion.** According to the results of experiment, akrofaze of albumin level in females accounted for 09.30 p.m. (45.67 mg per l), while batyfaze observed at 09 a.m. (38.62 mg per kg). Akrofaze batyfaze of males are shifted to one hour before relatively to females 10.30 p.m. and 10 a.m., respectively. On the background of paracetamol administration no significant changes of albumin level between intact and animals with model pathology were observed, but the conversion of akrofaze and batyfaze time confirming the development of desynchronosis in terms of pathology in violation of circadian rhythm. Akrofaze was at 04 a.m. in females and at 06 a.m. in males and batyfaze was at 04 p.m. in both sexes.

According to the total protein level it was found that females akrofaze was at 04 a.m. (79.60 g per l); 02 a.m. in males (89.80 g per l), when batyfaze of rates in both sexes was at 04 p.m. Introduction of parecetamol has caused desynchronosis of preset rate, according to the time of akrofaze and batyfaze onset. There were no significant differences in total protein level between the intact animal and rats with control pathology, due to insufficient depressing action of xenobiotics on protein sunthesis of the liver in case of its single injection.

**Conclusions.** Thus, according to the data obtained the total protein and albumin level is characterized by circadian dynamics of content in blood serum, with specific akrofaze in the dark period of the day: 09 p.m.-11 p.m. – albumin; 02 a.m.-04 a.m. – total protein level; and batyfaze in light period of day 09 a.m.-10 a.m. – albumin; 04 p.m. – total protein level. Paracetamol introduction causes desynchronosis above the threshold rate, with the time dislocation of akrofaze and batyfaze.

The received data should be considered in the formulation of experimental study of prospective hepatoprotectors and adequate interpretation of experimental results.

# SCREENING RESEARCH OF NEW PYRIMIDINE DERIVATIVES ANTICONVULSANT ACTIVITY

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The prevalence of epilepsy among diseases of central nervous system is third. The number of patients in the world exceeds 50 million. Treatment of epilepsy is a difficult task, up to 25-30% of patients have multi-drug resistance and a significant number of antiepileptic drugs have dangerous side effects (eg. phenytoin, carbamazepine, lamotrigine, phenobarbital). Therefore, the development and preclinical study of potential antiepileptic drugs is problematic. Under supervision of prof. V. Georgiyants 43 original compounds of pyrimidine derivatives were synthesized at the Department of Pharmaceutical Chemistry, National University of Pharmacy, which are promising for clinical study. Some of these compounds on the results of PASS-forecasting have high probability of anticonvulsant activity.

**Aim.** Rate anticonvulsant activity of pyrimidine derivatives compounds on basic screening model.

**Materials and methods.** It has been used basic screening model – pentylenetetrazole (PTZ) seizure test in mice. Control group received PTZ at a dose of 90 mg/kg subcutaneously. Bioactive compounds were administered at a dose of 50-100 mg/kg through a tube into the stomach 20-30 minutes before PTZ injection. As a reference drug used valproate sodium ("Depakin", Sanofi-Aventis, France) at a dose of 300 mg/kg into the stomach.

**Results and Discussion.** As a result of screening bioactive compounds were proved two leaders with codes KS78342 and KS78303 (100 mg/kg), which significantly increased the survival rate at the level of valproate sodium. Compound KS78553 (50 mg/mg) significantly reduce the number of generalized tonic-clonic seizures one animal. Another 6 compounds proved tend to increase survival and/or reduce the severity of seizures, 29 – proved proconvulsant effect of varying degrees, and 5 were indifferent.

**Conclusion.** The results allow to predict the potential anticonvulsants presence among leading compounds. For in-depth study leading compounds and their anticonvulsant activity must continue pharmacological study of their mechanism of action, spectrum of anticonvulsive action, others concurrent pharmacological activity, dose-dependent effect and safety.

# HEPATOPROTECTIVE ACTIVITY LIPOPHILIC AND HYDROPHILIC LIME LEAVES EXTRACT RESEARCH

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Paracetamol is the one of the most used non-prescription drugs in Ukraine. As one of the most effective analgesics and antipyretics, paracetamol is nevertheless a potential hepatotoxic agent.

Not only overdose of paracetamol, but even its long-term use contributes to the development of drug hepatitis, especially for people with hepatitis of various etiologies or patients with diabetes mellitus.

Paracetamol hepatotoxicity caused not only by the result of covalent binding of its highly reactive metabolite N-acetyl-4-benzohinonimin with macromolecules of hepa:-ocytes, but also by activation processes of free-radical oxidation (FRO) with enzymatu and non-enzymatic dysfunction of antioxidant systems.

**The purpose of the research.** Hepatoprotective activity lipophilic and hydrophik. lime leaves extract research.

**Materials and methods.** This work is devoted to the experimental research of the hepatoprotective properties of hydrophilic (PL**-1)** and lipophilic (PL-2) lime lea\. extracts. Investigations have been carried out on the paracetamol hepatitis model o: rats. White mongrel male rats with weight **1**80-220 g have been used in this research.

**Obtained results.** As a result of these experiments revealed that the use of PL-**1** anc PL-2 in drug-induced hepatitis caused by paracetamol reduces the intensity of cytoh: . and free radical processes in the liver, increases the activity of the antioxidant syste~ of hepatocytes and contributes to the normalization of carbohydrate, protein and lip | metabolism, and recovery processes bile production and secretion.

Efficiency of researched extracts is 20% higher on average than the efficiency of the reference drug silibor in the intensity of the hepatoprotective action.

**Summary.** Conducted research testifies the advisability of further preclinical lime leaves extracts studies to create new domestic plant hepatoprotector on their basis.

# THE USAGE OF THICK BEANS EXTRACT, METFORMIN, GLIBENCLAMIDE FOR CORRECTION OF DITHIZONE DIABETES COMPLICATIONS IN RABBITS

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Acute complications of diabetes mellitus are diabetic ketoacidotic, hyperosmolar and lactatacidotic coma and the chronic ones are vascular changes observed in the long course – diabetic microangiopathy. Despite a fairly wide range of modern antidiabetic agents, the problem of treatment and prevention diabetes is not completely solved, that encourages the search and development of new drugs for the correction of complications of the disease. The effect of a thick bean extract (TBE), metformin and glibenclamide on glucose and ketone bodies level in urine, urine pH was explored on the model of dithizone diabetes in rabbits. Dithizone diabetes was induced by intravenous injection of dithizone (35 mg/kg body weight) to male Chinchilla rabbits weighing 2.5-3.0 kg. The presence of glucose and ketone bodies in urine, and urine pH was dtermined after sampling the material using diagnostic test strips «Phan Laura» for urine analyzer «Laura Smart». Starting from 2 days of research animals with dithizone diabetes administered orally for two weeks TBE at a dose 40 mg/kg and the reference drugs – metformin at a dose of 30 mg/kg and glibenclamide at a dose of 5 mg/kg. We have studied the influence TBE, metformin and glibenclamide on the level of glucose and ketone bodies in urine, urine pH model dithizone diabetes in rabbits. 7, 10, 12 and 14 days later of the study of the TBE has reduced glucose levels in the urine of animals and prevailed over the effect of metformin in 9.8%, 9.7%, 31.2% and 37.4%, but has given in to the action of glibenclamide by 4.5%, 5.9 %, 1.3% and 0.7%. The TBE has reduced the level of ketone bodies in the urine of the animals in 7, 10, 12 and 14 days of the study, and prevailed over the effect of metformin in 5.5%, 10.2%, 8.4% and 12.0%, but has given in to the action of glibenclamide through 7, 10 and 14 days of the study by 4.1%, 3.8% and 3.3%, and in 12 days – the TBE has predominated over the effect of glibenclamide by 2.4%. On the 14th day the study the TBE has facilitated the normalization of urine pH in the animals, which corresponded (8.4±0.38) to alkaline environment. In the group of the animals for which treatment the glibenclamide has been applied, urine pH has been close to the original data (7.9±0.40), and the urine pH has been still acidic (7.5±0.51) when metformin has been used in the treatment of the animals. It has been found that a long-term administration of the TBE, starting of 7 days and during 14 days of the study, has decreased blood glucose and ketone bodies in urine, helped to normalize the pH of the urine in the animals with dithizone diabetes, prevailed over the action of metformin and has been approaching to the glibenclamide action. The TBE is a promising hypoglycemic agent in the complex treatment of acute insulin deficiency, as well as the treatment of diabetes type 2, which will prevent the development of the disease complications.

# EFFICACY OF INTERLEUKIN 1 RECEPTOR ANTAGONIST (IL-1Ra) IN ACUTE CHEMICAL INJURY OF ORAL MUCOSA

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Introduction. Inflammatory diseases of oral mucosa (OM) are widely distributed in all age groups and permanently occupy the leading position in dental diseases. The drugs influencing on the different phases of pathological process, namely antiinflammatory, immunotropic, wound healing et al., are widely used in the treatment of the aforesaid diseases. Non-steroidal antiinflammatory drugs (NSAIDs) are widely prescribed in this case. Receptor antagonist of interleukin-1 (IL-Ra) designed developed at the Research Institute of Highly Pure Preparations corresponds to this concept. The results of the last years investigations indicate the significant changes of cytokine profile in the oral cavity in inflammatory diseases. This makes possible to suggest the efficiency of antycytokine therapy in the inflammatory diseases of OM. Still the experimenatal and a fortiriori, clinical verification of this hypothesis has not been done. The purpose of the present study was to compare the efficacy and safety of the experimental therapy of the acute chemical injury of OM with IL-Ra and traditionally used NSAIDs in systemic administration.

Objects. The research was conducted on 42 randombred female albino rats (body weight 130–200 g) using the model of acute chemical injury of OM by the application of 10% solution NaOH on the underlip. The animals were randomly divided into 4 groups: intact control, untreated animals (chemical injury), animals treated with IL-1Ra (3 mg/kg subcutaneously) during 3 days after chemical injury, and animals treated with diclofenac sodium (8 mg/kg intramuscularly) in the same regimen. The doses of the drugs equaled $ED_{50}$ for antiinflammatory action. Body weigth and rectal temperature were determined on the 1, 3, 4, 8 days; erythrocytes and leukocytes count, haemoglobin content, ESR, total protein, AlAT AsAT, and catalase activity, concentration of TBA-reactants in blood were determined on the 3$^{rd}$ and 8$^{th}$ days. The status of OM was assessed macroscopically on the 3$^{rd}$ day, affected area of OM was harvested for histological study (light microscopy).

Results. Edema and hyperemia of the vestibule mucosa were observed in all animals. Apparent necrosis signs were absent in the untreated animals; the body weigth was increased by 3.5–7.9 g, the temperature was augmented in the first three days compared with intact control ($p<0.001$, $p<0.05$ respectively), the normal bowel movements were observed, there was no lethality.

Under the action of IL-1Ra clinically significant necrosis was absent in the damaged tissues. Initial body weigth was increased by 0.8–5.0 g, statistically significant hyperthermia compared with the intact control data was absent, lethality was also not registered.

Under the action of diclofenac sodium the macroscopically evident necrosis was found in 33.3% of samples; the body weigth was acutely reduced – the decrease was more than 15g in 50% of animals, and more than 25 g – in 33.3% of animals; progressive decline in body temperature compared to the untreated group and intact control data ($p<0.05$, $p<0.01$ respectively); diarrhea was observed in 50% of cases. It indicates the significant toxic effect of diclofenac sodium.

Leukocytosis and the increment in ESR ($p<0.05$) were seen in the untreated animals. Against the background of diclofenac sodium treatment anemia with the reduced haemoglobin content, as well as the increase in ESR were determined. Under the action of IL-1Ra these changes were not so significant as in diclofenac sodium group ($p<0.05$ and $p<0.01$; $p<0.001$ respectively).

Biochemical blood indicators in the untreated group did not differ significantly from the intact control data. Statistically significant differences from this group data were also absent in animals receiving IL-1Ra, except for TBA-reactants reduction ($p<0.01$). Under the influence of diclofenac sodium marked hypoproteinemia and increase in AlAT and AsAT activity, indicating augmentation in cytolysis, was observed. Activation of lipid peroxidation as evidenced by the increment in TBA-reactants in blood serum by 78% was registered as well as the reduction in antioxidant system (namely, the decrease in catalase activity).

Macroscopically extensive ulcerative necrotic lesions of all mucosa layers, submucosa, and sometimes muscular fibers were observed in the untreated animals, edge epithelization of the surface defects was not seen in these samples.

Under the action of IL-1Ra minor defects of mucosa were observed histologically. Necrotic dystrophic changes were less expressed in length and depth. Under the anticytokine therapy influence, edge epithelization was registered. After diclofenac sodium administration mucosa defects extended on submucosa and there were no evidences of the edge epithelization.

Conclusion. IL-1Ra exerts a pronounced antiinflammatory effect in acute inflammation of oral mucosa and does not demonstrate side effects inherent in traditional NSAIDs. Efficacy and safety shown in the present investigation experimentally substantiate the expediency of IL-1Ra usage in the treatment of mucosa inflammation processes.

# THE SCREENING STUDY OF STRESSPROTECTIVE EFFECT OF NEW OLIGOPEPTIDES

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Life of a modern human is related to a huge amount of stress influences, which are the basis of the pathogenesis of diseases of the cardiovascular, endocrine and central nervous systems. A long effect of stressors significantly reduces the adaptive capacity of a human body and leads to the development of a disease adaptation. Based on this a topical problem of the modern pharmacology is the search for new stressprotectors.

The purpose of the study. To screen a stress protective effect of new oligopeptides – the analogues of adrenocorticotropic hormone (ACTH15-18) ciphers under KK-1, KK -2, KK -3, KK -4 KK -5, KK-6, KK-9 KK -10.

Materials and methods. Screening studies have been carried out on the model of neuro-muscular tension by Selye by immobilizing the animal for three hours on a operating table, fixing antraumatically by their limbs. The studied drugs have been administered at a dose of 20 mg / kg intranasal, the drugs of comparison semax and glycine at doses of 20 mg / kg and 10 mg / kg, respectively, in the same mode. The presence of stress protective activity has been determined by the weight coefficients of the adrenal glands and thymus, the frequency of ulceration in a stomach.

Results. The presence of the stress protective activity has been found in oligopeptides ciphers under KK-1, KK-2, KK-3, KK-5, KK-10, because in these experimental groups we have revealed some statistically significant differences from the control pathology group of animals in all investigated parameters. These peptides have significantly reduced the adrenal mass index, increased the thymus weight ratio, reduced the incidence of ulceration in a stomach, exceeding the effect of the drugs of comparison. In the groups of animals treated with oligopeptidies KK-4, KK-6 and KK-9 with the expressed stress protective action has not been observed, because of the fact that no differences have been observed in all investigated indices.

Conclusion. According to the results of the screening tests for the further in-depth study of stress protective actions the most promising peptides are KK-1, KK-2, KK-3, KK-5, KK-10.

# THE INFLUENCE OF COMBINATIONS GEROPROTECTIVE DRUGS ON LIFESPAN OF C57 BLACK MICE

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Purpose of experiment

Purpose of experiment was to investigate the effect of combination of prospective geroprotector drugs on life expectancy and physiological parameters of laboratory animals. Combinations are selected according to the published data to prevent age-related pathologies.

Materials and Methods

Study was conducted on experimental animals – males and females of C57/BL6 aged 16-17 and 22-23 months. Animals were divided into groups depending on the geroprotective drugs that were incorporated in their daily food ration (165 mg nutriment to g of body weight a day): group 1 – Aspirin (2,13 mg/kg body weight a day), Everolimus (3,01 mg/kg), Metformin (10,64 mg/kg) (only females), group 2 – Aspirin (2,13 mg/kg), Everolimus (3,01 mg/kg), Metformin (10,64 mg/kg), Metoprolol (33,53 mg/kg), Simvastatin (20 mg/kg) and Ramipril (5 mg/kg) (both males and females), group 3 - control (food chow without drugs; both males and females). Mice were assigned to each group after randomization according to their body weight and open field test performance. Survival analysis included Kaplan-Meier plotting and Gehan-Wilcoxon $U_w$-test. Data analysis was performed with the «STATISTICA 7» software package.

Results

Statistically significant increase in life expectancy of group 1 was observed compared with other females (both control and experimental group 2). The average time of staying alive after beginning of experiment was more than 310 days, while the control group did not exceed 270 days.

Combination of drugs from the group 2 was able to extend the life expectancy of males (life expectancy animals after beginning of the experiment in the control group is 65 days and in group 1 - 270 days), but significant effect on life expectancy of females was not observed.

Conclusions

Established that complexes geroprotective drugs increase the life expectancy of control animals and therefore there are prospects for further research and practical applications of complexes of these drugs in geriatric practice.

# PRE-CLINICAL RESEARCHING OF NEW ANTIHELMINTHIC DRUGS

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In Ukraine the annual index of morbidity onhelminthiasis presents 1333 cases on each 100 thousand of population. Child's morbidity presents 2025.6 cases on each 100 thousand children. 30 of 342 types of helmints in the world meets in Ukraine: 90% cases are enterobiasis, 7.5% consistsascaridiasis and thrichocephalosis takes 1.5% of cases. At Ukrainian pharmaceutical market of antihelminthic drugs foreign production presents 90% and domestic one has only 10%. So, creating of new antihelminthic drugs is the actual medical and pharmaceutical problem. Requirements to new drugs are: low toxicity, high pharmacological activity, low suction in a gastrointestinal tract, high coefficient of elimination, absence of resorbtion action, injuring influence on organs and tissues, cumulation.

The aim of research was studying of experimental models, used in pre-clinical investigations of new antihelminthic drugs.

The clinical displays of helminthisms are: pain, diarrhea, nausea, itch, allergic reactions, oncologic process as a result of chronic inflammation. Modeling starts from choosing laboratory animals (hamsters, guinea-pigs, rats or dogs) and infection them by invasion material. In modeling of opisthorchiasischamsters, PCR, histological researches of liver are used; in case of ascariasis (guinea-pigs or rats are used) and thrichocephalosis (rats are used) researches make incision on different terms of infection. On the different stages researches apply such methods of laboratory diagnostics: serum reactions, histological research and PCR. So, laboratory animals (hamsters, guinea-pigs, rats, mice, dogs) are used in experimental investigations. Researches study state of internalss (depending on localization of parasites), setting the mechanism of action and properties. Methodology of modeling of opisthorchiasis is most valuable, as requires the use of PCR-analysis.

# STUDY OF ETHANOLIC AND WATER EXTRACTS OF BUPLEURUM AUREUM ON SPONTANEOUS HEMOLYSIS UNDER THE METHOD JAGER F.S.

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Today medicine has made considerable progress in the treatment of many diseases. However, many drugs, except medical action, have a number of side effects, leading to sensitization of the organism. Main organ, that sureference drugorts detoxification and excretion of drugs and their metabolites is liver. Drug-induced liver injury is about 10% of all adverse reactions and today remains one of the major problems of hepatology and pediatrics. Despite the rather wide arsenal of hepatoprotective drugs, the problem of effective therapy for liver injury remains unresolved, which causes the urgency of finding or creating new efficient drugs. From this perspective herb Bupleurum aureum draws attention. In traditional medicine this plant is used as an effective remedy for diseases of liver, gallbladder and pancreas. However, the main indications for use are cholecystitis and hepatitis. In view of the above, Bupleurum aureum is a promising object for development of new drugs of hepatoprotective action.

Aim of work was to determine the properties of water and ethanolic extracts of Bupleurum aureum on a model of spontaneous lysis of erythrocytes. Experiments were conducted on white outbread male rats weighing 180-200 g. As a reference drug was used antioxidant vitamin E (50 mg / kg) and pellets of quercetin (50 mg / kg). Study drugs were administered intragastric to animals in doses of 5 mg / kg daily. Control animals received water. On 14 day of the experiment in blood samples obtained from the tail vein of rats was determined the degree of lysis of erythrocytes by the method Jager FS.

According to the received data, the most pronounced membrane stabilizing action showed ethanolic extract, its activity was 37%, slightly lower 25% - reference drug vitamin E, and the lowest - water extract (13%) and reference drug quercetin (12%). It should be noted that concerning the expressive membrane stabilizing action ethanolicic extract of Bupleurum aureum was significantly higher than the water extract and reference drug quercetin and was equal to reference drug vitamin E. Taking into consideration, that membrane stabilizing action is the result of antioxidant properties, we can assume the presence of the latter in the ethanolic extract of Bupleurum aureum.

So, on the model of spontaneous lysis of erythrocytes was determined membrane stabilizing properties of studied extracts, as for expressive action, ethanolic extract of Bupleurum aureum was equal to vitamin E and exceeded the activity of water extract and reference drug quercetin.

# DEFINITION OF ANTIEXUDATIVE ACTIVITY OF WATER AND ETHANOLIC EXTRACTS OF SALSOLA COLLINA PALL. ON A MODEL OF ZYMOSAN-INDUCED EDEMA OF PAWS IN RATS.

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Today is increased interest to medicinal plants as a source of biologically active substances to create on their basis highly effective drugs with a wide range of pharmacological actions. From this point of view, Salsola collina Pall. is a perspective plant, hepatoprotective properties of which have been known in traditional medicine for a long time. Object of the research became water and 30% and 50% ethanolic extract of Salsola collina Pall.

Aim of this work was to determine the anti-inflammatory properties of extracts of Salsola collina Pall. on the model of exudative inflammation caused by zymosan (0.1 ml per animal in 2% suspension) in rats. Examined drugs were administered intragastric prophylactically during 4 days daily at a dose of 5 mg / kg. Last administration was made in 40 minutes before simulation of inflammation. As a reference drug were used granules of quercetin 50 mg / kg, which were administered in the same mode. Efficiency of the extracts was assessed by the ability of the extracts to reduce edema compared to positive control animals in dynamics within 3 hours.

It is established, that prophylactic administration of extracts prevented development of paw edema of rats. The biggest effectiveness was identified in 50% ethanolic extract of Salsola collina Pall., anti-inflammatory activity of which in average was 32%, less expressive effect showed water extract - 24%. Ethanolic extract of Salsola collina Pall. 30% showed weak antiexudative effect by inhibiting paw edema in animals for only 9%.

Since the major mediators of the development of zymosan inflammation is are leukotrienes, obtained results suggest the presence of antileukotriene activity in ethanolic and water extracts of Salsola collina Pall. as a part of anti-inflammatory action. Research of phytochemical composition of plants found, that along with a high content of various amino acids, Bupleurum aureum contains large amounts of quercetin for which is proven the ability to inhibit the release of leukotrienes in inflammation. Perhaps, the presence of quercetin in water and ethanolic extracts of Salsola collina Pall. provides a clear antiexudative effect on this model. It should be noted that for the expressive antiexudative action 50 % ethanolic extract of Salsola collina Pall. is equal to reference drug - granules of quercetin.

# CHANGE OF TRIGLYCERIDE LEVELS IN RATS WITH HYPOTHYROIDISM WHEN USING EXTRACT OF LAMINARIA

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One of the most promising ways to improve the treatment of major diseases of the thyroid gland (TG) – hypo- and hyperthyroidism – is using of herbal medications, which pharmacodynamic properties contribute to the increasing effect of basic medicines that address them a for manifestations of these pathologies and improve the safety of their use during long courses.

Well-known is that the lack of thyroid hormone leads to the decreasing of basal metabolism. Hypothyroidism is usually accompanied by lipid metabolism disorders, which include increasing of total cholesterol, very low density lipoproteins, low density lipoproteins and triglycerides.

The purpose of our study was to investigate the mechanisms of the effect of the aqueous extract of Laminaria on lipid metabolism in animals with hypothyroidism.

Experimental hypothyroidism was reproduced by administering of Merkazolilum in a dose of 5 mg/100 g body weight during 30 days. The aqueous extract of Laminaria saccharina was administered intragastrically at a dose of 1 ml/100 g body weight. The reference drug Iodomarin was used in a dose of 1.2 mg/100 g body weight in a similar mode. The degree of development of hypothyroidism was determined by measuring of thyroid hormones - thyroxine and triiodothyronine blood levels and by the data of morphometric evaluation of the TG functional state. Triglycerides were determined by the classical method.

In experimental hypothyroidism decreasing of thyroid hormones thyroxine and triiodothyronine, and increasing of triglycerides (2 times) serum levels were observed compared to control animals. Morphological structure of TG was typical for hypofunction. With the introduction of the aqueous extract of Laminaria there was a significant decrease in the concentration of triglycerides compared to the levels in rats with hypothyroidism. Iodomarin had less pronounced similar effect. The positive dynamics of morphological and functional changes of TG is observed.

Laminaria extract, which is being studied as a potential drug for the prevention and treatment of diseases associated with hypofunction of TG, showed a normalizing effect on the level of triglycerides in the blood of rats with hypothyroidism.

# CYTOPROTECTIVE ACTION OF THE RIBES NIGRUM

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There are many different factors that can lead the red bone marrow cell to increase the frequency of the toxic damage. In the clinical and experimental practices phenolic substances that were got from the plants are widely used as antioxidants, particulary the substances of the flavonoid nature. That's why the searching of the new effective cytoprotectors that have membrane stabilizing activity is topical. So if the last ones are the part of the leaves of the Ribes nigrum, we guess that we should explore its membrane-stabilizing properties.

With the choosing the optimal model, the red bone marrow cells, that had been got before every experiment, were used. The number of this cells in a gotten suspension was counted by the method of determination the number of the white blood cells (leukocytes).

40% ethanol was used as a toxical substance. The leaves of the Ribes nigrum were explored as 40% tincture doses 0.1, 0.3, 0.5, and 1.0 ml. A Shrek's method was used for estimation the quality of cytotoxic and cytoprotective action. The essence of this method lies in the fact that the living bone marrow cells don't skip a pigment when it's being painted by the 1% water solution of the methylen blue while the membrance of the damaged cells are fixing the color.

0,5 ml of the bone marrow cells (with the concentration $2.43*10^5$) and a dose of the exploring substance was imported to the tubes for determination of the cytoprotective action of the leaves of Ribes nigrum. A control was the bone marrow cells with the adding 0.5 ml of physiological solution.

The received information found out that the 0.5 ml dosed tincture of the Ribes's nigrum leaves has the most expressed membrane-stabilizing activity. So we can make a conclusion that an exploring preparation has membrane-stabilizing activity on the isolated red bone marrow cells.

# PHARMACOLOGICAL STUDIES OF THE INFLUENCE OF DICLOKOR ON ZYMOSAN-INDUCED PAW OEDEMA IN RATS

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Zymosan, which is a glucan with repeating glucose units connected by β-1,3-glycosidic linkages, is used to induce experimental sterile inflammation for further assessment of antiexudative action of a new drug. Zymosan inflammation is mostly leukotriene-mediated. Diclokor is a new drug, which is being developed by Borshagivskiy HFZ and containing 40 mg of quercetin and 25 mg of diclofenac.

The aim of this study was to assess the influence of Diclokor on zymosan-induced paw oedema in rats.

40 rats were divided into 4 experimental groups: group 1 – animals with control pathology; group 2 - animals receiving Diclokor at a dose of 17.8 mg/kg; group 3 - animals receiving quercetin at a dose of 11.0 mg/kg and group 4 - animals receiving Voltaren at a dose of 6.8 mg/kg. All drugs were administered orally in one dose 1 hour before induction of the pathology. Aseptic exudative inflammation was caused by subplantar injection of 0.1 ml of zymosan suspension in the right paw of the animals. The volume of oedema was measured by digital plethysmometer in dynamics in 0.5, 1, 2 and 3 hours after zymosan injection. Anti-inflammatory activity was expressed in percentages and measured by comparing the volumes of oedema in animals receiving test drugs and animals from the control group.

The results of the study showed that after 0.5, 1, 2 and 3 hours Diclokor had the most pronounced antiexudative activity (%), which equaled 35.6±2.1, 45.5±2.7, 32.3±1.9 and 24.4±1.5, respectively. Corresponding figures for quercetin were 25.4±1.5, 33.2±2.0, 22.2±1.3 and 19.6±1.2, and for Voltaren – 7.3±0.3, 14.8±0.7, 17.5±0.8 and 10.1±0.5, respectively. Antiexudative activity of Diclokor was reliable in comparison with the control group and reliably higher than that of the reference drugs. The ability of quercetin to inhibite zymosan inflammation is due to its antiluekotriene properties, which is consistent with the literature data. In this model, Voltaren had the lowest antiexudative activity.

Thus, Diclokor at a dose of 17.8 mg/kg exhibits a pronounced inhibiting effect on zymosan-induced paw edema in rats. This effect is due to the presence of quercetin in its composition, since quercetin inhibits lipoxygenase pathway of arachidonic acid metabolism, the mechanism responsible for the development of zymosan inflammation.

# CHRONOOPTIMIZATSIYA THERAPY OF ONCOLOGIC DISEASES

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The main purpose of chronooptimization of antitumor treatment is the selection of the time of day where we receive an optimal balance between the sensitivity of the tumor to the drug and its toxicity.

A desynchronization (violation) of biorhythms is an early sign of functional disorders that occur long before the malignant tumors progression. In patients with malignant neoplasms the circadian rhythm synthesis of the main synchronizer of time of melatonin is disturbed which indicates desynchronosis. Thus, in case of cancerous lesions of the esophagus in the later stages (3-4) there is an increase melatonin synthesis at 9 times and absence of the characteristic peak at night. The increase in the number of breast cancer in women working at night. This is due to the inhibitory effect of light by night melatonin production, which is known to be a powerful anti-cancer agent in the body.

The presence of diurnal and seasonal rhythms of proliferative processes in a variety of tumors is the basis for chronodiagnostics, chronoprophylacsis and chronotherapy of cancer.

According to experimental and clinical data, it is advisable to prescribe cytostatics for the hours of the day when the tumor cells are in a phase of mitosis and are most sensitive to drug influence. In addition, it must be remembered that these drugs affect the activity and proliferation rhythm of normal tissues. Therefore, the main dose is administered during the greatest resistance of the organism to cytostatics. For a man this is in a morning and the first half of the day.

The principles of the chronotherapy of malignant neoplasms:

• In the phase of the mitotic cycle, when the tumor is most sensitive to the drug;

• When proliferating cells of normal tissues are most sensitive to the drug;

• When a toxic effect on the entire body cytostatic is less pronounced.

Radiation therapy of malignant tumors of the human skin gives the maximum effect when providing it in 12 hours, and in breast cancer – from 7 to 10 hours.

# THE POSSIBILITIES OF METFORMIN COMBINING WITH THE HERBAL PREPARATIONS ON THE MODELS OF DIABETES MELLITUS (LITERATURE REVIEW)

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Introduction. The new approaches of combined treatment of diabetes mellitus and metabolic syndrome are necessary. Herbal drugs may stipulate polytropic favourable effects simultaneously influencing on several pathological pathways. Phytotherapy in the most cases is supplementary method, but it may increase the efficacy of known antihyperglycemic drugs. Still the verified data about efficacy and safety of such combinations are limited, and it is rational to summarize them.

Objects. Medline and elibrary.ru were searched up to January 2015. The search terms were 'metformin', 'herbal medicine', 'medicinal plant.' The search subsequently was extended.

Results. It has been found that several herbal preparations increase efficacy of metformin on the model of alloxan-induced diabetes (it should be emphasized that there is strong evidence of meformin efficacy on this model). These preparations include ethanol extract of Carica papaya L. (Caricaceae) leaves (at doses of 5 and 10 mg/kg), methanol extract of Catharanthus roseus L. (Apocynaceae*)* leaves (at a dose of 250 mg/kg), water extract of Terminalia chebula Retz (Combretaceae) fruits (at a dose of 500 mg/kg), while water extract of Cinnamomum cassia Nees ex Blume (Lauraceae) does not influence on hypoglycemic effect of metformin.

The ability to increase metformin efficacy under the conditions of streptozotocine-induced diabetes has been proved for fruit juice of Momordica chrantia L. (Cucurbitaceae, at a dose of 20 ml/kg), extract of Allium sativum L. (Alliaceae, at a dose of 500 mg/kg), ethanol extract of Scutellaria baicalensis L. (Lamiaceae) roots (at a dose of 400 mg/kg), while ethanol extract of Rehmannia glutinosa (Scrophulariaceae) does not increase hypoglycemic effect of metformin on this model, still it enhances the reduction in plasma C-reactive protein level.

Conclusion. Data available in literature show that herbal preparations are able to significantly increase the hypoglycemic effect of metformin on the models of alloxan-induced and streptozotocine-induced diabetes. Thus, there are prospects of success in the search and further studies of combinations of known antihyperglycemic drugs with herbal preparations. Further research is needed to establish the mechanisms of action and biopharmaceutical factors.

# THE PHYSIOLOGICAL ROLE OF $CO_2$ IN AN ORGANISM AND PHARMACOLOGICAL EFFECTS OF CARBOXYTHERAPY

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Carbon dioxide long time was considered as the final metabolism`s product, harmful for an organism, of which it is necessary to get rid completely. However at the end of the last century it was proved that $CO_2$ is very important product of an exchange which is necessary for normal organism`s activity. In recent years new data which characterize $CO_2$ role as the most important regulator of many processes, including, ensuring preservation of a homeostasis at adaptation to the most various conditions collected.

Therefore more detailed studying of physiological and pharmacological properties represents essential interest for medicine and pharmacy.

Physiological properties: expansion of vessels; microcirculation acceleration; relaxation of muscle fibers of vessels; improve a tone of veins; stimulate angiogenesis, respiratory reflexes, functions of fibroblast; raise a tone of smooth muscles; stimulate secretion of hormones, functioning of digestive glands; interfere with lipid peroxidation; reduces a threshold of excitability of nervous cages; regulates cellular respiration, electrolytic balance.

Thus, carbon dioxide, contrary to a popular belief, is necessary for an organism not less, than oxygen. It is the powerful physiological regulator of numerous systems of an organism: respiratory, transport, cardiovascular, secretory, haematogenic, immune, hormonal, etc.

Pharmacological effects.

Carboxytherapy thanks to the natural action`s mechanism $CO_2$ and a rich pharmacodynamics, solves many complex and unresolved problems of medicine. Use of carbon dioxide allows to improve blood circulation, tissue respiration, to regenerate fabrics, to bring toxins and slags out of an organism, to split fats.

Medical effects: hypotensive (secondary), cardiotonic (positive inotropny), metabolic, reparativno-regenerative, toning, anti-spastic, anti-inflammatory (primary), antianginalny.

Carboxytherapy promoting updating and clarification of an organism, increase of immunity and working capacity, normalization of work of internals, and also improvement of quality of life.

# ANTIOXIDANT ACTIVITY OF HYNALONAMYDITIN

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Conducted research showed that use of hynalonamyditin significantly reduced the content of primary molecular products of lipid peroxidation in cardiac tissue and blood, reduced cholesterol/phospholipids ratio [2, 6], and stimulated superoxide-dismutase activity of myocardial tissue and superoxide-entraining activity of blood serum.

By its impact on lipid peroxidation processes, hynalonamyditin had greater impact than vitamin E.

The purpose of the research were confirmed by submicroscopic examination of myocardium, when attention was paid to ultrastructure of cardiomyocyte nucleus, sarcoplasm, availability of mitochondria in juxtanuclear area, borders of "insert disc" between sarcomeres, etc. After administration of hynalonamyditin in animals, number of mitochondria significantly increased, borders of "insert discs" between sarcomeres slightly "expanded", a lot of different organelles appeared in sarcoplasm. Restoration of myocardiocyte ultrastructure was confirmed by detected changes which appear as a result of hypoxia and in case of antioxidant action of both, tocopheryl acetate and hynalonamyditin.

Materials and methods of research Acute regional myocardial ischemia was caused by RB Jennings method under ethaminal-sodium anesthesia (40 mg/kg intravenous). Activity of lipid peroxidation and key anti-oxidase system enzymes was determined by means of sampling in decapitated animal blood serum and myocardium.

Analysis of data in literature, which speak of the ability of tocopheryl acetate to improve metabolism and contractive activity of myocardium, reduce oxygen consumption by myocardium, take part in tissue respiration and in other important processes of cell metabolism, allows with great probability, while taking into account results of own research, assuming that hynalonamyditin possesses similar properties.

Summary. Antioxidant effect of hynalonamyditin is realized as a result of reduction of primary molecular products of lipid peroxidation in myocardium and blood, stimulation of superoxide-dismutase activity of cardiac muscle and superoxide-entraining activity of blood serum.

# HERBA OF SHEPHERD'S PURSE IS PERSPECTIVE RAW MATERIAL FOR THE CREATION OF NEW DRUGS

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Nowadays search for new medicines in plant materials is actually because a herbal medicines have fewer side effects and equal synthetic drug activity. Most modern drugs are synthetic origin and may cause and positive pharmacological effects and side effects. Herb of Shepherd's purse Capsella Bursa-Pastoris (Brassicaceae) is interesting for investigation. Moreover, this plant has traditionally been used as a diuretic and for the treatment of dysentery, furuncle, gonorrhea, menstrual disorders, and fever. In particular, plants belonging the Brassicaceae family contain high levels of sulforaphane (SF). SF is an isothiocyanate, and SF has received extensive attention for its potent chemopreventive activity. SF is not only effective in preventing chemically induced cancers in animal models, but also effective in inhibiting the growth of established tumors. In addition, a sulforaphane-containing solution (SCS) isolated from broccoli had an antioxidant effect. Furthermore, shepherd's purse contains vitamin A, ascorbic acid, linoleic acid, and omega-3 polyunsaturated fatty acids, which are beneficial for human health. To date, several classes of phenolic compounds have been isolated from shepherd's purse, such as flavonoids, alkaloids, calystegines, glucosinolates, and saponins.

So, the aim of this work is studying of pharmacological action of extract of the herb of Shepherd's purse (EHSP) in laboratory animals. Known that damage cell membranes of tissues and organs causes a disturbance of their functions and development of the disease. So, was studied membrane stabilizing effect of EHSP in doses 10 mg/k, 50 mg/kg and 100 mg/kg kg in method of erythrocyte hemolysis (Jager F. C.).

It was found that EHSP in all doses have membrane stabilizing effect in 27-58%% which increases with grows of the dose values. Thus membrane stabilizing activity of EHSP in dose 10 mg / kg is 27%, in dose 50 mg / kg is 50% and in dose 100 mg / kg – 58 %. It shows that the EHSP may be effective for the treatment of diseases pathogenesis of which is have damage to cell membranes (inflammatory diseases of the respiratoty and GI tract, liver, kidney, hart, metabolic disorders and others).

So, the results show that EHSP is promising for further study in order to create a new effective and safe drugs for use in medical practice.

# COMPARATIVE STUDY OF ANXIOLYTIC PROPERTIES OF GEL WITH GLUCOSAMINE HYDROCHLORIDE AND SUPPOSITORIES WITH ESTRIOL IN SPAYED RATS

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Anxiety, as one of neurosis signs, is an attributive symptom of psychoneurological disturbances, emerging at climacteric syndrome in women.

The goal of research is study of anxiolytic activity of glucosamine HCL (5% vaginal gel) and estriol ("Ovestin" vaginal suppositories) at intravaginal introduction to spayed rat females.

**Materials and methods.** The experiments have been carried out on spayed rats of 180-200g weight. The exposure to the drug at vaginal introduction to animal anxiety has been studied with help of "elevated plus maze" test, based on natural acrophobia of rats and their ability to avoid lighted spots. An animal has been placed to the maze center and its moves have been being registered within 5 minutes. The experiment has been carried out in hours of darkness, because of circadian rhythm of rats. Anxiolytic properties have been evaluated on such parameters as follows: latent period of entry to the dark tube (s), duration of staying in light tubes (s), duration of staying in dark tubes (s), number of transfers.

**Results and Discussions.** Spayed animals of control pathology group showed sharply amplified anxiety. Latent period of the dark tube entry and duration of staying in light tubes of the maze have been 5 times and 2 times correspondingly lower than in the females of intact control group. However, time of staying in the dark tube was 2 times more, and the number of transfers between tubes of the maze got 3 times less ($p < 0.05$)

Vaginal introduction of 5% gel with glucosamine hydrochloride to spayed rat females results in reduction of their anxiety: increased latent period of the maze dark tube entry, duration of staying in light tubes of the maze, time of staying in the dark tube has been reduced correspondingly. Number of transfers between tubes of the maze was 2 times more, than of untreated animals. Rats, which were given hormone replacement therapy with estriol, had decreased anxiety, and had improvements in locomotor activity. The obtained data were consistent with indicators of intact animals.

**Conclusions**. This way, the studied preparations showed almost the same anxiolytic effect and normalizing impact on locomotor activity in spayed rat females.

# CARBOXYTHERAPY INDICATIONS, POSSIBLE SIDE EFFECTS AND CONTRAINDICATIONS FOR IT

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A new direction in medicine - carboxytherapy treats so many diseases with $CO_2$. Carboxytherapy was a real breakthrough in modern cosmetology and solutions to complex medical problems. Throughout the world, this technique is becoming the most popular way to rejuvenate the skin. Carboxytherapy turned all the laws of beauty and youth, because the desired effect is achieved by "harmful" carbon dioxide. Today carboxytherapy found good use in many areas of medicine, but especially a lot of experience of its application in cosmetics and orthopedics. Carboxytherapy helps when the signs of skin aging, promotes correction eliminates many cosmetic defects and even allows you to fight cellulite. $CO_2$ therapy is indicated for the treatment of skin diseases such as atopic dermatitis; acne; scleroderma; plaque psoriasis; eczema; scars of different origin; applied to improve circulation, enhancing the protective properties of the skin, healing of wounds and burns, inhibition of inflammation. Analysis carboxytherapy indications show that it corrects all body systems. Diseases of the circulatory system - coronary heart disease, myocardial infarction, hypertension. In the nervous system, improves the condition of neuritis, vegetative neurosis, vertigo of various origins. In diseases of the kidneys and urinary system used for chronic prostatitis, chronic pyelonephritis, erectile dysfunction in men. Effective for the treatment of respiratory diseases: chronic bronchitis, bronchial asthma, pulmonary fibrosis and emphysema. $CO_2$-therapy is used in ENT surgery, proctology, gynecology, and even oncology. Carboxytherapy, promotes purification and regeneration of the body, improve immunity and efficiency, the normalization of the internal organs.

Carbon dioxide is non-toxic, since it is naturally formed in the body and excreted through the lungs. Carboxytherapy using not noted any serious side effects. In the first few seconds after the session, a burning sensation, redness, edema, or swelling within an injection area. The main absolute contraindications are: acute inflammatory and dermatological process at the injection site; suppurative inflammatory changes of the skin; herpes; decompensated diabetes; the early period after a stroke or myocardial infarction; anemia; mental illness, epilepsy, pregnancy and lactation.

21st century - a time of high technology and unique discoveries, including carboxytherapy is a versatile and widely used technology. This unique method helps to triumph in many areas of medicine. Today is difficult to call the field of medicine, wherever carboxytherapy not yet been rated "excellent" for effectiveness and safety.

# NON-DRUG ARTERIAL HYPERTENSION TREATMENT FOR YOUNG PEOPLE WITH OVERWEIGHT

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Arterial hypertension (AH) treatment is an activation of organism internal reserves. The majority of patients with AH and overweight need lifestyle modification first.

The basic treatment for these patients is unloading dietary therapy. Dosed fasting has its complex effects on the patients suffering from AH. It restores self-regulation, compliance with the pumping function of the heart and level of peripheral vascular resistance, reduces cardiac output and blood pressure on the myocardium.

The purpose of the research. To study non-drug arterial hypertension treatment for young people with overweight.

Materials and methods. Patients with early stage of AH combined with overweight were prescribed a short absolute "dry fasting" for i-3 days with subsequent limitation of taking water at 10-12 ml / kg per day, throughout the whole discharge period. Starting from the first day of fasting drug therapy was revoked.

Obtained results. At the beginning of the third day of blood pressure (BP) was reduced by 10%, and to 10.9 days in 53% of patients blood pressure was close to the norm for this age group already. After the course carried out, if it is necessary to prescribe drugs, the dose of antihypertensive drugs is decreased by 39.5%. It is prescribed infusions and decoctions of herbs (valerian root, motherwort herb, fruit Aronia) as maintenance therapy. It is recommended to follow a vegetarian days, hypocalorie and hyposodium diet, reducing excess weight, avoiding harmful habits, sufficient physical activity of cyclic type (walking, jogging, skiing), that in the presence of contraindications in combination with diet, 58% of patients with early stage hypertension lead to normalization of ABP level. The basic treatment for these patients is unloading dietary therapy. Dosed fasting has its complex effects on the patients suffering from AH. It restores self-regulation, compliance with the pumping function of the heart and level of peripheral vascular resistance, reduces cardiac output and blood pressure on the myocardium.

Summary. Non-drug treatment for patients with AH combined with a healthy lifestyle have a positive effect, since more than half of the patients had a normalization of ABP level.

# NEW POTENTIAL OF RHEUMATIC DISEASES IMMUNOBIOLOGICAL THERAPY

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Chronic inflammation in rheumatoid arthritis (RA) and many other systemic dis-eas of connective tissue extend beyond the joints. Patients with RA have an increased **sk** of disease development in cardio-vascular system, lungs, eyes, musculoskeletalem. Effective control of inflammation becomes important and is the key to improv-| outcomes for patients with rapidly progressive RA. Traditional treatments are often effective for patients with RA, as they do not completely suppress the inflammation : causes its progression. Thanks to the appearance of biological agents, especially inhibitors of tumor necro -| UPE-a, there were alternative effective means obtained, which are characterized by efficiency and ensure rapid and sustained improvement.

**The purpose of the research.** To study the state of rheumatic diseases immunobi-2ical treatment.

**Materials and methods.** We have researched the effectiveness of the drug "Rituxi-- Mab-Thera for patients with an inadequate response to the ongoing complex lent in serum department 27 GKB Kharkov.

**Obtained results.** Mab-Thera application for 22 patients with RA is accompanied clinical improvement of state of the disease with a marked reduction in the im-le-inflammatory activity. Mab-Thera prescription for patients with systemic lupus iiematous with active lupus nephritis resistant to basic drugs leads to reduction of nephritic syndrome and stabilization of the nephritis course. Mab-Thera prescrip- for patients with Sjogren's syndrome, accompanied by high activity, leads to im-. ed clinical and laboratory parameters of the disease/

**Summary.** Thus, the use of new biological agents for the treatment of systemic ective tissue diseases can slow the progression of the disease, and also to achieve long-term remission of it in most cases

# INFLUENCE OF TINCTURE OF HERB OF BIDENS TRIPARTITE ON RAT'S DIURETIC FUNCTION

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Herb of bur-marigold (bidens tripartite) is interesting for investigation. Plants take up an important place in traditional medicine and scientific research confirmed properties about their use as alternative therapy. Bidens tripartita, commonly known as Three-lobe Beggarticks, Three-part Beggarticks, Trifid Bur-marigold, is a flowering plant in the genus Bidens, family Compositae, subfamily Asteroideae. Evaluation of the chemical composition of this plant has revealed the presence of flavonoids, xanthophylls, volatile oil, acetylene and polyacetylene, sterols, aurones, chalcones, caffeine and tannins. Shown in animal experiments that the drugs of herb of bur-marigold a series of hypotensive and sedative effect. Complex flavonoids–polysaccharide drug from herb of bur-marigold succession bile effect on exceeds flamin. The positive effect of herbs tinctures succession by 70% ethanol, with the use of an external ointment containing 2.5% of the extract of the herb of bur-marigold on the basis of a lanolin - petrolatum in patients with psoriasis. Advised of infusions and decoctions of herb of bur-marigold have a diuretic, diaphoretic, choleretic, inflammatory, reparative, antimicrobial, regulating of metabolism action. The herb of bur-marigold has been used in folk medicine as a diuretic, sudorific and anti-inflammatory agent. It is also used in the treatment of fevers, skin diseases, bladder and kidney troubles, and as a stimulant of the immunological system.

So, the aim of this work is studying of influence of tincture of herb of bidens tripartite on rat's diuretic function because in previous researches it was found that powder of the herb of bur-marigold have membranestabilizing action. So, was studied diuretic action of tincture of herb of bidens tripartite in doses 0,1 ml/kg after 2 week administration in spontaneous diuresis and in diuresis with water load.

It was found that tincture of herb of bidens tripartite in doses 0,1 ml/kg not changed spontaneous diuresis and increased diuresis with water load comparatively with control animal's group on 13%. It is showed low diuretic action tincture of herb of bidens tripartite in doses 0,1 ml/kg after 2 week administration. For the complete characterization of diuretic function tincture of herb of bidens tripartite is necessary to study its effect on glomerular filtration rate in the future.

So, the tincture of herb of bidens tripartite is promising for further study in order to create a new effective and safe drugs for use in medical practice.

# EXPERIMENTAL INVESTIGATION OF ANTIEPILEPTIC POTENTIAL AND MECHANISMS OF ANTICONVULSANT ACTION OF DRY EXTRACT OF *FUMARIA SCHLEICHERI*

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According to the data of WHO almost 0.68 per cent of world population suffers from epilepsy and this showing is only increasing. It is well known that treating chronic diseases including epilepsy is a rather long-term if not lifelong process. That is why in this case implementing medicinal plants is relevant as they are highly safe even in the situation of a long-term using.

**The aim of the present study** is to study the antiepileptic potential of perspective herbal anticonvulsant drug – dry extract of *Fumaria schleicheri* (FSDE) – taking into consideration its ability to prevent primarily generalized convulsions on the model of seizures induced by the maximal electroshock (MES) and the ability to inhibit epileptogenesis under the conditions of pentylenetetrazole-induced kindling, and also to examine the potential mechanisms of anticonvulsant action of FSDE analyzing the changes of neurotransmitter amino acids content in mice brain.

**Materials and methods.** For the MES test the animals of experimental group received intragastically the water solution of FSDE at the conditionally effective dose of 100 mg/kg during 3 days with the last time 30 minutes before conducting the experiment. The comparison groups received intragastically classic antiepileptic medications – sodium valproate at a dose of 300 mg/kg and carbamazepine at a dose of 40 mg/kg in the same mode. The control group of mice received intragastically the distilled water (0.1 ml for 10 g of body weight). Then the animals through the corneal electrodes were influenced by electric stimuli with the duration of 0.2 sec, frequency 50 Hz and current 50 mA.

For the pentylenetetrazole-induced kindling the animals of experimental group received intragastically water solution of FSDE at the conditionally therapeutic dose of 100 mg/kg in the treating and preventive mode during 27 days once a day 30 min before injecting the convulsant. The comparison group received intragastically a classic anticonvulsant drug of sodium valproate at a dose of 300 mg/kg in the same mode. Mice from control group received intragastically distilled water (0.1 ml for 10 g of body weight). The water solution of pentylenetetrazole (corasole) was injected intraperitoneally at the under-edge dose of 30 mg/kg in the same mode.

The influence of FSDE on the content of inhibitory and excitatory amino acids in the brain of intact mice has been studied. Water solution of FSDE at the conditionally effective anticonvulsive dose of 100 mg/kg and the reference drug of sodium valproate at the dose of 300 mg/kg were administered intragastrically in the preventive regimen for 3 days. Thirty min after the last injection mice were sacrificed, the brain was immediately removed and frozen with liquid nitrogen, powdered and extracted. The content of GABA, glutamate and aspartate was determined in the obtained extracts.

**Results and discussion.** In the MES test FSDE showed clear anticonvulsant properties. FSDE decreased the duration of convulsions in 2.1 times compared with control, and also decreased the time of recovery of the survived animals in 3 times.

On the model of pentylenetetrazole-induced kindling FSDE continued the latent period of the first convulsions occurrence with statistical significance, validly decreased the general amount of days with seizures and the percentage of mice with convulsions in the group from the $23^{rd}$ to the $27^{th}$ day including the last one.

Under administration of FSDE there were significant changes in the quantitative content of all studied amino acids in the mice brain. The GABA level was increased by 2.3 times, and the glutamate and aspartate levels were decreased by 8.3 and 30.8%, respectively. Sodium valproate significantly increased the level of GABA in the brain of mice 3.4 times, as well as a significantly decreased the content of glutamate by 34.6% and increased the level of aspartate by 8.9% compared to control group. Correlation analysis showed that there is a strong negative relationship between GABA and glutamate levels in the brain of mice treated with FSDE and sodium valproate. Between GABA and aspartate levels in the control group and in the background of sodium valproate there was a weak correlation and negative correlation of medium strength in the group of animals treated with FSDE.

**Conclusions.** Under the conditions of the MES test it was established that FSDE showed considerable anticonvulsant properties which were not inferior to the effect of sodium valproate though did not reach the level of carbamazepine. On the model of pentylenetetrazole-induced kindling it was shown that FSDE has an ability to prevent convulsions under the conditions of experimental chronic epileptogenesis. A pronounced influence of FSDE on the balance of neurotransmitter amino acids in the intact mice brain was indicated. Correlation analysis proved a significant intervention of FSDE in processes of the exchange of neurotransmitter amino acids in the CNS.

# EFFECT OF QUINOCARB SUBSTANCE ON BLOOD PRESSURE AND HEART RATE IN RATS AFTER A SINGLE DOSING

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**Introduction (relevance).** Pharmacological correction of arterial hypertension - one of the most common human diseases - is an urgent task of Cardiac Pharmacology. According to the information from the Ministry of Health of Ukraine, in the country is registered more than 9.8 million of hypertensive patients, representing 24% of the adult population and is observed a steady increase of this index. According to research by the Institute of Cardiology named after N.D. Strazhesk about 44% of the adult population has elevated blood pressure. In Ukraine level of cardiovascular mortality, which has always been closely associated with hypertension, is one of the highest in Europe - 2-4 times higher than in developed countries of the world.

**Aim of the research** – impact of Quinocarb substance on blood pressure and heart rate at experimental hypertensive rats after a single dosing.

**Materials and methods.** Research was carried out on female rats. During the experiment, animals were kept in a vivarium at the temperature 20-25 C, humidity less than 50%, natural light mode "day-night", in standard plastic cages, on a standard diet. Comparator drugs were Hydrochlorothiazide granules that contain 25 mg of Hydrochlorothiazide. After administration of a drug blood pressure and heart rate in rats was recorded in 2, 4, 6, 24 and 27 hours. Blood pressure and heart rate in the rat tail artery was recorded with a non-invasive method using blood pressure recorder BP Recorder («Ugo Basile», Italy). Effects of drugs that are compared, were evaluated by the change in blood pressure from baseline, taking it for 100%. Statistical analysis was performed using the spreadsheet package of statistical analysis. Probability of difference between mean values was determined using Student's t test. Validity of the

results was evaluated at the significance level of not less than 95% ($P \leq 0.05$).

**Results and discussion.** Quinocarb influence on blood pressure and heart rate in hypertensive rats was studied experimentally by measuring the baseline blood pressure and heart rate in all studied rats. Baseline blood pressure is on average 180,0 ± 2,90 mm of mercury, which is 38-50% higher than the physiological index of this indicator in normotensive animals (120-130 mm of mercury). Heart rate in all studied rats is on average 495 ± 8,9 beats / min.

Single dosing of Quinocarb to rats in a dose of 10 mg / kg resulted in all animals in the group gradually moderate and quantitatively different blood pressure reduction. Maximum anti-hypertensive effect of the drug reaches after 6 hours of observation, when the average blood pressure in the group decreased in average to 14%. Up to 24 hours of observation anti-hypertensive effect lasted up in 80% of the animals and the average blood pressure of rats in the group remained significantly lower than the initial level on 9.5%. In 27 hours after administration of Quinocarb substance average value of blood pressure returned to baseline. Comparator drug Hydrochlorotiazide caused similar to Quinocarb action in dynamics, but somewhat less pronounced. Over 27 hours of observation Quinocarb and Hydrochlorothiazide had no significant effect on the heart rate, levels of which were prone to minor fluctuations.

**Conclusions.** Thus, Quinocarb in single intragastric administration to experimentally hypertensive rats in a dose of 10 mg / kg provided a significant anti-hypertensive effect, maximum of which evolved after 6 hours, and its severity and duration exceeded anti-hypertensive activity of Hydrochlorotiazide.

# EFFECT OF QUINOCARB SUBSTANCE ON BLOOD PRESSURE AND HEART RATE IN RATS AFTER 7-DAY DOSING

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**Aim of the research** - study of blood pressure in experimentally hypertensive rats and prospects of correction with Quinocarb - new derivant of quinoline-2-carboxylic acid.

**Materials and methods of research.** Was carried out the research at the 7-day dosing of Quinocarba, Hydrochlorothiazide and Enalapril on male rats. During the experiment animals were kept in a vivarium at the temperature 20-25 C, humidity less than 50%, natural light mode "day-night", in standard plastic cages on a standard diet. Comparator drugs were Hydrochlorothiazide granules which contain 5 mg of Enalapril maleate. Blood pressure and heart rate in the rat tail artery was recorded with a non-invasive method using blood pressure recorder BP Recorder («Ugo Basile», Italy). Based on the data in each series of research were formed uniform groups according to the level of blood pressure. On the day of the experiment was recorded baseline blood pressure of the rats, and right after that into their stomach was administered Quinocarb and reference drugs. Effects of drugs that are compared, were evaluated by the change in blood pressure from baseline, taking it to 100%. According to conventional approaches in biology anti-hypertensive response of the drugs was calculated as a whole in each experimental group and separately in the subgroups of rats in which blood pressure under the influence of the studied drugs was reduced by 5% or more from baseline. This allowed to assess more deeply the potential anti-hypertensive properties of Quinocarb. The drugs, that are compared, were administered once a day for 7 days. To the control group of untreated rats was daily administered intragastrically 0.9% saline solution in an equivalent volume (0.2 ml / 200 g). On day 7 after the experiment and in 4 hours after the last administration was recorded heart rate and blood pressure of the rats. Statistical analysis was

performed using the spreadsheet package of statistical analysis. Probability of difference between mean values was determined using Student's t test. Validity of the results was evaluated at the significance level of not less than 95% ($P \leq 0.05$).

**Results and discussion.** Quinocarb during 7-day administration in 66,7% caused a significant decrease in blood pressure. Individual lowering of blood pressure in these animals susceptible to therapy with Quinocarb fluctuated in the range of 12,8-29,3%. Average anti-hypertensive effect of Quinocarb substance was 17.8%, ie. it was higher than after a single dose. Average blood pressure in this period in rats of the given subgroup was significantly lower than baseline. Two rats were resistant to the anti-hypertensive effect of Quinocarb (decrease in blood pressure have been less than 5%). In this connection, when calculating the overall in the group average effect of the studied substance in 4 hours after the last administration was at an average 13% and was expressed in the increasing trend toward a reduction in mean blood pressure from baseline. At the same time, average reduction in blood pressure (ΔAD) in group significantly exceeds ΔAD in the untreated control.

In the group of animals treated with Enalapril, on the 7th day of administration blood pressure of all rats reduced by more than 5%, it means, that all the animals were susceptible to the action of Enalapril. Average anti-hypertensive effect of the drug was 19.8%. Mean blood pressure during this period in the whole group in Enalapril was significantly lower as for relative to the initial control and as for the Quinocarb, Hydrochlorothiazide and untreated control groups, but not statistically different from blood pressure in the subgroup of rats sensitive to therapy with Quinocarb substance.

7-day administration of Quinocarb and reference Hydrochlorothiazide and Enalapril drugs had no effect on heart rate.

**Conclusions.** In general, drugs, which are compared in 7-day dosing in sensitive experimentally hypertensive rats can be arranged in the following sequence by reducing the magnitude of the anti-hypertensive effect: Enalapril (19,8%) ≥ Quinocarb (17,8%) ≥ Hydrochlorothiazide (14,1% ).

# THE RESEARCH OF INFLUENCE 1-(4-CHLORPHENYL)-N,N-DEMETHYLE-ALPHA-(2-METHYLEPROPYLE) CYCLOBUTANEMETHANEAMINE (SIBUTRAMINE) ON THE EXPERIMENTAL INSULIN-RESISTANCE COURSE AND ENDOTHELIAL DYSFUNCTION DEVELOPMENT IN RATS

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**Introduction.** Insulin resistance (IR) – is a pathological syndrome, which is accompanied by a decrease in the sensitivity of cells to insulin. It is associated with the development of a number of diseases: type 2 diabetes, obesity, metabolic syndrome, atherosclerosis, cardiovascular and some others. These diseases are widespread in the population and are characterized by high mortality rates. This point explains the urgency of finding ways of pharmacological correction of the disease developing on the background of IR. One of the promising methods of the pharmacotherapy is the use of 1-(4-Chlorphenyl)-N,N-demethyle-alpha-(2-methylepropyle) cyclobutanemethaneamine (Sibutramine) – anorectics means of central action, pharmacodynamics of which is due to the inhibition of the reuptake of serotonin and norepinephrine (normalization of eating behavior), as well as activating an effect on β3-adrenergic receptors of brown adipose tissue (the increase of thermogenesis). In a number of studies we have proved the marked therapeutic efficacy of the substance in IR's presence, but there has been a significant increase in the number of cardiovascular events (heart attacks and strokes). One possible reason for the development of cardiovascular disease is the development of endothelial dysfunction (ED).

**The aim** of this work has been to study the effect of sibutramine on individual rates of lipid and carbohydrate metabolism, the state of NO-synthase system during the experimental IR in rats.

**Materials and methods**. The researches has been performed on Wistar male rats of the line. The IR has been simulated by intraperitoneal injection of low doses of dexamethasone (Severino C. and co-author, 2002). The sibutramine that has been injected intraperitoneally at an effective therapeutic dose (assuming a ratio of specific resistance). The effect of the drug has been evaluated by the glucose content, immunoreactive insulin (IRI), triacylglycerol (TAG), free fatty acids (FFA),

cholesterol (CH), nitric oxide (NO), nitrate and nitrite (NO2 + NO3), arginine, citrulline.

**Results and discussion.** Intraperitoneal administration of dexamethasone has been accompanied by the IR syndrome development, which has been confirmed by a significant in glucose levels increase by 55.4%, IRI - by 44.12%, TAG - by 70.14%, FFA - by 91.11%, CH – by 25% compared to the intact animals. There has been the reduction of the blocking action of insulin on lipolysis, which has been accompanied by an increase in the content of free fatty acids, which has led to an increase in the concentration of TAG, cholesterol and aggravate IR. The sibutramine has generally normalized the studied parameters due to the correction of obesity as a trigger factor of IR. Moreover, the drug mediates the adiponectin level increase, which increases the sensitivity of tissues to insulin. The development of hyperglycemia and hyperinsulinemia has been associated with some significant pathological changes of the markers of NO-synthase system: NO content has increased by 1.22 times, $NO_2$ + $NO_3^-$ by 1.2 times, citrulline – by 1.26 times, the concentration of arginine has decreased by 1.48 times compared with the indicators of the intact rats. Such dynamics of parameters is characterized to the state of the ED. Insulin is a powerful inducer of NO-synthase (NOS) of endothelial cells that stimulates arginine entrering to the cells, thereby reducing its content in the blood. This resulted in increased formation of NO and the second reaction product – citrulline. Hyperglycemia and also increase of the content of NO, by activating the expression of iNOS and generation of reactive oxygen species. Hyperglycemia and hyperinsulinemia cause the formation of peroxynitrite ($ONOO^-$), which is accompanied by the development and progression of ED. When administered with sibutramine we have observed similar, though less pronounced dynamics of NO-synthase marker system. This is probably due to the formation of active metabolites of the drug during its biotransformation, which has a negative impact on these indicators.

**Conclusions.** The administration of low doses of dexamethasone is the cause of the IR syndrome, which entails some pathological changes in lipid and carbohydrate metabolism types, as well as in the NO-synthase system. The administration of the sibutramine has led to the normalization of rates accompanying the formation of IR, however, the lack of positive dynamics with respect to the changes in the NO-synthase system can be considered as one of the mechanisms of cardiovascular complications during the use of the drug.

# PHARMACOLOGICAL STUDY OF THE USE OF NANOPARTICLES OF CERIUM DIOXIDE IN THE DEVELOPMENT OF NEW GENERATION EFFECTIVE AND SAFE PHOTOPROTECTORS

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The effect of excessive solar radiation on the skin can be harmful and cause melanoma. Due to the bad environment, ozone depletion and increased solar activity, this problem has become very serious. By results of the researches which have been carried out by Institute of dermatology and cosmetology, every summer during holiday as a result of solar burns 10 thousand Ukrainians get sick of a cancer of skin. 95% of the patients in Ukraine with a melanoma perish that is connected with late diagnostics and untimely prevention. Protection of skin against sunshine by means of UV-filters is the most effective prophylactic of the photodermatosis, aging and a cancer of skin. For today as a part of modern photoprotectors are used physical light filters on the basis of oxide of zinc and dioxide of the titan which are effective, but have a high toxicity. Dioxide of cerium is promising new UV-filter that can be included in the sunscreens compositions. According to the literature it has low toxicity and is capable of screening the solar rays.

We have made detailed pharmacological studying of cream (developed on department of pharmacy drug technology named by D.P. Salo) contains 5% of nanoparticles of dioxide of cerium on model of a photodynamic trauma on guinea pigs. This cream had already proved us its efficiency early on the same model in normal conditions and exceed efficiency of existing photoprotectors presented in the market of Ukraine (Biocon) for 15% that is connected with a high shielding rate.

Experiment is made on 40 same-gender guinea pigs divided into 4 groups on 10 animals. We did radiation by an ultra-violet lamp at distance of 10cm within 15 minutes on shaven sites of skin of $3cm^2$ in size on three on each animal. Control of results carried out by Suvorov's calorimetric ruler, level of the histamine in blood, and quantity of leukocytes. Also we measured markers of lipid peroxidation in tissues (reduced glutathione, TBA-reactants, diene conjugates, catalase). In groups where we had protected skin by the way of studied cream the indicators were at the level of intact animals while at animals from groups which we radiated without photoprotector it was observed expressed erythema, the raised level of a histamine and quantity of leukocytes, the high level of TBA-reactants and diene conjugates.

As a conclusion this study showed that nanoparticles of cerium dioxide is a promising substance for further research and development factory dosage form of powerful and safe photoprotectors.

# THE STUDY OF PHARMACOLOGICAL ACTION OF BRIQUETTES WITH PULP OF PERSICA VULGARIS IN EXPERIMENTAL METABOLIC SYNDROME OF GUINEA PIG

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The generality of pathogenesis of cardiovascular pathologies, as well as their relationship to such metabolic disorders as obesity, insulin resistance and atherogenic dyslipidemia, suggest the totality of these metabolic and systemic changes, as an independent nosological unit – a metabolic syndrome. We should also note the role of cardiovascular disease as a major segment in the structure of overall morbidity and the main cause of mortality in young working population. A number of medical and social problems explain this unfavorable epidemiological situation: sedentary lifestyle, hyper-caloric diet with a number of high sugar and triacylglyceride foods, chronic stress, bad habits (smoking, etc.). In view of the said above, the search for new methods for correction of metabolic abnormalities, forming the basis of this condition pathogenesis, becomes relevant.

The aim of our research is to study the effect of functional food - briquettes with pulp of Persica vulgaris, on dynamics of protein, carbohydrate and lipid oxidative metabolism indices, on a background of experimental metabolic syndrome. Pathology in experimental animals (guinea pigs) has been modeled with daily injections of dexamethasone at hyper-caloric diet. It has resulted in numerous disorders of carbohydrate and lipid metabolism. The identified changes showed themselves in insulin resistance and hyperinsulinemia, increased blood serum glucose level, hypertriacylgliceridemia, increased level of blood serum free fatty acids, and significant increase in body weight in experimental animals.

We have discovered, that oral administration of functional food - briquettes with pulp of Persica vulgaris in experimental animals, has resulted in significant regression of negative metabolic changes. Particularly, we have noted significant reduction in free fatty acids and triacylglycerols level, as well as almost complete normalization of blood serum glucose level in experimental animals. There has also been a decrease of blood insulin level and a significant improvement of oxidative balance in experimental animals. As of the effect on multiple indicators, the functional food - briquettes with pulp of Persica vulgaris, under study, is equal to "Glibomet" reference drug.

**Conclusions**. The obtained results, indicating the presence of valuable metabolic and therapeutic effects in the functional food under research, suggest the feasibility of further deeper studies of pharmacological properties of briquettes with pulp of Persica vulgaris.

# INFLUENCE OF PEACH LEAVES EXTRACT ON THE CYTOKINE PROFILE IN EXPERIMENTS IN VITRO

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Cytokines are a group of polypeptide regulatory molecules the immune system (interleukins, interferons, growth factors) performing the functions of mediators of intercellular interactions in the regulation of the modulating effects on the immune system. The study of the levels of cytokines allows to obtain information about the functional activity of various types of immune competent cells. Moreover, the determination of cytokine levels are widely used in the study of new modulators of the immune system to participate in the process of implementing the mechanisms of natural and specific immunity. According to the literature the leaves extract of the peach ordinary has anti-inflammatory and immuno-biological activity.

Purpose. Study the effect of leaves extract of the peach ordinary to the level of pro-inflammatory and anti-inflammatory cytokines in experiments in vitro.

Materials and methods. Pharyngeal tonsil cells of children received after adenotomy prepared as a suspension by using the medium RPMI 1640 containing additives. For cell culture added solution of the leaves extract of the peach ordinary in dose of 10 mcg and 100 mcg per sample. Solution of the leaves extract of the peach ordinary passed through a filter of type Milipore. In control used similar concentrations of glucose. Through day of cultivation at $37^0$ C samples centrifuged and in the part above the sediment by enzyme immunoassay method using the enzyme immunoassay analyzer Lab Line (Austria) determined the concentration of interleukin-1beta (IL-1β), interferon gamma (IFN-γ), interleukin-4 (IL-4), interleukin-10 (IL-10).

Results. Research has shown that the leaves extract of the peach ordinary in dose of 10 mcg and 100 mcg reduced the level of pro-inflammatory cytokine IL-1β in cell culture of a pharyngeal tonsil in experiments in vitro and no significant effect on the level of IFN-γ and anti-inflammatory cytokines IL-4 and IL-10.

Known, that pro-inflammatory cytokines increase process of exudation and promotes to the high activity of inflammatory reaction, needed for formation of the adequate inflammatory response immediately after exposure to damaging factor. Later, however, the production of these cytokines should be reduced. Overexpression of pro-inflammatory cytokines can lead to the development excessive inflammatory reaction. The use of the leaves extract of the peach ordinary may have a positive effect in case of chronic inflammation. The positive side is the fact that the leaves extract of the peach ordinary does not change the levels of IL-10, which is cytokine IL-1β antagonist and IL-4, under the influence of which the immune response is shifts toward the formation of antibodies.

Conclusions. Leaves extract of the peach ordinary in vitro system is able to reduce the level of pro-inflammatory cytokine IL-1β. Immunomodulatory effect of leaves extract of the peach ordinary can be used in cases where the inflammatory response to the impact of the damaging factor is protracted.

# HEPATOPROTECTIVE EFFECT ON SPIROCYCLIC OXINDOLIC DERIVATE IN THE CONDITIONS OF ACUTE LIVER'S ISCHEMIA

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Hypoxic hepatitis, also known as ischaemic hepatitis or shock liver, is an acute liver injury caused by hepatic hypoxia. Cardiac failure, respiratory failure and septic shock are the main underlying conditions. In each of these conditions, several haemodynamic mechanisms lead to hepatic hypoxia. A shock state is observed in only 50% of cases. Current trends in modern medicine and pharmacy is to create, study and implementation in medical practice drugs with multiple organ action, namely anti-hypoxic, hepatoprotective and ability to restore energy metabolism in the damaged liver cells in the treatment and prevention of ischemic and reperfusion injury of the liver tissue and its microvasculature. Promising compound in this aspect can be considered a new substance - 4,3'-spiro[(2-amino-3-nitrile-4,5-dihydropyrano[3,2-c]chromen-5-one)-5-methyl-2'-oxindole], connection 77, by the structure of the nucleus of the molecule (4H-pyrano [3,2-c] chromen) is a structural analogue of melatonin. Influence was studied the spirocyclic oxindolic derivate in a dose 5 mg⁄kg and preparations of comparison vita-melatonin (5 mg⁄kg) and thiotriazolin (48 mg⁄kg) on lethality on animals, activity of cytolysis, free-radical oxidization and functional activity of the liver in the conditions of acute experimental ischemia is studied. At ischemia of the liver without pharmacological protection of animals groups control pathology there was a high mortality rate (64,3%), which was significantly indicating the severity of the condition and figure significantly higher than in the group of control rats (0%, $p<0,001$). Therapeutic and prophylactic administration of the compound 77 and comparator drugs significantly reduced the percentage of mortality in all three experimental groups, but it should be noted that the protective effect of compound 77 was the most pronounced and has reduced the mortality rate to 0%, what is significantly exceeded this figure vita-melatonin (40 %, $p<0,001$) and hepatoprotector thiotriazoline (25%, $p<0,01$). Compound 77 showed marked membrane protective effect of significantly reducing the cytolytic activity of enzymes in the blood serum. The expressed antioxidant, anticytolytic action spirocyclic oxindolic derivate in dose 5 mg/kg is established. It is found that the total hepatoprotective effect of new substance exceeds activity of preparations of comparison of vita-melatonin and thiotriazolin. It is proved that the a new substance to had significant hepatoprotective activity due to multicomponent mechanism of action, namely, antihypoxic, antioxidant, cytoprotective properties.

# THE HISTORY OF CARBOXYTHERAPY

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Carboxytherapy (pneumatic puncture or gas injection) - a modern method of treatment and rejuvenation via subcutaneous injection of carbon dioxide ($CO_2$).

Mentions of carbon dioxide therapy are dated the 1st century before our era. The ancient Romans used for medicinal purposes hot springs with $CO_2$. Hippocrates told patients to drink and bathe in water, saturated $CO_2$. In the 17-18 centuries the first time Robert Boyle and Antoine Lavoisier described antibacterial properties of carbon dioxide and in 1777 performed the treatment of chronic ulcers.

In 1932, the technique was first described the use of $CO_2$ in the Medical Spa Roy (Medical SPA of Royat, France). In 1953, the French physician Jean-Baptiste Romuef published his two decades of research in the field of carbon dioxide injection.

Subcutaneous injection of $CO_2$ used since 1970 in the Czech spas (Karlovy Vary).

In 1990 began to study the effects of carbon dioxide transdermal therapy for localized fat deposits (cellulite) in the SPA Institute Rabi (SPA institute of Rabbi, Italy). The Italian company Carbossiterapia Italiana in 1993, has developed a method of introducing $CO_2$ injection with a medical device, and there was the name of the therapeutic method - Carboxytherapy.

In 1994, the Institute of cardio-vascular pathology at the Medical Spa Roy (Medical SPA of Royat), France, began to apply the transdermal therapy of vascular insufficiency carbon dioxide. French Ministry of Health emphasized the importance of carbon dioxide therapy with vascular insufficiency, used by itself or in combination with other methods. The first clinical study method carboxytherapy process of lipolysis and activation of microcirculation were performed at the Institute of Plastic Surgery, University of Siena (Italy). In 2006 was introduced a university course studying carboxytherapy and in 2012 Europe was declared the Year of Carboxytherapy.

Due to the high security and efficiency of the method used during the 70 years of general medical practice and more than 30 years in aesthetic medicine, is absolutely safe and suitable for people of different age groups.

## SECTION № 8

# MODERN ASPECTS OF PHARMACEUTICAL MICROBIOLOGY AND IMMUNOLOGY

# ANTIMICROBIAL ACTIVITY OF ONION AND GARLIC PHYTONCIDES

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Onion and garlic phytoncides possess a high bactericidal activity. They are known to kill almost all kinds of pathogenic microbes. They have fatal effect on many pathogenic bacteria, including agents of dysentery, diphtheria, tuberculosis, Staphylococcus aureus, and Trichomonas. By the strength of action only highly effective antibiotics can be compared with them.

The chemical composition of garlic and onion phytoncids is unknown. Aliin is a substance extracted from garlic and it inhibits bacteria in a dilution of 1:250000. Garlic and onion juices are non-volatile at ambient temperature, differ in composition from the volatile phytoncids of these same plants.

To determine antimicrobial action of plant phytoncids, we used bulb onion, white onion, Crimea onion and garlic. These samples were peeled, washed with soap in running warm water and wiped with 70% alcohol to remove dirt and foreign microorganisms. Then a sterile knife was used to remove the top layers, to cut and the core was triturated in sterile mortar to obtain juice.

Antimicrobial activity was studied using agar diffusion method with subsequent determination of growth inhibition zones and the serial dilution method. Museum culture of E.coli and S.aureus were used as test strains. Initially the bactericidal action of phytoncids of different species of onion and garlic were studied using agar diffusion method. However, in the experimental and control inoculations identical result was obtained: no growth inhibition zone.

Then antimicrobial effect of herbal phytoncids was investigated using the serial dilution method. Pieces of plant tissues were placed in tubes with a liquid medium to prevent violation of the phytoncids. But in this case, the results were negative: antimicrobial effect was not identified.

Conclusions. There are no doubts in high bactericidal activity of phytoncids, but it can’t be confirmed using general methods for of antimicrobial activity of antibiotics detection. Onion and garlic tissues expend almost all of their volatile phytoncides in the first minutes after grinding. To study their bactericidal activity special methods are required. An alternative option to identify the bactericidal action of phytoncids is to determine the number of microorganisms in the air.

Scientists from different countries have carried out many experiments to study the chemical nature and mechanisms of action of phytoncids’ antimicrobial activity, and yet it is necessary to assume that research in this area remain relevant and promising.

# ANTIMICROBIAL ACTIVITY OF B-LACTAM–BILE ACID CONJUGATES

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β-Lactams are a large class of antibiotics characterized by the presence of an azetidine-2-one ring, which is the core of biological activity. The azetidine-2-one (β - lactam) ring system is a common structural feature of a number of broad spectrum β - lactam antibiotics, like penicillins, cephalosporins, carbapenems, nocardicins and monobactams, which have been widely used as chemotherapeutic agents for treating microbial diseases. It also shows many other interesting biological properties, such as cholesterol absorption inhibitors, human cytomegalovirus protease inhibitors, thrombin inhibitors, antihyperglycemic, anti-tumour, anti-HIV, antiinflammatory, analgesic activities9 and serine-dependent enzyme inhibitors. However, microorganisms have built up resistance against the most traditional b-lactam antibiotics due to the wide-spread overuse of antibiotics. Therefore, the phenomenon of bacterial resistance forces the continuous modification of structure of known active compounds and the development of new ones. Azoles are the largest class of antifungal agents in clinical use. 1,2,3-Triazole moieties are attractive connecting units, as they are stable to metabolic degradation and capable of hydrogen bonding, which can be favorable in binding of biomolecular targets and solubility.

Target molecules were synthesized using 1,3-dipolar cycloaddition reaction of β-lactams containing azide and bile acids containing terminal alkyne, in the presence of Cu(I) catalyst (click chemistry). The cycloaddition reaction of propargyl esters and with azido β-lactams in the presence of Cu(I) catalyst (click chemistry) under microwave irradiation furnished diastereomeric mixture of novel conjugates in excellent yields (85-97%). All the newly synthesized azido β-lactams, steroidalalkynes and 1,2,3-triazole-linked β-lactam–bile acid conjugates were tested in vitro for antifungal and antibacterial activity.

The antifungal activity was tested using isolate fungal strains *Candida albicans*, the antibacterial activity was evaluated against *Escheirchia coli* and *Staphylococcus aureus*. The MIC and IC50 values were determined using standard broth microdilution technique described by NCCLS. In comparison with the antimicrobial activity, amphotericin B and fluconazole were used as the reference antifungal agents, while tetracycline and ampicillin were used as the reference antibacterial agents. From the biological data, it was observed that azido β-lactams and steroidal alkynes were almost inactive against all the tested strains. The MIC value for all these compounds was >128 mcg/mL. The activity of compounds conjugates was higher or comparable to that of fluconazole against *C.albicans* with MIC value of 16–32 mcg/ml. Furthermore, those compounds showed good antibacterial activity against *E. coli* having MIC value of 16 mcg/ml. The compounds derived from cholic acid having 7-hydroxy group showed moderate antibacterial activity against *S. aureus*. However, the compounds derived from deoxycholic acid in the absence of 7-hydroxy were less active against *S. aureus* with MIC value of >128 mcg/ml. From the overall activity results, it was observed that the ester or amide linkage and chloro substituent on phenyl ring of β-lactam part did not affect the activity of the compounds.

# PROSPECTS OF CREATING COMPLEX ANTIMICROBIAL DRUGS FOR EXTERNAL USE

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Due to acquired tolerance of microorganisms to anti-viral, anti-microbial, and anti-fungal substances, search, development, and introduction of new drugs remains relevant today.

The purpose of the work is to investigate antimicrobial activity of some inorganic, natural, and synthetic materials, as well as their combinations.

Materials and methods. For study purposes, the following materials have been selected: copper sulfate, zinc sulfate, boric acid, aluminum chloride, ammonium aluminum alum, lead acetate, iron chloride III, alizarin, and quercetin.

Antimicrobial activity of drugs has been determined by the diffusion method of "wells" with the determination of the diameter of microorganism growth delay zone. In order to evaluate antimicrobial activity of the formulations, the following six test strains of microorganisms have been used:

*Staphylococcus aureus ATCC 25923*, *Escherichia coli ATCC 25922*, *Pseudomonas aeruginosa ATCC 27853*, *Proteus vulgaris ATCC 4636*, *Bacillus subtilis ATCC 6633*, and *Candida albicans ATCC 885/653.*

Results and discussion. Below there are the comparison results of antimicrobial activity of substances in order of descending.

Aqueous solutions of copper sulfate and zinc sulfate demonstrate significant antimicrobial activity. Ethanol solutions of boric acid, calcium chloride+Alizarin, Alizarin+aluminum chloride, quercetin, quercetin+aluminum chloride, and alizarin show medium-range activity. And aqueous solutions of iron chloride III, ammonium aluminum alum, lead acetate, and aluminum have weak activity.

Conclusions. The most promising as antimicrobial agents for external use are copper and zinc cations, as well as soluble complexes of aluminum or boric acid with quercetin. However, this requires careful toxicological and pharmacological studies.

# STUDY OF MICROBIOLOGICAL STATE OF THE TAP WATER IN KHARKIV

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Water is a unique and irreplaceable source of human existence, and all water bodies should be safe in epidemic relation. Sanitary and microbiological analysis of pathogenic microorganisms present in water is performed on epidemiological indications. Such pathogenic and opportunistic microorganism as Salmonella, Shigella, Pseudomonas (Pseudomonas aeruginosa), Staphylococcus aureus, enteroviruses, fecal streptococci (enterococci), spores of sulphite-reducing clostridia, Proteus, thermophilic microorganisms, coliphages (viruses, bacteria) and certain protozoa should be detected in water bodies depending on their type according to the regulations. Identification of sanitary indicator is based on detection and quantification of sanitary indicator microorganisms (SIM) and certain pathogenic microorganisms in the probe of the tested water source.

Qualitative sanitary indicators (SI) answer the question, if target microorganisms are present in the fixed volume of water probe or not. These SI are used in detection of pathogenic, potentially pathogenic, and certain opportunistic microorganisms, such as Salmonella, Shigella, Listeria, Pseudomonas aeruginosa, and others. Their presence in fixed volume of drinking water is unacceptable.

Quantification of SI gives idea about the extent of water body contamination or disinfection procedure efficiency. Quantitative SI is a content of target SIM in fixed volume of the probe. The number of SIM is expressed as SIM index: number of CFU (colonies forming units) of microorganism per unit of the fixed volume (CFU/mL, CFU/20 mL, CFU/100 mL).

We've studied 5 tap water probes taken in different areas of Kharkiv. For quantitative SI identification we used method of deep inoculation of water probes in Petri dishes with MPA (incubation time – 24 h., at 37°C): probe No 1 - 178 CFU/mL; probe No 2 - 144 CFU/mL; probe No 3 - 149 CFU/mL; probe No 4 - 279 CFU/mL; probe No 5 - 73 CFU/mL. All the harvested colonies were described; detected microflora was studied bacterioscopicaly (using Gram-staining) in order to obtain general qualitative identification. According to the study results, all the tested probes contained high number of opportunistic microflora, except for the probe No 5. Coliform bacteria were detected in probes No 2 and No 4, which indicates poor purification of water, secondary contamination or presence of excess organic pollution. Thus, probes No 1, 2, 3 and 4 do not conform to corresponding sanitary and hygienic standards.

# EFFICIENCY OF THE HOUSEHOLD ANTISEPTICS

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Skin of human's hand is colonized by various microorganisms. Hand sanitizers are used in order to follow basic rules of hygiene and prevent transmission of pathogenic microorganisms in conditions where the sink and soap are not available. They are recommended for use in living conditions, particularly in areas with large concentration of people. Household hand sanitizers are available in small bottles, plastic bottles with dispenser, in the form of liquid solutions, gels, sprays or foams to be used in the workplace, office in public places. Usually, household hand sanitizers contain skin softening excipients and fragrances.

The aim of this study was to determine the efficiency of the household antiseptic Arnica, antiseptics Horosten and Neosteril, liquid soap and 70° alcohol. The study was conducted using the method of washings from hands' skin before and after treatment with these substances and determining the total number of microorganisms. Washings were made with sterile cotton swab dipped in 1% peptone water, poured by 5 ml into tubes. Then tampons were shaken, squeezed and transferred into tubes with 6.5% saline broth, incubated in temperature-regulated chamber at 37°C for 24 hours and inoculated on solid nutritional media.

The study results identified the following. The number of microorganisms on the skin before treatment with antiseptic or washing the glass was on average $10^5$. After application of alcohol-based household antiseptic "Arnika" the number of microorganisms decreased by 2 orders from $10^6$ to $10^4$. Application of 70° ethanol, combined preparation Horosten, which contains decamethoxin and alcohol, and Neosteri, which is a mixture of alcohols, reduced microbial contamination of hands by 4 orders from $10^6$-$10^7$ to $10^2$-$10^3$. The same result was obtained after washing hands with soap and water: the number of microorganisms decreased from $10^6$ to $10^2$.

Conclusions. The most reliable way to remove microorganisms from the skin is hand washing with soap and water, and further processing with antiseptics. Alcohol-based antiseptic are considered to be more effective means for microbial elimination than soap. They destroy many different species of bacteria, fungi, and are characterized by a high virucidal activity. However, alcohol-based hand antiseptics may be ineffective in low amounts or concentrations, because of the rapid evaporation it doesn't comply with required duration for destruction of microbial cells. Thus, in the absence of access to water and soap, use the hand sanitizer containing at least 60% alcohol.

# CHANGES IN SENSITIVITY TO METHICILLIN AT MRSA UNDER THE INFLUENCE OF LACTOBACILLI EXOMETABOLITES

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Modern industrial technologies of cultivation of agricultural animals, birds, fish suggest widespread using of antibiotics, which are not only used for the treatment and prevention of various diseases of bacterial etiology, but also as feed additives, stimulating the growth and development of young animals, increase safety and productivity of livestock. However, antibiotics are used for these purposes accumulate in excessive amounts in foods - meat, milk, eggs, posing a threat to human health, causing dysbiosis, allergies and reducing immunity. Moreover, antibiotic therapy which is used for decades to treat bacterial infections has led to the emergence and spread of antibiotic-resistant strains. Therefore, in the developed countries more and more attention is paid to the development and implementation of alternative methods of prevention and treatment of bacterial infections.

One of the alternative replacement ways are pro-, pre- and synbiotics. They have a wide spectrum of antagonistic activity and help restore normal flora and colonization resistance of the mucous membranes.

The aim of the work was to study the effect of lactobacilli exometabolites for resistance to oxacillin at methicillin-resistant strains of Staphylococcus aureus (MRSA).

Strains of MRSA were isolated from healthy bacteria carriers among medical staff, co-cultured with lactobacillus exometabolites. Sensitivity to methicillin was determined by disco-diffusion method.

It is established that after 3 passages in medium with exometabolites zone of growth inhibition around the disc with an antibiotic in 46.3% of the strains varied from 0 mm to 7,3 ± 2,6 mm. After 5 passages in medium with lactobacilli exometabolites 62,8% MRSA become sensitive to methicillin (zone stunting ≥13 mm) and 8.6% of the strains were killed. After 10 passages, the number of dead strains was 21.4% and the number of strains have become sensitive to methicillin - 78.3%. Only one strain does not change its sensitivity.

Thus, the antimicrobial substance secreted by the lactobacilli could be used as alternative means for sanitation bacillicarriers aureus.

# TRICHOMONIASIS: ACTUAL QUESTION OF TODAY

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According to the WHO annually 170-180 million of people in the world suffer from trichomoniasis, which far exceeds the rate of gonorrhea and chlamydiasis. In the US 10 million of people are infected by trichomoniasis, while in Europe there are 11 million of infected. Over 150 million of people are infected in developing countries. These indices can be much higher (according to other sources there are 270 million of people infected in the world). Actually, it is the only one sexually-transmitted disease, which is not subject to registration and reporting in majority of countries.

The prevalence of the disease depends on socio-economic conditions of the population and the availability of timely high-quality care, good hygiene, education level of people. For example, in the US black-skinned residents are more often infected with trichomoniasis. All over the world the number of teenagers with trichomoniasis increases, because many of them are sexually active. Trichomonas infection occurs in 29.84% of women (depending on the region), and half of these women have no complaints and symptoms of the disease. Women who have casual sex suffer from trichomoniasis 3.5 times more often than women, having one sexual partner. As for trichomoniasis in men, there a lot of gaps in the medical literature: Trichomonas infection in men is almost unexplored.

Trichomoniasis (trichomonosis) is called by protozoa of the genus *Trichomonas*. Normally, in the oral cavity lives T. tenax, in the colon - T. hominis. Vaginal parasite Trichomonas vaginalis is pathogenic to humans and cause trichomoniasis, which is characterized by a complete injury of the genitourinary system.

Trichomonas vaginalis have a pear-shaped body of 14-30 microns in length, at the front end it has 4 flagellum, undulating membrane to the middle of the body, axostyle through the whole body. After attachment to epithelial cells Trichomonas transform to amoeboid shape. Trichomonas are facultative anaerobes, obligate parasites that have lost the ability to synthesize many macromolecules. These components they obtaine from vaginal and other secretions, during phagocytosis of bacterial cells of the normal flora of the urogenital tract. For cultivation of Trichomonas on artificial media such additives as blood serum lipids containing

essential fatty acids, amino acids, vitamins and minerals are necessarily used. Optimal conditions for growth are 35-37°C and pH-5.5-6.3. T. vaginalis are able to phagocytose red blood cells, bacteria, which are usually digested, but it incomplete phagocytosis is possible and long-term persistence of bacteria inside the Trichomonas, which has captured bacteria (phagosome). Factors of pathogenicity of Trichomonas include adhesins, hemolysins, and proteases. T. vaginalis infects only the squamous epithelium of the urogenital tract. Trichomonas are bladder and tissue parasites, because may inhabit superficial layers of the epithelium, imitating its relief, and penetrate deep enough into the tissue, thanks to the presence of proteases.

Urogenital Trichomonas outside the human body are unstable. Obligatory condition for their viability is the presence of moisture; upon drying they die quickly. These protozoa are highly susceptible to many other environmental factors: temperature increase to 40°C, direct sunlight, osmotic pressure violations, influence of antiseptics and etc. These parasites are more resistant to lower temperatures. Optimal temperature for their growth is 36.5 – 37°C. At 60°C Trichomonas die immediately; at 55°C they die in 30 seconds; at 50°C in 2-4 min; at 45°C in 10-15 min. At a temperature of 5°C they remain viable for 1.5 hours; at 10°C up to 20-45 minutes.

Urogenital Trichomonas live in the human saliva up to 48 hours, in the urine up to 24 hours. In the vaginal secretions they remain for 1-2 days, if the pH is not less than 4.8. Optimal environment for them is pH 5.2-6.2, but they can remain viable in a neutral, acidic and alkaline environment. In Ringer-Locke solution at ambient temperature they retain their mobility and vitality for 96 hours. The latter circumstance is very important in the diagnosis of trichomoniasis, as it helps to avoid using temperature-regulated chamber in the study of these protozoa in native preparation. In fresh water of rivers, lakes and ponds the viability of Trichomonas is maintained for 15-60 minutes. Lifetime of these protozoa in water depend on its osmolality. In the tap water they live for 15-20 min; in 0.1% sodium chloride solution for 1-4 hours; in 0.2% solution for 2.6 hours; in 2% solution for 1 h. In distilled water parasites die almost immediately. In natural water bodies, where there are many swimmers, these protozoa are not found. The disease is transmitted sexually, from mother to fetus during passage through the birth canal. Rarely, contact-household transmission is possible through towels, sponges, contaminated surface. On average, 25-67% of women and men, who are sexually active, are infected with Trichomonas. Both asymptomatic carriage and clinically apparent disease course are possible.

Carriers of T. vaginalis pose a greater epidemiological danger. The disease is ubiquitous and occurs with equal frequency in men and women. In girls trichomonas invasion is extremely rare. Incubation period is usually from 4 to 28 days in approximately 50% of infected individuals, but can be reduced to 1-3 days.
Realization of T. vaginalis pathogenic and virulent properties depends on the state of immune, nervous and endocrine systems of the infected person.

In the clinical practice urogenital trichomoniasis is mainly a mixed protozoal-bacterial infectious process in which initial etiological role is played by T. vaginalis. Primarily, this due to incomplete phagocytosis inside trichomonads: capture and reservation a of great variety of pathogenic and opportunistic microorganisms, leading to their persistence in the cells of Trichomonas. Moreover, since Trichomonas are able to adhere to epithelial cells, and in the area of attachment to the epithelial cells they cause degradation of cellular plasma membranes, which leads to significant loosen of tissue, they facilitate penetration of various microorganisms of accompanying microflora into intercellular spaces, complicating the inflammatory process. Urogenital trichomoniasis as monoinfection occurs only in 10.5% of patients with trichomoniasis, and its mixed forms in association with other infections, are observed in 89.5% of patients: in association with mycoplasmas (47.3%), gonococci (29.1%), gardnerellami (31.4%), ureaplasma (20.9%), chlamydia (18.2%) and fungi (15.7%). It is proven that in trichomoniasis there is a pronounced contamination of genital tract with various nonspecific opportunistic microflora: streptococci and enterococci - 47.2%, fungi of the genus Candida – 30.1%, and staphylococci.

Trichomonad’s ability to phagocytosis of gonococci, chlamydia, mycoplasma, fungi and viruses contributes to quantifiable reduction of the latter in the genital tract, which may lead to a decrease in antigenic and toxigenic effect on the organism, suppression of phagocytic reaction and body's immune response to the infectious factor. In the vagina content sample in female with urogenital trichomoniasis lactobacilli are usually undetectable (normally, present in an amount of more than 107 cells/mL, and 90% of all bacteria inhabiting the vagina). This is due to the fact that Trichomonas are able to utilize lactobacilli, seriously disrupting vaginal microbiocenosis.

Currently, the peculiarity of trichomoniasis is that it occurs three times more often than syphilis, chlamydia and HIV, and pronounced clinical manifestations of the disease are becoming increasingly rare, dominated by sluggish, low-symptom forms, which complicates timely diagnosis and treatment of this insidious disease.

# ARBOVIRUS INFECTION IN UKRAINE

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The problem of arbovirus infections is currently relevant to the health of many countries, including Ukraine. These diseases account for each year hundreds of thousands of uncontrolled system health cases that they are not etiologically diagnosed and treated. Along with other infections important for Ukraine (tuberculosis, HIV, hepatitis, leptospirosis, and others.) Arboviral diseases are constantly mentioned in official documents as a disease, which epidemic supervision is a priority for health authorities to protect the health of the population. Arboviruses represent a special group of viruses, including several families: Togaviridae, Flaviviridae, Bunyaviridae, Arenaviridae, Rhabdoviridae and Reoviridae. Viruses multiply in the body of arthropods (mosquitoes, ticks, etc.) and transmitted by the bite of a vertebrate. Arboviruses can cause pathological processes in the body, which manifest themselves in the form of fever with pain in the muscles and joints or severe lesions of the meninges and the brain - meningoencephalitis, or in the form of hemorrhagic fever with systemic vascular disease. The natural reservoir of most arboviruses are small rodents, wild animals and birds, ticks and mosquitoes. A man is the intermediate host of the virus, and only for a short period of time enters the chain of natural circulation of the virus. Among arbovirus infections in Ukraine there are more frequent and severe in tick-borne encephalitis and West Nile fever. Quite often there are hemorrhagic fever with renal syndrome and Crimean-Congo haemorrhagic fever. Currently endemic tick-borne encephalitis is founded in 18 administrative regions. The endemic foci of the virus are detected in the Transcarpathian, Poltava and Cherkasy regions. Circulation of the virus is observed in Vinnytsia, Zhytomyr, Lviv, Ivano-Frankivsk, Kharkiv and Khmelnytsky regions, as well as at the territory of the Black Sea Biosphere Reserve in the Kherson region. The incidence of arbovirus diseases in Ukraine is significant, because the diagnosis and the treatment of diseases are often not made in a timely manner, as health practitioners generally do not take them into account when making a diagnosis. In the absence of major outbreaks epidemiological surveillance is often weakened and control of communicable diseases, thus creating a serious public health problem. The part of such diseases in the structure of acute seasonal neuroinfections, according to experts, makes 23.5%. For the prevention of infectious diseases of arbovirus it's necessary to carry out the activities within the framework of epidemiological surveillance of especially dangerous infections. These activities include: annual epizootological monitoring of areas of increased risk of human infection, rapid identification of patients with arbovirus infections, conducting pest work, reducing populations of some species of birds and rodents, increasing health education and organization of the laboratory diagnosis of arboviral infectious diseases in the institutions of practical public health. Widespread, mass outbreaks, the difficulty of their etiological decoding due to the large antigenic diversity, but bound by laboratory confirmation, the absence of specific treatment and prevention today – all this defines the extreme urgency of study of modern problems of epidemiology, clinics, diagnosis of arbovirus infections.

# BIFIDUM- AND LACTOBACTERIA IN EUBIOTICS, BIOYOGURT AND YOGURT

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Microbial ecosystem of human's intestine can be disbalanced by wide range of factors: administration of antibiotics and other drugs, alcohol abuse, stress, diseases, toxic substances, and even the use of antibacterial soap. Probiotic bacterial cultures (usually bifidobacteria and lactobacilli) are intended to help the body restore impaired intestinal flora and are able to show antagonism against pathogenic and opportunistic microbes. Bifidobacteria synthesize vitamins B (B1, B2, B12, folic acid), vitamin C, essential amino acids. Lactobacteria are non-pathogenic Gram-positive large rods. They are always present in the vagina and digestive tract.

The aim of the study is determination of initial bifido and lactobacteria strains growth properties in commercial preparations and dairy products. Probiotic "Yogurt" of Pharma science, spoon yogurts "Activia classic", "Rastyshka", and kefirs were investigated.

Study results. The number of lactic bacteria in "Yogurt" was $10^2$ CFU/g, lactic streptococci – $10^3$ CFU/g, whereas according to the manufacturer it should be at least $10^8$ CFU/g.

Dairy products "Activia" should contain a special strain of bacteria Bifidobacterium ActiRegularis® in an amount of $10^8$ CFU/g. In our experiment the number bifidobacteria was $10^6$ CFU/g, lactobacteria - $10^7$ CFU/g, lactic streptococcus - $10^8$ CFU/g. The same results were obtained for spoon yogurt "Rastyshka" with strawberry taste. Kefirs TM "Romol" and "Zarechie" contained lactic streptococci in the amount of $10^3$ CFU/g.

Conclusions. Probiotics are recommended by physicians and more often nutritionists after course of antibiotics or as a part of fungal diseases treatment. However, single dose of probiotics may not contain the same number of viable microbial cells as claimed by manufacture (according to the instructions, 1 dose of preparation should contain not less than 1 billion of viable lactobacteria). In our opinion, this can lead to their ineffective actions. In some cases the quality of dairy products is controversial as they can actually contain inadequate number of certain microorganisms. However, even taking into consideration this fact, based on the results of our research it is more efficient to use probiotics present in natural sources, such as yogurt, kefir, sauerkraut, in management of the abovementioned conditions.

# MODERN CONCEPTS OF EPSTEIN-BARR VIRUS

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In recent years, an increasing number of patients suffering from chronic recurrent herpes virus infections are observed. In many cases it is accompanied by a marked disturbance of general health and a range of therapeutic complaints. Pathogen of the most common latent infection is Epstein-Barr virus (EBV). Nevertheless, general practitioners are not well informed on chronic infection caused by Epstein-Barr virus and its forms.

Epstein-Barr virus is a ubiquitous herpes lymphotropic virus, affecting about 95% of the adult population. It is an etiological agent of infectious mononucleosis, as well as causative pathogen of Burkitt's lymphoma, nasopharyngeal carcinoma, lymphoproliferative syndrome associated with the X-chromosome, and chronic fatigue syndrome. Transmission of the virus mainly occurs at the contact with infected secretions from the oropharynx. Usually, infection with this virus takes place in the early childhood or adolescence, and persists in the form of a latent infection almost throughout the whole life of infected individual. The source of the infection is a sick person, including those with blurred forms of the disease. B-lymphocytes are the main reservoir of the pathogen in the human body. Replication of the virus in the human body can cause exacerbation (occurrence) of the secondary immunodeficiency. Numerous studies confirm that EBV is associated with malignant transformation of the infected cells. It is proven, that such types of cancer as cancer of the nasopharynx, larynx, circulatory system, kidneys, sexual organs and nervous system, often is associated with Epstein-Barr virus. Infection with Epstein-Barr virus in adolescence in 75% of cases leads to infectious mononucleosis development. Chronic course of the disease can be in the form of subtle disease or masked with other chronic diseases. In this case diagnosis of the disease is difficult due to lack of specific clinical markers.

Except for the general physical examination, the study of immune status (antiviral immunity), DNA diagnosis of infection in different materials in dynamics, serological testing (EIA) are required to establish the diagnosis.

# ANTIMICROBAL ACTIVITY OF PHYTOSUBSTANCE OBTAINED FROM ALNUS GLUTINOSA LEAVES

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Development of the phytopreparations remains to be a promising trend in pharmaceutical production. Despite their long-term use in traditional and officinal medicine actual potential of the medicinal plants is yet not completely discovered. Recently, new original aspects have emerged in terms of application as well as technology of phytopreparations, using new raw materials, extracting agents, ways to intensify the process of extraction, etc. Extension of the national phytopreparations' range, produced according to the sophisticated economical technologies with comprehensive utilization of the raw materials and waste products is still relevant.

From the earliest times and currently phytosubstances derived from Alnus glutinosa attract high interest due to their wide spectrum of pharmacological activity, including antimicrobial action.

The aim of this study was to investigate in vitro antimicrobial properties of the new phytosubstance's experimental samples derived from the shrot of Alnus glutinosa leaves and predict further extended study using clinical strains, such as pyoinflammatory and antibiotic-resistant pathogens, with the prospect of its further clinical use as an antimicrobial drug.

Antimicrobial activity of the new preparation was studied using a modified agar well diffusion method, which is generally accepted in microbiological practice. Typical strains of American Culture Collection: S. aureus ATCC 25923, E. coli ATCC 25922, P. aeruginosa ATCC 27853, B. subtilis ATCC 6633, C. albicans ATCC 885-653 were used as reference test-strains.

Obtained results indicate that phytosubstance of Alnus glutinosa leaves has a broad spectrum of antimicrobial activity. It is worth mentioning, that there is a higher susceptibility of Gram-positive cultures of bacteria, including S. aureus and B. Subtilis, which is evidenced by a more pronounced zones of growth inhibition of these cultures compared with Gram-negative bacteria. Thus, growth inhibition zone diameter around the well containing extract ranged from 22.4 to 28.0, relative to cultures S. aureus and B. subtitles, which is significantly higher than its activity against other test-strains. At the same time the extract showed indifference against the culture of fungus C. albicans.

# BACTERICIDAL ACTIVITY ASSESSMENT OF ULTRAVIOLET RADIATION

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Ultraviolet radiation of bactericidal spectrum is widely used for treatment of air and premises in each health care setting in order to ensure epidemiological regime, prevent infection of the staff and visitors. Ultraviolet radiation with wavelength 205 to 315 nm has bactericidal effect, which results in destructive-modifying photochemical damage of DNA synthesis causing microbial cell death in the first or subsequent generations. Waves ranging 254 to 257 nm have the maximal bactericidal effect.

Bactericidal properties of UV-rays depend on biochemical peculiarities of microflora (species and even stain of the microorganism, thickness of microbial cell membrane and etc.), environmental characteristics (pH, transparency and etc.), characteristics of the UV radiation source (wavelength, intensity, and etc.), exposure time and other factors. UV-flow density reduces depending on distance in quadratic progression and decreases by 10 times when the distance from the source increases from 2 cm to 50 cm, and is insignificantly small at 3 m distance.

Aim of the study is to identify experimentally the effective exposure time for bacteria elimination.

Museum cultures E. coli, S. aureus, P. aerugenusa, C. albicans and B. subtilis were inoculated on Petri dishes (solid nutrient medium) and were left in UV-light on the bank at 250 cm from the source of light for 30 and 60 minutes. Negative control and experimental cultures were incubated during 24 and 48 hours in temperature-regulated chamber.

Obtained results have shown that after 30 min. of UVR exposure bactericidal action on the studied microorganisms was not observed, in control and studied inoculates the uniform lawn-like growth was observed. After 60 min. exposure we obtained S. aureus growth of 12 colony forming units (CFU), E. coli - 107 CFU, C. albicans 113 CFU, P. aerugenusa and B. subtilis more than $10^3$ CFU.

High efficiency of UVR in disinfection of the surfaces has been proved, yet there is no robust scientific methodology for air-flows disinfection using UVR. When using UV-radiation the limiting factor is the maximum permissible dose for people, but not the dose needed to kill microorganisms in the air of premises. In laboratory experiments UVR reaches high rates of microorganisms' mortality while creating ideal conditions. In real application efficiency of the equipment is much lower and depends on many factors. Even prolonged for 60 minutes exposure to UV-radiation does not kill blue purulent infection and spore-forming microorganisms. Duration of exposure must be at least 60 minutes, as sublethal doses of UV-rays have mutagenic action on bacteria and viruses. Each organism has biochemical mechanisms that can completely or partially restore the damaged original structure of the DNA molecule. Due to mutagenesis the survived bacteria can form new colonies with a lower susceptibility to radiation.

# RESISTANCE OF TRICHOMONADS AND OTHER PATHOGENS OF SEXUALLY TRANSMITTED INFECTIONS (STIS) TO ENVIRONMENTAL FACTORS

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Sexually transmitted infections (STIs) have a significant impact on sexual and reproductive health all over the world, and are among the 5 major disease categories for which adults seek health care. According to WHO estimates every year 500 million of people acquire one of four STIs: chlamydia, gonorrhea, syphilis, and trichomoniasis. Untreated and persistent STDs can cause severe complications, male and female infertility, prostatitis, inflammatory diseases of the uterus and appendages, epididymitis, and genital tumours. In order to determine the likelihood of domestic route STIs transmission, we analysed the resistant of STI to environmental factors according to available literature. Of a great practical importance is the study of Trichomonas vaginalis stability in certain environmental conditions, efficiency of antiseptics and so on. Previously it was believed that Trichomonas are extremely stable in the environment, especially in water reservoirs, but currently it is not supported. Trichomonas vaginalis is very sensitive to changes in osmotic pressure and in fresh water of different reservoirs it dies within 15-60 minutes, rapidly loses its viability at 45-50°C and at 60°C dies immediately. These protozoa can not tolerate drying, but can remain viable for a long time in a humid environment, especially on cotton fabrics and sponges, they can aslo tolerate low temperatures. Chlamydia is quite sensitive to the action of short- and long-wave ultraviolet radiation, as well as high temperature. Thus, at 37°C extracellularly located Chlamydia loses its infectivity within 24-36 hours. Concentrated suspension of Chlamidia is inactivated within 1 minute at 95-100°C. At the same time, the ability of the infected material to maintain its infectiveness within 2 days at 18-19°C was established. Agents of syphilis are susceptible to different environmental factors. They rapidly die at drying. Outside the human body in biological substrates, on household items pale treponema retains its infectiousness before drying. In the external environment at 40-42°C they are killed within 3-6 hours, and at 55°C within 15 minutes. In the whole blood or serum at 4°C microorganisms remain viable for a day, which is important for the blood transfusion. Treponema pallidum is resistant to low temperatures. It is very sensitive to chemical substances. Different antiseptics are lethal for syphilis agent. Causative agent of gonorrhoea is not stable in the environment. Outside the human body gonococci are unstable and die after drying of the substrate in which they reside. Neisseria does not tolerate cooling, and as the temperature rises to 56°C it dies within 5 minutes. Almost immediately they die in soapy water, are sensitive to preparations of antibacterial and antiseptic solution.

Prevention of the STIs is important in maintaining of reproductive health of the sexually active population. Majority of STIs pathogens can survive long enough in a warm and humid environment, biological substrates, as well as at low temperatures, which results in probable infection through domestic route. At the same time, sensitivity of microorganisms to drying, heating and many antiseptics, this predisposes the non-specific ways of STIs prevention.

# SECTION № 9

# CLINICAL PHARMACY

# PHARMACEUTICAL CARE FOR PATIENTS WITH IRON DEFICIENCY ANEMIA OF DIFFERENT ORIGIN, INCLUDING HEMOPHILIA

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Iron deficiency anemia (IDA) one of the most frequent pathology in medical practice and worldwide medical and social problem. Frequency of this sometimes severe disease reach up to 50-80% (especially in child age in developing countries). Range of health problems, which can cause this pathology is very wide starting from some cosmetic disorders (such as hair loss, nails fragility), continuing in cardiovascular and respiratory disorders, development and growth retardation in child age and foetus if IDA occurs in pregnant woman. In severe cases IDA can cause irreversible change in organs of the human body.

The list of causes of IDA include big amount of different factors, last can be gathered in two big groups – poor supply with iron (alimentary, dismetabolism) and overrun (any types of acute or chronic bleedings). One of the major causes of chronic bleedings in childhood is hemophilia – severe disease involving clotting. Whatever cause of IDA iron containing drugs (ICD) are essential for its treatment. Along with necessary positive pharmacological effect they have some adverse effects, and its crucial for the patients to be aware about them, thus it is the duty of the physician and pharmacist to give full information about it to patients.

Task of our project was to estimate efficacy and safety of treatment with ICD of patients with IDA in the Bagdad Preceptorial Hospital (Bagdad city, Iraq). to perform this task we provided analyses of case histories of the patients of this hospital, also we developed questionnaireand provide interview of those patients. Major part of questionnairewas dedicated to the questions of the adverse effects of ICD and patients awaring about them. It was estimated that up to 60 % of patients had no information about adverse effects of ICD. Last fact lead to discontinuing of drug treatment by patients themselves of 20% in investigational group.

We can conclude that its essential to provide patients with proper and full information for further prevention of selfdiscontinuing of drug treatment.

# NONANTIBIOTIC PROPERTIES OF TETRACYCLINES

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Tetracycline antibiotics include a number of drugs related in chemical structure, antimicrobial spectrum and mechanism of action, the features of which still continue to be refined. Among the new applications of tetracyclines is their widely use as a tools for studying the mechanisms of disorders of the various structures of the body, as well as to develop the new approaches to the use of these drugs in the diagnostics and treatment of various human diseases, such as rheumatoid arthritis and other systemic diseases. Currently one of the rapidly developing areas of researches is the study of immunomodulatory and anti-inflammatory effects of antibiotics. While studying the effects of tetracyclines in the therapy of noncommunicable diseases, particularly in the treatment of immune and skin diseases, some authors have been concluded that the therapeutic action of this drugs is realized due to the influence on immune system. Nonantimicrobial effects of tetracyclines also includes pro-apoptotic, anti-tumor, neuroprotective, genotropic and other effects on the macroorganism.

Tetracyclines – a relatively low toxic substances, but long-term use leads to the development of side effects of varying severity. One of the possible way to improve the safety of this group is to create combined drugs containing tetracycline antibiotics and biologically active substances that modify their toxic properties.

The tasks of this study were to conduct the comparative analysis of safety as well as finding the median lethal dose ($LD_{50}$) of tetracycline hydrochloride, doxycycline hydrochloride, methacycline hydrochloride and to determine the optimal remedy for the further studies as anti-inflammatory and chondroprotective drug.

Materials and Methods. A study of acute toxicity of the oral forms of tetracycline hydrochloride, doxycycline hydrochloride, methacycline hydrochloride were conducted according to the V.B. Prozorovsky method in 108 white outbred rats of both genders with the body weight 180.0-200.0 g divided into three series of 6 groups, there were 6 animals in each group. Animals of experimental groups received tetracycline hydrochloride, doxycycline hydrochloride, methacycline hydrochloride in doses ranging from 500 mg/kg to 5000 mg/kg. Drugs were administered intragastrically in appropriate doses dissolving them in the necessary amount of saline solution. For the calculation of the median lethal dose ($LD_{50}$) was determined the percentage of mortality in each group after 14 days. Using tables and calculations

in accordance with the V.B. Prozorovsky method of probit-analysis of the curves of lethality the value of $LD_{50}$ was determined.

Results. The observation of the animals has been carried out within two weeks after drug administration. Already on the second day after drug administration in groups of rats used doxycycline in doses 2000 – 5000 mg/kg the first fatal cases were observed. At the end of the first week a certain level of lethality has been observed in all groups, except the group of rats used the drug in the dose 500 mg/kg. Then the average mortality rate reached its maximum at 8-9 days of the experiment. The median lethal dose was calculated based on the activity of the drug depending on the applied dose by probit-analysis. Using the tabular data the percentage of mortality in each group were transferred into probits and then the weight coefficients and place of doses were determined carrying out further necessary calculations. According to experimental data was plotted the graph of probit analysis of the dependence "dose-mortality".

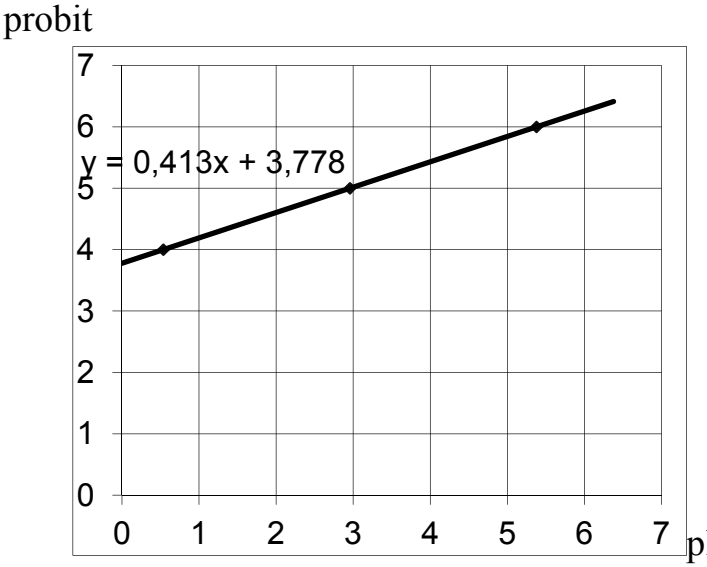


Figure 1. Graph of the probit analysis of dependence "dose-lethality" of the tetracycline

Conclusion. 1. The results of the conducted investigations and calculations lead to the conclusion that the $LD_{50}$ level of tetracycline hydrochloride after single oral administration in rats is 1478.22±201.67 mg/kg; $LD_{50}$ of doxycycline hydrochloride – 1893.03±286.2 mg/kg; $LD_{50}$ of methacycline hydrochloride – 1635.73±199.36 mg/kg. Thus, doxycycline is significantly safer than tetracycline and methacycline.

2. The obtained results allow to refer the studied drugs to the IV class of toxicity – the low toxic substances according to the standard K. K. Sidorov classification.

3. It is recommended to carry out the further studies of the mechanisms of anti-inflammatory and possible anti-rheumatic effects of tetracyclines and their combinations with potential anti-inflammatory and chondroprotective substances.

# THE STUDIES OF ALDOSTERONE ANTAGONIST EFFECTIVITY IN THE TREATMENT OF CONGESTIVE HEART FAILURE

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Heart failure is a clinical syndrome characterized by the functional inability of the ventricle to meet the metabolic demands of the body.

Renal hypoperfusion occurs as a result of reduced cardiac output, resulting in the activation of the renin–angiotensin–aldosterone system which plays an important role in the pathophysiology in heart failure by way of its effects on sodium retention and potassium loss. Aldosterone is a major prognostic determinant in heart failure. As the rise of aldosterone in bloodstream causes increase in atrial and perivascular fibrosis of the pulmonary artery, as well as in the aorta.

In the Randomized Aldactone Evaluation Study (RALES) trial there is a proof of principle that aldosterone possesses pathophysiologic importance in patients with heart failure that is caused by systolic left ventricular dysfunction. This trial demonstrates the effect of spironolactone in doses of 12.5 and 25 mg and analysis suggested a uniform effect of spironolactone without regard to age, gender, cause of heart failure, use of concomitant potassium supplements, creatinine levels, and serum potassium level.

There was also a significant improvement in New York Heart Association Functional Classification (NYHA) as well as a 35% reduction in hospitalization for heart failure. But the only notable side effect in the RALES trial was an excess of gynecomastia and breast pain in males when increases the doses.

British National Formulary (BNF) presents the indication of spironolactone for oedema in congestive heart failure; moderate to severe heart failure as adjunct.

But in the most reliable electronic database like PubMed and different literatures recourses there have not been considered much of the existing evidence, and therefore the recommendations of these drugs are more restrictive in the type of heart failure patients. It is unclear how useful this class of drugs is in patients with mild and moderate heart failure. In 52 departments of internal medicine of the Spanish RICA there was performed an investigation of patients with heart failure and preserved ejection fraction (HFPEF). It has shown that the administration of spironolactone was associated with an increase in all-cause readmission, perhaps due to the higher rate of hyperpotassemia.

Therefore in Iraq hospital I am going to conduct an analysis of cardiologists' opinion for uses of aldosterone antagonists (spironolactone), their approach to the standard treatment of heart failure, as well as the way this class of drugs affects the CHF patients and the appearance of adverse events for standard dosage regimen.

# STUDY OF THE CONDITIONS FOR PHARMACEUTICAL CARE OF HYPERTENSIVE PATIENTS IN IRAQ

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Hypertension is one of the most spread chronic diseases that can lead to dangerous complication like heart and kidney diseases, and hypertension considered essential factor in occurrence strokes and heart failure. There are a lot of hypertensive patients in Iraq but nowadays a lack of qualified medical care to such patients. So, the role of a pharmacist may be decisive in the treatment of chronic diseases such as hypertension.

**The aim** of our research was to investigate pharmaceutical care condition for hypertensive persons in Iraq.

**Material and methods.** We conducted 50 special questionnaire for pharmacists in 50 pharmacy and 50 for hypertensive patients in Iraq. There are necessary question and all information about pharmacies available and the most antihypertensive drugs commonly in Iraq.

**Results.** There are 15 (30%) hospital pharmacy, 23 (46%) branch regional city pharmacy and 12 ( 24%) village pharmacy in Iraq; and big sizes are 18 (36%), middle sizes are 20 (40%) and small sizes are 12 (24%) pharmacies. The 62 % of pharmacies has a device for measuring blood pressure. From 50 pharmacies 32 (64 %) have more than 30 different antihypertensive drugs: ace inhibitors were in 48 (96 %) of pharmacies, beta-blockers were in 39 (78%), calcium channel blockers were in 42 (84 %), diuretics were in 29 (58 %), and angiotensin II receptors blockers were in 32 (64 %) pharmacies retrospectively. Diuretics and angiotensin II receptors blockers were found mostly in hospital pharmacies. Pharmacists in Iraq mostly know about indication, contraindication and side effects of antihypertensive drugs. However, 24 % of pharmacists do not tell the patients how to use the drugs, 84 % of pharmacists do not consult about side effects of the drugs, 52 % of pharmacists give the antihypertensive drugs without prescriptions.

From questionnaire for patient, we discovered that 34 % of hypertensive persons in Iraq do not check their blood pressure, in spite of 60 % of the patients has severe course of hypertension and usually use combined antihypertensive treatment.

**Conclusion.** Condition for qualified pharmaceutical care in Iraq needs to future development due to increasing of educational level of pharmacists in area of chronic illness such as hypertension.

# CLINICAL AND PHARMACEUTICAL APPROACHERS TO RATIONAL USE OF DRUGS IN PATIENTS WITH DIABETES MELLITUS TYPE II

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Diabetes mellitus is a group of metabolic diseases, that are charecterized by hyperglycemia due to insuline secretion deficiency, insuline action defect or to both of these factors. **T**he number of people with diabetes is increasing due to population growth, aging, urbanization, and increasing prevalence of obesity and physical inactivity. Quantifying the prevalence of diabetes and the number of people affected by diabetes, now and in the future, is important to allow rational planning and allocation of resources. In 2000, according to the WHO, at least 171 million people worldwide suffer from diabetes, or 2.8% of the population. Its incidence is increasing rapidly, and it is estimated that by 2030, this number will almost double.

Materials and Methods. The experimental part of the master thesis was conducted in collaboration with Kharkiv Regional Hospital (endocrinological department, head of the department Dr. Ivan Smirnov) and State Institute of Problems of Endocrine Pathology named after Danylevskiy (Kharkiv, Ukraine). For the purposes of the master thesis was developed a questionnaire for surveying of patients and endocrinologists in English and translated into Russian. For the purposes of survey were pooled 25 endocrinoligists and 30 patients with diabetes mellitus type 2 (not insulin-users), that were hospitalized in the endocrinology department of Kharkiv Regional Hospital. The aim of this thesis is: to investigate the epidemiology and pharmacoepidemiology of diabetes mellitus type 2; to develop practical recommendations for healthcare professionals to increase efficiency and safety of diabetes treatment. The tasks were: to investigate the epidemiology of diabetes mellitus; to investigate the International Guidelines for diabetes control (ADA, EASD) and pharmacoepidemiology of diabetes mellitus; to study the opinion and beliefs of endocrinologists concerning efficiency criteria and essential factors of diabetes control; to study the opinion and beliefs of patients with DM type 2 concerning efficiency criteria and essential factors of diabetes control; to develop practical recommendations for healthcare professionals.

Results. The obtained survey results and complex analysis of the literature data enable to develop some practical recommendations for the doctors, pharmacists and patients for the improvement of the diabetes control. Practical recommendations for endocrinologists include: Older patients can be treated with the same drug regimens

as younger patients, but special care is required in prescribing and monitoring drug therapy. Metformin is often contraindicated because of renal insufficiency or heart failure. Sulfonylureas and other insulin secretogogues can cause hypoglycemia. Thiazolidinediones should not be used in patients with congestive heart failure. α-Glucosidase inhibitors are safe but may not be well tolerated and may not be effective as monotherapy. Drugs should be started at the lowest dose and titrated up gradually until targets are reached or side effects develop. Control of blood glucose level is essential for the prevention and decrease of the complication development. It is necessary to control 3 parameters: fasting and post-prandial glucose and HbAc level. Post-prandial glucose is a evident factor for complications development. It is important explain to the patient the importance of the regular blood glucose and HbAc measurements to ensure the definitive therapeutic result. Following of the dietary recommendations and increase of physical activity are essential for improvement of the diabetes control. Together with the choice of appropriate medication it is necessary to explain to the patient importance of the regular medication administration. It is important to control the use of herbal medicines with hypoglycemic activity by the patients, explain the low efficiency of it and motivate patient not to stop the medication intake while using the herbal medicines.

Practical recommendations for pharmacists are the next: the essential element of the communication with patients with diabetes mellitus type 2 is increase of patient's compliance to treatment and diabetes control (regular medication administration, regular blood glucose measurement – at least 1 time a day); the specific focus should be done to patients that take more than 1 medicine; it is necessary to ask patient about the safety aspects of use of hypoglycemic medicines (especially about hypoglycemia and change of weight). The hypoglycemia that is experienced by the patient increase the cardiovascular risk and risk of complications. Increase of weight can show the hidden hypoglycemia that are associated with use of sulfonylurea. Decrease of weight lower the recommended BMI can show the decompensation of diabetes; by the dispensing of the medical herbs and herbal medicines with hypoglycemic activity is important to ask patient about other medication that he is taking and explain that he shouldn't stop prescribed diabetes mellitus treatment; pharmacist should be able to consult the patient with diabetes type 2 concerning the diet and recommended physical activity.

Conclusion. The role of the pharmacist in diabetes managenest must be directed to the increasing of patient' compliance (regular medication administration, regular blood glucose measurement), safety aspects (decrease of risk of hypoglycemia, decrease or increase of weight, use of herbal medicines).

# QUALITY ASSURANCE DURING REALIZATION OF CLINICAL TRIALS IN THE CLINICAL AND DIAGNOSTICS CENTER OF THE NATIONAL UNIVERSITY OF PHARMACY

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Clinical and Diagnostic Center of the National University of Pharmacy (CDC of NUPh) is a medical and preventive establishment of higher accreditation category where clinical trials of Phase I-II and bioequivalence studies are conducted. During the realization of clinical trials quality assurance is provided at all stages.

Basic principle of clinical trial conducting is compliance to requirements of "Good Clinical Practice" (GCP). Confirmation that study is conducted in accordance with these rules must be expected results of quality assurance, but it is impossible to achieve it at once. Right from the start of clinical trial, from the moment of study protocol signing, from the moment of its submittion to Ethics Committee, Investigator is under an obligation to meet all requirements of International Conference on Harmonization of Good Clinical Practice (ICH GCP), Sponsor's and Ukrainian legislation requirements.

Specialist in quality is an important factor of quality assurance. His professional skills, proper qualification before the start of a clinical trial and ability to co-operate with the personnel of CDC of NUPh, quality of his official duties implementation are the most reliable in this process.

Let's focus on the key positions that require the hundred-per-cent monitoring during clinical trials conducting. Compliance with ethics principles is a basis of clinical trials therefore the forms of the informed consent must be strictly checked up (100%). Not only the fact of informed consent obtaining from patient, but also the accuracy of its obtaining and documenting of this procedure is examined.

The special attention is drawn to source documentation of patients who experienced adverse events or adverse reactions (AE/AR). Besides a verification of accuracy and completeness of AE/AR data, it is necessary to make sure that the corresponding information about the degree AE/AR severity, its relation to the investigational medicinal product (IMP) in source documentation, in a report and in the Case Report Form (CRF) is provided properly.

A key aspect of any clinical trial are the procedures of IMP handling which include the verification of the fact of IMP receipt, compliance with its storage terms, transmission of unused IMP to the Sponsor and many other aspects that also are the object of intent attention of assurance specialist in quality.

"There are no tufles in a clinical trial" is a thesis which is an axiom for the clinical research team of Clinical and Diagnostic Center of the National University of Pharmacy.

# ASSESSMENT OF QUALITY OF LIFE IN HEALTHY VOLUNTEERS WHO PARTICIPATE IN CLINICAL TRIALS

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In many areas of medicine there is used the concept of quality of life which is a health-related issue. Assessment of the patient's quality of life includes physical, psychological, social, economic, and spiritual aspects of his life. Improving the quality of life is either a main or an additional goal of any treatment. The criteria of treatment efficacy in clinical studies take into account the physical findings and laboratory data. At the same time the studies of quality of life are held in many areas of medicine, particularly in palliative medicine, cardiology, oncology, psychiatry, endocrinology, neurology and others. The main areas of such research include the standardization of methods of treatment, examination of new methods of treatment and medicines, the development of predictive models of disease and economic feasibility methods of treatment.

In certain diseases volunteer's assessment of his condition is the most important indicator of health. The 36 – item short form of the Medical Outcomes Study questionnaire (SF-36) was designed as a generic indicator of health status for use in population surveys and evaluative studies of health policy. It was set to assess the quality of life of the patient, widely used in the clinical trials. It is widespread in Europe and in the USA, it can also be used in conjuction with disease-specific measures as an outcome measure in clinical practice and research. According to the study protocol requirements we have experienced the use of this questionnaire in patients with rheumatoid arthritis. We consider that it is necessary to submit the quality of life surveys to healthy volunteers as well. We have developed the special questionnaire which is based on the approved quality of life surveys and covers 10 questions about physical functioning, general health, vitality, social functioning, emotional state, mental health. Within the quality assurance procedures we have introduced this questionnaire to the healthy volunteers who took part in the bioequivalence studies which are run in the Clinical and Diagnostics Center of the National University of Pharmacy. The time range was specifically calculated according to the standard schedule of bioequivalence study and it may describe how the volunteers' quality of life has changed during the trial. We think that the developed quality of life questionnaire will reflect the special aspects of the general well-being and health of the participants of the clinical study. This information will represent the comprehensive approach to the quality assurance of the given study.

# COMPARATIVE STUDY OF TREATMENT STANDARDS HELICOBACTER PYLORI INFECTION IN GEORGIA AND EUROPE

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The end of the twentieth century. took a significant step towards changing the principles le-tion of gastric ulcer (GU) and duodenal ulcer (DU). The success of modern approaches to treatment is associated with the recognition of etiology and logical role Helicobacter pylori (HP), which was proved in 95% of the PUD, 90% of non-drug GU and 60-70% of cases stomach cancer, as well as the use of new circuits and antisecretory drugs HP eradication. However, the selection of the most effective treatment of H. pylori infection is still an important issue. Modern approaches to the treatment of H. pylori infection, which meet the requirements of evidence-based medicine are given in Recommendation IV-th (2010) Maastricht consensus

The aim of the work was a comparative study regimens Helicobacter-associated diseases in Georgia and Europe.

Materials research is the history of the disease in patients with gastric ulcer and duodenal ulcer, chronic and erosive gastritis, gast-roezofagealnoy reflux disease who were treated in 3 croup-Nation health facilities in Batumi (Georgia): Regional Centre lo Mein Medicine, Naval Medical Center and Health center.

Conducted the study showed that the scheme therapy of H. pylori in Georgia correspond to the scheme proposed in the IV-th Maastricht Consensus. But in Europe, it is recommended Duration of treatment of 14 days, which increases the effectiveness of eradication of HP by 12%, while in Georgia, 80% of the duration of treatment is 7-10 days. The recommendations I and 2nd Maastricht consensus to suppress gastric secretion were recommended proton pump inhibitors (PPIs) in appropriate doses 1 time a day, but in Recommendation IV-th (2010) Maast-rihtskogo consensus PPI recommended 2 times a day. It is proved that took away chenie doses of PPIs standard protocols triple therapy is accompanied by increased effectiveness of eradication, but increases the cost of treatment. Pharmacoeconomic is optimal to use double dose PPIs (omeprazole for - 40 mg 2 times a day) using a 1-week protocol, which allows to achieve eradication rates comparable to that at 2 weeks of treatment.

Conclusions: Based on the foregoing, it should be more actively work to supplement and implement treatment protocols in Georgia Correspondingly-dance with international standards.

1. Therapy of H.pylori-infected patients should be carried out in accor-dance with the recommendations of the Maastricht 4-2010.

2. In the first part of the base line therapy of H.pylori antibiotic in all cases be clarithromycin 500 mg 2 times a day, as second preference should be given antibiotic amoxicillin (1000 mg two times a day); nitroimidazoles (metronidazole, ornidazole) unwillingness to use-enforcement.

3. Compliance with these recommendations can significantly improve ef ciency therapy of H.pylori and the frequency of eradication of Hp infection.

# THE ANALYSIS OF COMPLIANCE OF BIOETHICAL NORMS OF SIGNING THE INFORMED CONSENT DURING ORGANIZING CLINICAL TRIALS OF DRUGS

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Clinical trials (CT) are the essential step in development of medicines in the whole world, which goes before its registration and wide medical usage. Informed consent (IC) is a process that allows a patient or a healthy volunteer reaffirm their will freely to participate in CT. The volunteers should understand all the procedures and risks of participating in CT. Such information is provided by a researcher to a potential volunteer during signing the IC.

The interview of 44 volunteers was held for the evaluation of volunteers' awareness during signing the IC.

The questionnaire for respondents consisted of two parts: the first part had general questions and questionnaire that allowed volunteers to assess themselves their knowledge of terms which could be got across during CT, and the second – test questions of closed type for evaluating real knowledge of terms. The verification of the test in the questionnaire was conducted by the key.

The analysis of results showed that from 44 volunteers more than a half (52.27%) were aged 36 – 45 years. 52.17% of respondents aged 36 – 45 years took part in 3 – 5 CT, 60% of volunteers aged 18 – 25 years – in 1 – 2 CT. The majority of respondents (86.36%) didn't have questions during reading the information, but 34.09% asked questions about unfamiliar or unclear terms, the answers on the raised questions were provided to 56.82% of cases and were satisfactory to 68.18% of respondents.

The statiscal analysis by Student's test of relations between volunteers' self-rating and evaluation of their real knowledge of CT's terms was carried out. It showed that the volunteers' self-rating is significantly higher than their test results ($P=0.29<p\text{-level}=0.05$).

The results of analysis demonstrate the necessity of the proper explanation of terms by researchers to volunteers and then making sure by asking volunteers questions how well they understand the received information. In future it is planned to analyze the impact of different factors on degree of the IC information understanding during signing it by the volunteers.

# ACNE – MEDICAL OR COSMETIC PROBLEM?

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Acnes – it is a chronic inflammatory disease of sebaceous glands, that appear in result of it's plugging and high level of the produsing of sebum. From the literature, about 80% of citizens at the age from 12 to 25 years has this problem, and about 40% of people older 25 years. There are many reasons of appearance of acnes such as ecologicas conditions, the tipe of feeding, the way of life. Acne is one of the most wide spread dermal diseases. The following factors play role In the formation of acne : hormonal changes, increased levels of male sex hormones (androgens), diseases of the stomach and intestines; liver disease; genetic predisposition. Basis of treating - regular facial cleansing by spesial means for the skin. Medical opinion. Acne is a disease, rather than a cosmetic defect of the skin. Treatment of acne not by the dermatologists in beauty salons and aesthetic centers undesirable. None of cosmetic methods are not superior to medical treatment of acne. Opinion of beautician. It's nesessary to remember the golden rule: you can not squeeze tumors, because it contributes to the spread of infection on the skin surface and leads to the appearance of new spots.

Acne treatment: nitrogen, cryotherapy, facial cleansing, exfoliation, home care. Daily skin care should include: gel cleaner, toner, cream of light texture that does not clog pores, mask (1-2 times a week). That can not be used to treat acne: soap that includes an alcohol; patch soda, toothpaste, vitamins.

The aim of our work was to identify the problems of acne on the basis of a survey among the students 1-5 courses of National Pharmaceutical University and correction of acne stage 1 by adhering to a healthy lifestyle, with or without cosmetics. Objects were students of 1-5 courses of National Pharmaceutical University with and without acne problems.

Objectives: To find out the number of students who have acne problems. To work out a set of procedures aimed at correcting the problems of acne. To work out a profile.

Conclusions: The problem of acne is relevant in our time, as a large number of people face it. After the experiments and surveys we'll make a conclusion: if you want to have beautiful and healthy skin, keep a healthy lifestyle, combined with a visit to experts. The problem should be solved both inside and outside. The place of doctors and beauticians important to maintain your health and beauty.

# SIDE EFFECTS OF LONG-TERM USE OF AROMATASE INHIBITORS

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Aromatase inhibitors (AI) have proven effective drugs in the treatment of breast cancer during the postmenopausal period. In recent years, they are in the top line of the complex medical treatment of hormone-positive tumors of various prevalence and stage of disease. It should be noted that currently used in practice solely AI third generation (letrozole, anastrozole and exemestane) as earlier design allowed a significant number of serious side effects. At the same time over the past few years, a growing number of clinical publications in which there is a serious discrepancy between the accumulated data from controlled clinical trials on the safety profile of these drugs with the data obtained from medical practice. It should be remembered that AI often take elderly patients who have a variety of comorbidities, therefore, the presence of additional adverse effects associated with taking any medication, should be reduced to a minimum level.

The aim of our study was to evaluate the nature and frequency of side effects long-term use of AI and their possible prevention according to clinical trials and literature data.

Materials and Methods: We analyzed data from clinical trials available results at the beginning of 2015 (5198 study). This included testing of exemestane (159), anastrozole (228) and letrozole (273). In addition, analyzed the available literature on AI side effects and effectiveness of the methods to prevent them.

Results: The most frequent side effects of AI were increasing the frequency and intensity of hot flashes, joint pain of varying severity, weakness, mood changes, sore throat, dyspepsia and vomiting, depression, high blood pressure, osteoporosis, swelling of extremities and headache. Moreover, the intensity and frequency of most of them increased respectively terms of reception of AI. For example, if after two years of taking the drugs serious difficulties due to the side effects observed approximately 10% of the patients, after 3 years were not less than one third.

Analysis of the data revealed significant differences in the defined frequency and spectrum of side effects during clinical trials and clinical publications on the topic. For example, in clinical trials the frequency of arthralgia and myalgia varying intensity observed in 15-21.8% of patients. At the same time, practical publications

indicate the level of comparable intensity of symptoms in 35-58.5% and even 63.9% of the patients. In addition, half refused to taking the AI patients (50.4%) did so because of the severity of pain. But in general, failure rates is, according to various estimates, from 27.8 to 36% of patients. It is interesting that in pilot clinical trials of the last century, these effects were recorded in only 5% of patients. As the therapeutic methods of arthralgia and myalgia, indicate certain (albeit modest) positive effect of the reception of ibuprofen, the use of physical therapy, massage and acupuncture. At the same time, increase the risk of fractures is reliably prevented parallel use of bisphosphonates and denosumab (Prolia) reception.

If the frequency is fixed by clinical trials and clinical publications side effects comparable with regard to the development of dry mucous membranes (3-7.2%), osteoporosis (2.7-10%), the intensification of hot flashes (25-33%) and general weakness (18-24.1%), the effects of a number of other effects, there is considerable differences again. In particular, it concerns the increase in anxiety and depression (clinical trials - about 1.5%, and clinical publications - 14-17%), memory impairment (respectively, 2% and 48%). Furthermore, clinical trial data taken into account when receiving AI only a limited number of side effects. At the same time outside of the results is a significant number of them quite significant, because of which many patients are forced to refuse treatment. Among these side effects: a significant decrease in libido - up to 24%, sleep disorders - to 53.4%, increased sweating - 16,4-17%, diarrhea - 9-12%, vaginal bleeding - 3.8%, and so on. In particular, after two years of receiving AI observed, although relatively rare, and other significant side effects, such as "dry eye syndrome" (3%), "carpal tunnel syndrome" (1.5%), numbness of fingers extremities (1.2%) and some other.

Conclusions: It was found significant differences in the incidence of side effects is determined during chronic administration of AI during clinical trials and clinical publications. Apparently, they were associated with the peculiarities of design and selection of patients when preparing for the clinical trials, when the inclusion criteria included a limited number of comorbidities, and the refusal of treatment (including due to the severity of adverse symptoms) patients were excluded from the calculation obtained results. Inclusion in the number of dropouts due to side effects of the course of clinical trials would increase the incidence of side effects in two or three times. Most likely, the perform clinical trials sponsored by the manufacturer of medication of is not ideal to obtain objective results.

# RECOMMENDATIONS EUROPEAN ASSOCIATION (ESC-ESH, 2013) IN HYPERTENSION – WHAT'S NEW?

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**Actuality.**Currently arterial hypertension (AH) is one of the most common chronic diseases and also those that hardly proceeds. The main diagnostic feature is the steady increase of blood pressure (BP).

Numerous recent studies have shown that hypertension occurs on the backdrop of a complex interaction of genes and surrounding factors. We found many common genes that have little effect on blood pressure, as well as some rare genes that greatly affect blood pressure, but the genetic side of hypertension is still poorly understood.

Increased peripheral vascular resistance at constant hypertension, mainly associated with the structural narrowing of the small arteries and arterioles. Reducing the number or density of capillaries also affects the peripheral resistance. Hypertension is also associated with a decrease in the elasticity of peripheral veins, which can increase blood flow back to the heart, the end diastolic pressure and subsequently lead to diastolic disorders. High pulse pressure in elder people who suffer from hypertension or isolated systolic hypertension can be explained by increased arterial rigidity, which usually accompanies the aging process and may deteriorate because of high blood pressure. The mechanisms that affect arterial system increasing resistance in hypertension are: violations of water-salt metabolism in the kidneys, in particular disorder intrarenalnoyi renin-angiotensin system and the sympathetic nervous system disorders. These mechanisms are not mutually exclusive, but rather to some extent combined in most cases of essential hypertension. We can assume that endothelial dysfunction and vascular inflammation also may increase peripheral vascular resistance and vascular damage in hypertension.

Thus, considering the characteristics of the pathogenesis, the main goal of treatment is to reduce hypertension cardiovascular risk, the risk of heart failure and chronic renal failure. In 2013, at the Congress of the European Society of Hypertension (ESH) in Milan the new ESH and the European Society of Cardiology (ESC) guidelines for the treatment of hypertension was presented.

**Results.**Recommendations for treatment of hypertension presented by European experts (ESC-ESH) in 2013 didn`t experience a significant correction from the previous guidance.

Pharmacological treatment is needed by most patients with hypertension. In the treatment the 5 classes of antihypertensive drugs are most often used: diuretics, calcium channel blockers, ACE inhibitors, Sartany, beta-blockers.

The decision to start drug therapy in patients with hypertension depends on blood pressure. Immediate start drug therapy is recommended for all patients with hypertension 2 and 3 degrees (SBP ≥160 or DBP ≥100 mmHg. In.) or at any level of cardiovascular risk, as well as in patients with grade 1 hypertension with high cardiovascular risk (destruction of target organs, diabetes, chronic kidney disease).

In elder patients pharmacotherapy is recommended for SBP ≥160 mm Hg. c. Also, pharmacological treatment can be offered to elderly patients (younger than 80 years) with SBP 140-159 mm Hg. c. if they tolerate it well. Treatment starts with a combination of two antihypertensive drugs that are recommended at greatly elevated blood pressure (SBP ≥160 mm Hg. In.), and in patients with moderately elevated blood pressure (SBP ≥140 mm Hg. In.), but with high cardiovascular risk. Combined treatment gives better control of blood pressure in many patients. In addition, patients prefer combined therapy much higher than monotherapy. The list of the best combinations of antihypertensive drugs includes those who have proven their advantages in large randomized trials: 1. ARA + diuretics + ACEI 2. 3. ARA + diuretics, calcium antagonists, ACE-I + 4. 5. calcium antagonists Calcium antagonists + diuretics.

It`s necessary to provide antihypertensive treatment to pregnant women with severe hypertension (SBP> 160 mm Hg. Art. Or DBP> 110 mm Hg. In.). In this case the preference should be given to methyldopa, labetalol and nifedipine. For urgent reduction of blood pressure in preeclampsia intravenous labetalol or nitroprusside is recommended.

The recommendations of the ESH / ESC 2013 changed the target levels of blood pressure in patients with diabetes, that are defined at the level of <140/90 mm Hg. c. In hypertensive patients with diabetes can be used all classes of antihypertensive drugs, with the preferred RAAS blockers, especially in patients with proteinuria or microalbuminuria. Assignment of two blockers of the RAAS is not recommended.

**Conclusions.** In the approach of treatment recommendations the beginning of antihypertensive therapy, target BP level and liberalized approach to the selection of initial monotherapy were changed, scheme priority combinations of antihypertensive drugs was revised. We propose a new algorithm for a long-term care and blood pressure control achievement, advance recommendations for the treatment of hypertension in different clinical situations including elderly patients and patients with resistant hypertension.

# ORAL ANTIDIABETIC DRUGS

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Type 2 diabetes is a global public health concern, its prevalence in Europe, especially Ukraine, rising every year. Type 2 diabetes mellitus is a progressive and complex disorder that is difficult to treat effectively in the long term. The majority of patients are overweight or obese at diagnosis and will be unable to achieve or sustain near normoglycaemia without oral antidiabetic agents; a sizeable proportion of patients will eventually require insulin therapy to maintain long-term glycaemic control, either as monotherapy or in conjunction with oral antidiabetic therapy. Drugs used in diabetes treat diabetes mellitus by lowering glucose levels in the blood. With the exceptions of insulin, all are administered orally. There are different classes of anti-diabetic drugs, and their selection depends on the nature of the diabetes, age and situation of the person, as well as other factors. Diabetes mellitus type 2 is a disease of insulin resistance by cells. Type 2 diabetes mellitus is the most common type of diabetes. Treatments include agents that increase the amount of insulin secreted by the pancreas, agents that increase the sensitivity of target organs to insulin, and agents that decrease the rate at which glucose is absorbed from the gastrointestinal tract. The main classes are heterogeneous in their modes of action, safety profiles and tolerability. These main classes include agents that stimulate insulin secretion (sulphonylureas and rapid-acting secretagogues), reduce hepatic glucose production (biguanides), delay digestion and absorption of intestinal carbohydrate (alpha-glucosidase inhibitors) or improve insulin action (thiazolidinediones). Today proved the benefits of intensified glycaemic control on microvascular complications in newly diagnosed patients with type 2 diabetes. The most promising direction control hyperglycemia yalyaetsya use of complex oral antidiabetic drugs. The recent clinical trial Steno-2 Study showed that intensive target-driven, multifactorial approach to management, based around a sulphonylurea, reduced the risk of both micro- and macrovascular complications in high-risk patients. The insulin-sensitising thiazolidinedione class of antidiabetic agents has potentially advantageous effects on multiple components of the metabolic syndrome; the results of clinical trials with cardiovascular endpoints are awaited. Combinations of certain agents, for example a secretagogue plus a biguanide or a thiazolidinedione, are logical and widely used, and combination preparations are now available in some countries. Clinically effective are combination metformin added to a sulphonylurea. Promising direction of diabetes therapy is to create a comprehensive anti-diabetic drugs.

# PHARMACEUTICAL CARE OF PATIENTS TAKING FLUOROQUINOLONES

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Fluoroquinolones (FQ) recently, but quickly took leading positions in sales due to the high germicidal power and broad-spectrum. Therefore, patients who are prescribed fluoroquinolones should be aware of and adhere to the principles of rational use of this group of drugs.

In the appointment and the reception FQ must follow these rules:

-To patients under 18 years are appointed only in case of exciter resistance to other chemotherapeutic drugs.

- When long-term therapy requires regular monitoring of peripheral blood and the functional state of of indicators liver and kidney.

- Older patients or patients with hepatic dysfunction is recommended to to conduct a thorough medical supervision.

- During the period of the week before the of treatment, during treatment and within at least 3 days from the end should avoid prolonged of sun exposure or of artificial actions of UV radiation due to the possibility of the occurrence photosensitization.

- Patients who engaged in potentially hazardous activities that should be applied with caution because of a possible of vertigo, especially early in treatment.

- Be used with caution FQ patients with diseases known or suspected CNS disorders.

- Preparations of quinolones at intake need to drink a full glass of water. Accept no less than 2 hours before or 6 hours after antacids and preparations of iron, zinc, bismuth.

- During the period of of treatment is sufficient to comply with the water regime (1.2-1.5 l / day).

- Strictly observe the schemes and regimes of treatment during the whole course of therapy, not to skip a dose and take it at regular time intervals. If you miss a dose take it as the soon as possible; not to accept if almost time for your next dose; do not double the dose. Withstand prolonged therapy.

- Do not use preparations of expired.

- Consult the with your doctor if improvement does not occur within a few days or new symptoms appear. At occurrence the pain in the tendonsshould consult a doctor.

If the pharmacist will use this algorithm when with talking patients who are prescribed FQ, will enhance the effectiveness and safety of drug therapy.

# TYPE 2 DIABETES IN UKRAINE: CLINICAL GUIDELINES AND PRACTICAL REALITY

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According to international statistics, the World Health Organization (WHO), the National Health Systems, professional associations and the International Diabetes Federation (IDF Diabetes Atlas) type 2 diabetes is one of the most widespread endocrine diseases all around the world (382 million patients in 2013) and in European countries (52.8 million patients, the average prevalence is 8.1%). WHO further projects diabetes will become the seventh leading cause of death in 2030.

According to the Center of Medical Statistics of the Ministry of Health of Ukraine as at 01.01.2014 has been registered more than 1.3-million patients with diabetes (9% of the adult population aged 18 and older), among them – 90% of patients with type 2 diabetes. Constantly progressive increase in number of people with type 2 diabetes, gives reason to call this disease «Noninfectious epidemic of the 21st century». A modern therapeutic strategy of treatment of diabetes has been directed at the most effective prevention of progression of the disease and its complications and achievement of the maximum disease control. For this purpose in EU countries decision on creation of an integrated registry of patients with diabetes was taken in March 2012. This registry includes data collection, monitoring, complications and costs of treating patients with diabetes. The project was named EUBIROD (European Best Information through Regional Outcomes in Diabetes). The Ministry of Health of Ukraine has planned to begin creating an integrated Ukrainian registry of patients with diabetes already in the 2015. Ratification of «Unified Clinical Protocol of primary and secondary (specialized) medical care «Type 2 diabetes» has become one of the most significant steps in the unification of medical care for patients with type 2 diabetes in Ukraine (Order of the Ministry of Health of Ukraine № 1118, 21 December 2012).

Estimate of conformance of drug therapy in patients with type 2 diabetes to recommendations of «Unified Clinical Protocol» was the purpose of this study.

Materials and Methods. The practical part of this study was conducted in collaboration with Scientific and Practical Medical Center of Kharkiv National Medical University «University Hospital» (Department of metabolic disorders). Retrospective analysis of 83 medical histories of patients with type 2 diabetes (primary clinical diagnosis) was made by us. All patients were hospitalized in the department of metabolic disorders in January – March 2015.

Results. 7 groups of oral hypoglycemic drugs (OHGD) have been registered and used in Ukraine. All of them have been presented in «Unified Clinical Protocol». These are sulfonylurea derivatives, biguanides, thiazolidinediones, meglitinides, inhibitors α – glucosidase, glucagon-like peptide-1 (GLP-1) agonist – incretin mimetics, DPP-4 inhibitors. A new group of OHGD has been registered in Ukraine not long ago (in late 2013). They are called oral sodium glucose cotransporter type 2 (SGLT2) inhibitors. This group is not included in the «Unified Clinical Protocol» in the absence of substantial evidence base and is a second-line therapy.

Listed below results have been gotten after the analysis of medical histories. Patients with type 2 diabetes of moderate severity (75%) and severe (25%) were treated with OHGD and insulin preparations that are registered in «Unified Clinical Protocol».

The drug from the group of sulfonylurea derivatives Glimepiride was administered most often – in 45%. Glimepiride was administered as monotherapy (in 10%) or in combination with Metformin (in 33%) and only 2% in the form of fixed combination (Tripride – Glimepiride, Pioglitazone, Metformin). Gliclazide is second in frequency of prescribing (20%). Gliclazide was administered as monotherapy (in 3%) or in combination with a Saxagliptin, Vildagliptin, Sitagliptin (in 2%), in combination with Metformin (in 15%). Glibenclamide was administered as a fixed combination with Metformin (Glibomet, Glukovance, Glibofor) in 5%. DPP-4 inhibitors was administered in 13%, in which connection drugs of this group were administered as monotherapy in 4% (Saxagliptin, Vildagliptin, Sitagliptin) or in form of fixed combination with Metformin (Janumet, Galvus Met, Kombiglyze). Dapagliflozin (SGLT2 inhibitors) as second-line monotherapy was administered in 1.2%. Insulin therapy was administered in 15.8% due to severe type 2 diabetes as a combination with Glimepiride, Metformin and in a fixed combination (Glibomet, Kombiglyze).

Conclusions. According to international recommendations Metformin and/or DPP-4 inhibitors are first-line drugs in the initial therapy, as in the debut of type 2diabetes, and at any stage. In prescription of two drugs preference should be given to benefit of fixed combinations. On the Ukrainian pharmaceutical market, such combinations have been presented in sufficient quantities. A combination of several drugs in one dosage form significantly simplifies the use of the drug regime and leads to increase of compliance of the patient to therapy and allows support long-term glycemic control, preventing the progression of diabetes and development of complications. Another important factor is reduction of cost of treatment. All this eventually will lead to an improvement of the life quality of patients with type 2 diabetes.

# CLINIC AND METABOLIC EFFECTS OF LOSARTAN VERSUS CANDESARTAN IN PATIENTS WITH METABOLIC SYNDROME

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Metabolic syndrome is a disorder includes three out of five of the following medical conditions: abdominal obesity, hypertension, impairment of glucose metabolism due to insulin resistance and dyslipidemia. The number of such patients is increasing every year, which initiated the question of the choice of the antihypertensive agent, which will have not only antihypertensive effect, but also have a positive metabolic effect.

**The aim of our research** was to investigate the effects of losartan and candisartan (angiotensin II receptor antagonist) on Blood pressure and serum uric acid in hypertensive patients with metabolic syndrome.

**Material and Methods.** We studied 44 Case History of newly diagnosed mild hypertensive patients, having markers of metabolic syndrome. The hypertensive patients were divided into two groups. Group 1 (22 patients) was given losartan (50 mg/ day) and group 2 (22 patients) candesartan (8 mg/ day) for a duration of 2 months. Metabolic syndrome was diagnosed according to diagnostic criteria of metabolic syndrome related to the American National Cholesterol Education Program-Adult Treatment Panel III.

**Results.** We have investigated significant antihypertensive effect of losartan and candesartan. The level of blood pressure were in group 1 before treatment 143.60 ± 7.72/ 92.18 ± 6.21 mm Hg and after 2 month treatment by losartan it become 136.82 ± 8.4/ 83.92 ± 6.3 mm Hg ($p<0.001$). The level of blood pressure were in group 2 before treatment 145.78 ± 5.39/ 91.44 ± 6.15 mm Hg and after 2 month treatment by candesartan it become 136.82 ± 8.4/ 86.07± 5.0 mm Hg ($p<0.001$). Significant drop of uric acid was noted after treatment with losartan but not with candesartan. The level of uric acid in group 1 before treatment was 306.69 ± 67.72 mmol/L, after losartan treatment it was 275.92 ± 61.63 mmol/L ($p<0.001$). The level of uric acid in group 2 before treatment was 302.94 ± 56.86 mmol/L, after candesartan treatment it was 289.99 ± 50.28 mmol/L ($p=0.132$(NS)).

**Conclusions:** Losartan can be useful therapeutic agent to control blood pressure and to reduce serum uric acid level in hypertensive patients having markers of metabolic syndrome and hyperuricaemia.

# CLINICO-PHARMACOLOGICAL APPROACHES TO TREATMENT OF ANEMIA IN PREGNANT WOMEN IN ANTENATAL CLINICS

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For many countries, anemia is a medical and social problem, since it leads to a violation of a condition of patients, reducing their efficiency and causes functional changes in the organs and systems of the body. Of particular importance, this problem gets during pregnancy, due to the high rate of pregnancy complications.

**Objective:** To analyze the clinical and pharmacological action of oral iron drugs used for anemia in pregnant women's clinic.

**Methods:** To conduct a clinical assessment 57 women attended the antenatal clinic Outpatient Department The Scientific Center Kharkov National Medical University about anemia in pregnant women. In a retrospective analysis took into account the action of drugs that are administered in case of anemia in pregnant women. Drugs of choice are two drugs ferrous iron. "Sorbifer Durules" - a combination of iron and ascorbic acid. "Gino - Tardiferon" - iron complex preparation of prolonged action that restores iron deficiency and folic acid in the body. Thanks to the combined composition, they significantly increase the concentration and maintain long serum iron, have fewer side effects.

**Results:** As a result of treatment in 49 pregnant women showed a significant increase in hemoglobin in the clinical analysis of blood. The high content of ferrous iron in these preparations, their high therapeutic efficacy and good tolerability with minimal side effects allow us to recommend them in terms of standards of proof-based medicine for the treatment of anemia in pregnant women in outpatient conditions.

**Conclusions:** Clinical and pharmacological properties of oral preparations containing ferrous iron and recommended the Ministry of Health of Ukraine have significant pharmacodynamic efficiency, lower incidence of side effects and have advantages over other dosage forms.

# THE INFLUENCE OF GLUCOSAMINE DERIVATIVES ON APOPTOSIS OF CELLS IN EXPERIMENTS

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Today, apoptosis has an essential role in both physiological and pathological processes. In many cases, apoptosis is initiated by radiation, oxidative stress, viral infection, the influence of chemical agents including various medicines. However, in the literature there are reports on the possibility of regulation of apoptosis by various substances of synthetic and natural origin, in particular natural metabolites of the organism which include glucosamine.

The aim of our study was to investigate the effect of combinations of glucosamine derivatives with quercetin and ketoprofen on apoptosis of cells in experiments on rats.

The influence of combination of derivatives of glucosamine with quercetin on hepatocytes apoptosis was studied in doxorubicin-induced liver damage in rats. Experiment was carried out on 18 mongrel white rats weighing 200-250 g. Animals were divided into 3 groups with 6 animals: group 1 – intact, group 2 – control animals received single i.p. doxorubicin (DOX) at a dose of 10 mg/kg body weight on $8^{th}$ day of the experiment, 3 group were the rats that received combination aminosugars GA h/ch and N-acetylglucosamine with quercetin at a ratio of 3:1 in recolculation on GA h/ch (CA+Q) in conventionally-therapeutic dose of 82 mg/kg daily per os during 10 days. At the end of the experiment, tissue samples of liver were taken for further immunohistochemical study. Assessment of apoptosis in liver micropreparations was performed for quantification bcl-2 positive cells (containing the anti-apoptotic protein bcl-2) per 1000 hepatocytes and expressed by ‰.

It was found that administration of DOX in dose 10 mg/kg to rats leads to significant increased expression of the antiapoptotic protein bcl-2, as evidenced by increased number of bcl-2-positive cells with respect to the group of intact animals and agreed with the literature data. Although the antineoplastic antibiotic doxorubicin is inducer of apoptosis, such changes can be explained starting compensatory mechanisms of cell protection on administration of cytotoxic agent. Preventive administration of CA+Q to animals with DOX increase the number of bcl-2-positive hepatocytes and increased expression of anti-apoptotic protein bcl-2 relative to the control pathology group, and these changes were not statistically significant

difference. It was testifies to the mobilization of protective reserves of cells under the influence of CA+Q and causes anti-apoptotic effect in a cytotoxic lesion.

Also derivatives of glucosamine improves the metabolism of cartilage. These compounds are a substrate for the synthesis of glycosaminoglycans, stimulates the synthesis of proteoglycans. Despite the high chondroprotective activity of derivatives of glucosamine it should be noted the lack of efficacy of this group on anti-inflammatory and analgesic effect, which somewhat limits the possibilities of their use in patients with osteoarthritis (OA).

Today the most promising direction is the development of third generation chondroprotective drugs based on combinations derivatives of glucosamine with drugs of other groups (non-steroidal anti-inflammatory drugs (NSAIDs), vitamin, micronutrients, etc.). This can significantly extend the pharmacodynamics derivatives of glucosamine.

The resulting combination drug influences on the several pathogenic links of destructive-dystrophic lesions of cartilage. The study of the combination of glucosamine hydrochloride and ketoprofen as a topical dosage form was carried out on a model of systemic steroid osteoarthritis (SSOA) in rats. The object of the present research was glucosamine hydrochloride and ketoprofen combination in the form of a cream-gel (G\K cream-gel). Fastum gel 5%, glucosamine cream gel 5% were used as a comparison agents that were applied in a similar way with equivalent therapeutic dose of 50 mg. The 60 white male rats aged 4-5 months, weighing 250-300 g. had been used in the study.

The rats were divided into 5 experimental groups. Experimental osteoarthritis was reproduced by three times intramuscular injections in the thigh muscle of dexamethasone in a single dose of 7 mg / kg at intervals of 1 week. In the study of the ultrastructure of articular cartilage in rats standard methods of electron microscopy were used. In the study of the ultrastructure of rat articular cartilage pathology in the control pathology group were observed micropreparations expressed degenerative-dystrophic changes corresponding to the development of OA. Most micropreparations chondrocytes found in various stages of the so-called "dark-cell" death. Its main sign is full heterochromatization cell nucleus. Information from literature indicate that the described "dark" cells are exposed apoptosis. Unlike the control pathology group in ultrastructure of cartilage of animals treated with G\K cream-gel, were not observed "dark" cells, with signs of classical apoptosis.

The obtained results could detailed view of the mechanism of action of glucosamine derivatives, which are caused by the presence of a regulating effect on apoptosis.

# THE MAIN ITEMS ON DIAGNOSIS AND TREATMENT OF ASIDEROTIC ANEMIA IN CHILDREN

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**Actuality.** According to epidemiological researches nowadays 35-45% of grown-ups and 40-48% of children suffer from latent lack of iron and asiderotic anemia. Asiderotic anemia remains one of the mostly common forms of anemia in childhood, forming 80-90% of all kinds of anemias. According to this fact the elaboration of modern programmes of diagnosis, treatment and prophylaxis of ironlacking states is an extremely urgent task.

**Results.** A healthy worn out new-born child has enough reserves of iron for maintaining a normal growth until 4 months. Most children do not have the symptoms of ironlacking until the moment of forming of the asiderotic anemia. For all that even if children have, as a rule, anemia of mild case (Hb=100-90 г/л), they cannot have symptoms of the disease, and the exposure of anemia represents an accidental find (godsend, windfall).

It is well-known that if kids have the lack of iron, it may lead not only to asiderotic anemia but also to the delay of the mental development, which is accompanied by the breach of cognitive, motive and socially-emotional development. The ironlacking leads also to the breach of immunity which can be revealed through the raising in 3-4 times of virus influenza and intestinal diseases, lingering and after-effect flow of bacterial infections. There are facts which show that the vaccination of children who has the lack of iron can be ineffective until carrying out the course of irontherapy.

The reasons of infants and older children's asiderotic anemia are different.

The common causes of infants are: prenatal iron deficiency (placental abruption, premature birth); insufficient intake of iron in the body (defects of feeding, milk intolerance); blood loss (tumors, abnormalities of the gastrointestinal tract); violation of iron transport (hypo- and atransferrinemiya).

The older children's causes are hemorrhage (gastrointestinal pathology, helminth infections, endometriosis, thrombocytopathy, coagulopathy); endocrine

diseases (hypothyroidism, ovarian disfunction); hematuria; tuberculosis; violations of iron transport ;, extracorporeal therapies, nutritional deficiency.

The diagnosis of asiderotic anemia should be based on history, physical examination and laboratory studies. Nowadays the main method of determining iron deficiency is a common clinical blood test that can be done in 2 ways: manual and automatic. However, modern diagnostic programs require a broader range of indicators:

- for the evaluation of erythropoiesis it is necessary to count the erythrocytes in the peripheral blood, to determine the concentration of hemoglobin, the content of Hb in erythrocyte (MCH), mean corpuscular volume (MCV) and to a study a bone marrow and cytochemical iron identification;

- the assess of the ability of serum to transport iron should be carried out on the content of serum transferrin and transferrin saturation percentage, based on the total iron-binding capacity of serum;

- it is also necessary to determine the content of serum iron and serum ferritin;

- modern diagnosis also requires determining of the absorption in the bowels with the help of diagnostic $59Fe^{2+}$ -absorbtion test**.**

The treatment of iron deficiency states includes the elimination of iron deficiency and the restore of its reserves in the body. To do this, on the one hand it is necessary to eliminate the causes that led to the development of the IDA, and the other - to carry out compensation of iron deficiency in the body.

IDA therapy should be carried out mainly by preparations for oral taking, as the dynamics of increase in hemoglobin levels when administered orally is behind parenteral taking only 2-4 days.

Abroad, particularly in the US, by the detection of infants anemia iron therapy at a dose of 3 mg / kg for a month is conducted**.** The increased hemoglobin of 10 g / l by the end of the month of therapy is the convincing evidence of the patient's IDA and justifies the continuation of therapy, the duration of which depends on the severity of anemia. It must be remembered that the normalization of hemoglobin levels cannot justify the abolition of iron supplementation.

**Conclusions.** Modern, correct and timely laboratory diagnosis and nosological diagnosis (the identification of the causes) is the key to the effective treatment of the most common syndrome of anemia - IDA.

# SECTION № 10

# MODERN PHARMACOTHERAPY

# PHARMACOTHERAPY PLAGUE

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Plague - an acute infectious disease characterized by severe general condition of the patient, inflammation in the lymph nodes, lungs and other organs.

The highly contagious and very high mortality provided the basis attributed to plague especially dangerous, quarantine infections. For the plague is characterized by epidemics and pandemics with a very high mortality rate.

The disease is quite specific and less common, but due to the fact that the plague is to quarantine infections, the development of effective pharmacotherapy remains relevant in today's world.

Patients plague subject hospitalization in a special plague hospital. Treatment of patients should be integrated with the inclusion etiotropic and detoxification therapy.

Antibiotic therapy is prescribed to laboratory confirmation of the diagnosis. The main drugs for the treatment of all forms of plague are: streptomycin use to 1.0g, intramuscular or intravenous for 7-14 days; gentamicin to 5 mg / kg body weight, intramuscular or intravenous for once a day for 10 days; Doxycycline use to 200 mg followed by 100 mg 2 times a day for 10 days; Chloramphenicol (alternative drugs) use to 25 mg / kg body weight every 6 hours for 7 days. Alternative, modern drugs, is levofloxacin. Levofloxacin use to 500 mg once a day for 7-14 days.

To decrease intoxication and hemodynamic disorders use intravenous drip solutions, Ringer-Locke "Trisol", "Kvartasol", 5% glucose solution, hydroxyethyl starch (HES) derivatives (ionosteril). These solution administer bolus to recovery heart rate and blood pressure, and after the elimination of acute vascular insufficiency - drip.

If the introduction of therapeutic solutions in the vein cannot normalize blood volume and development of infectious-toxic shock, further added catecholamines (epinephrine, norepinephrine, mezaton) and glucocorticoids (100-150 mg of prednisone of other drugs). Infusion use with speed 40-60 drops per minute until complete and permanent eradication of acute vascular disorders.

Convalescents with bubonic plague, is discharged from the hospital or after 4 weeks from the date of clinical recovery, after two (5-6 days) control puncture buboes with negative results when bacteriological examination punctate.

For the pneumonic form of plague recovering discharged under normal chest radiograph and the presence of a normal body temperature for 6 weeks, and after three negative sputum-smear and mucus from the throat, held every two weeks. Also use vaccination.

Plague vaccination is of limited use and is not mandatory for entry into any country. The vaccine is not effective against the pneumonic form of plague. Plague vaccine is recommended for field workers in endemic areas and for scientists and laboratory personnel who routinely work with the plague bacterium.

# FIRST AID IN ELECTRIC SHOCK

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Electrocution is a violation of the anatomical relationships and functions of tissues and organs, accompanied by local and general reaction of the body, caused by the action of an electric current. The result of electric shock to persons affected by many factors. The most important are the magnitude and duration of the current generation, and frequency of the current and the individual properties of the organism.

The first necessary aid activities with electrical accident is the elimination of the current action on the body. To do this, turn off the power supply. When providing first aid for electrical accident should be to abide by the rules-saving electrical safety. After a preliminary dead must pull the victim of clothing at a safe distance. After the liberation of victims of the electric current necessary to call an ambulance. Assess the condition of the victim: to assess the state of consciousness, breathing and circulation. For this it is necessary to determine the magnitude and pupillary response to light them, and to identify the pulse in the carotid artery. If the victim is unconscious but breathing and pulse is present, it must be given the position of "lying on its side," control pulse and breathing before arrival of "first aid". If the victim is not breathing and consciousness, but is determined the pulse of the carotid artery it is need to start urgent mechanical ventilation. In the absence of the victim consciousness, breathing and carotid pulse embarking on cardiopulmonary resuscitation. Performance criteria in cardiopulmonary resuscitation are the following: the emergence of the carotid pulse; restoration of respiration; the appearance of the reaction of pupils to light. When the effective conduct of cardiopulmonary resuscitation affected attach a stable position "lying on its side," sheltering veil and holding control of breathing and heart rate before the arrival of the ambulance. Upon detection electrical burns impose a dry aseptic bandage. In a matter of urgency with electrical transport the victim to a hospital.

Thus, the timely provision of first aid at electrical accident will help save the lives of the victims.

# PHARMACOTHERAPY OF GENITAL HERPES

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Genital herpes is an infectious disease caused by the herpes simplex virus (HSV) type 1 or 2. HSV is well distributed worldwide. According to WHO Genital herpes takes third place among the diseases, sexually transmitted diseases. Half a billion people worldwide are infected with herpes simplex virus type 2, which causes genital herpes. With almost 24 million new cases recorded annually. The disease occurs in all population groups, with the highest incidence was registered in the age groups 20-29 and 35-40 years. Deaths from herpes infections in second place in the structure of mortality from viral diseases and is 15.8%.

The goals of pharmacotherapy are to reduce morbidity and to prevent complications. Medical treatment of HSV infection is centered around specific antiviral treatment. Among the group of antiviral drugs recommended nucleosides and nucleotides, except reverse transcriptase inhibitors. Pharmacotherapy is carried out depending on the course of genital herpes. The drug is administered orally or parenterally depending on the severity of the disease. First episodes of genital herpes are frequently associated with a prolonged disease course. In view of the potential for more severe disease, prompt treatment with aciclovir 400 mg orally, 5 times daily for 7 to 10 days is recommended. Alternative regimens are valaciclovir 1 g orally twice daily for 5 to 10 days or famciclovir 250–750 mg orally 3 times daily for 10 days. In patients with severe cutaneous disease or systemic complications, aciclovir 5–10 mg/kg IV every 8 h should be considered. For treatment recurrent Genital Herpes recommended regimens for suppressive antiviral therapy include: aciclovir 400–800 mg orally 2 or 3 times a day; valaciclovir 500 mg orally twice daily; or famciclovir 500 mg orally twice daily. Systemic therapy with either IV foscarnet 40 mg/kg bd or tid IV has been shown to be effective for aciclovir resistant strains with the length of therapy depending on treatment response. In rare cases with aciclovir and foscarnet resistance cidofovir topically or IV 5 mg/kg weekly infusion is the preferred agent.

Thus, the modern pharmacotherapy of genital herpes will significantly reduce the number relapses of the disease.

**RATIONAL PHYTOTHERAPY OF PEPTIC ULCER**

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Peptic ulcer and duodenal ulcer are the leading pathologies of the gastrointestinal tract diseases. A large number of modern drugs do not solve the problem of successful treatment of peptic ulcer disease, highlighting the problem of relapses. Despite the high efficiency, synthetic drugs have a number of side effects, which reduces their tolerance as well as the results of treatment of peptic ulcer. Therefore, the attention today is given to phytomedicines.

Herbal medicines can be administered continuously for a long time without the risk of complications. They positively effect on the diseases of gastrointestinal tract as well as on the symptoms of nervous system disorders. The importance of this fact becomes clear if we remember that peptic ulcer diseases are often combined with nervous and cardiovascular disorders. These systems are interconnected and disorder of the first leads to disorder of the second.

Plants contain biologically active substances, which therapeutic effect is many-sided. Biologically active substances that affect on the gastrointestinal tract show anti-inflammatory, reparative, covering, antioxidant, membranestabilizing, antimicrobial effects, which explain the expediency and pathogenetic reason of their use in the treatment of peptic and duodenal ulcers.

In the basis of the anti-inflammatory effect of astringents is their ability to form films with mucus proteins on the surface of the mucous membrane of the stomach. These films play a protective role, and have vasoconstrictive effect, reducing local inflammation.

To prevent possible complications, especially bleeding administration of hemostatic drugs is required. Spasmolytic effect of medicinal plants is widely used as symptomatic remedy for spasm elimination in different parts of the gastrointestinal tract.

Taking this into account, medicines are created on the base of these biologically active drugs (for example, liquiriton, flacarbin, biogastron, alanton, quercetin et al.). However, the limited range of these medicines explains the need for the development and creation of new phytomedicines to treat peptic and duodenal ulcers.

# FIRST AID AND PHARMACOTHERAPY OF HYPERTENSIVE CRISIS

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Hypertensive crisis is a clinical syndrome of sudden uncontrolled rise in blood pressure, leading to progressive dysfunction of target organs or a real risk of its development, as well as to the appearance of neurovegetative disorders. Under these conditions, blood pressure must be reduced by more aggressive course of a few minutes to several hours. On January 1, 2011 in Ukraine there are more than 12 million. Hypertensive patients, accounting for about 32% of the adult population. According to information of Medscape due to the appearance antihypertensive agents, the incidence of hypertensive crises decreased from 7% to about 1% of patients with arterial hypertension. In addition, the survival rate for 1 year increased by more than 90%.

The main activities of first aid are the following: it is necessary to put the patient in a comfortable position with the head slightly raised and lowered feet; to measure blood pressure. Call to local emergency department. Provide a complete psychological comfort, do not allow the patient to move independently to reduce the load on the myocardium. Find a medication that the patient takes before, find previous patient's ECG and show HCP team ambulance. All patients with suspected hypertensive crisis, regardless of gender, age and other factors to be urgent hospitalization. Transportation carried out on a stretcher after stabilization of the patient.

List of drugs that are recommended for the relief of hypertensive crises are somewhat different in the European and Ukrainian guidelines.

Comparative recommendations for relief of hypertensive crises according to the European and Ukrainian guidelines.

| Group of medications | Medication (European guidelines) | Medication (Ukrainian guidelines) |
|---|---|---|
| Vasodilators | Sodium nitroprusside, hydralazine, itroglycerine | Nitroglycerine |
| B-blokers | Labetalol, esmolol | Propranolol |
| Calcium channel blockers | Klevidipin, nicardipine | Nifedipine |
| ACE inhibitors | Enalaprilat | Captopril |

Thus, we see that the European guidelines recommended the use parenteral forms of drugs with rapid onset of action and a short half-life.

# HYPERTENSION PATIENTS CARBOHYDRATE METABOLISM DISORDERS AFFECTED BY OBESITY

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Obesity affects the overall morbidity and mortality rates, and the reason of such consequences recorded in more than 10% of the cases, is associated with high risk of cardiovascular complications and mortality. Overweight and obesity have become the reasons for the increasing number of patients with diabetes, hypertension, coronary heart disease.

**The purpose of the research. To study** hypertension patients carbohydrate metabolism disorders affected by obesity

**Materials and methods.** 47 patients with essential hypertension (HTN) were examined, including 35 (74,5%) patients with obesity and 12 patients (25,5%) without obesity. The age of patients ranged from 30 to 67 years (average age 51, 17 ± 1,35 years). There were 19 men and 28 women examined. HTN duration ranged from six months to 35 years, the average increase in blood pressure was about 8,2 ± 0,67 years. A study of anthropometric indexes changes (body mass index, waist and hips and their relationship), hemodynamic and metabolic parameters (fasting blood glucose, HbA1s) was held. The presence and degree of obesity was assessed by body mass index (BMI (kg / $m^2$) = weight (kg) / height ($m^2$)). Patients were examined comprehensively, including general clinical and additional methods. Glucose was determined by glucose oxidase test.

**Obtained results.** It was proved that the average BMI was statistically higher in HTN patients with obesity compared to the group of HTN patients without obesity. Insulin concentration increased sustainably ($p < 0,05$ in all cases), but in patients with the 3rd degree of obesity it decreased slightly, however, it was significantly different from the group with the standard body weight ($p < 0,05$). Glycated hemoglobin rate in compared groups was significantly elevated in the 1-3 rd obesity degrees ($p < 0,05$ in all cases). Fasting glucose rate was characterized by a similar growth trend in obesity groups, the highest indicator was marked in patients with obesity of the 3rd degree ($p < 0,05$ in all cases). IP Index – NOMA probably increased significantly in patients with varying degrees of obesity.

**Summary.** HTN patients have carbohydrate metabolism disorders along with increasing degree of obesity. This results in hyperinsulinemia, increased rates of glucose and glycated hemoglobin, and in increased insulin resistance (according to the increase in HOMA index).

# STRONTIUM RANELATE IN TREATMENT OF POSTMENOPAUSAL OSTEOPOROSIS

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Increased interest in osteoporosis is mainly caused by high incidence of the disease and its consequences, such as peripheral bone and vertebral fractures, which cause temporary incapacity, disability, and increased mortality in the population.

The question of osteoporosis medical treatment remains relevant despite the large variety of approved medications. Side effects and poor adherence to long-term therapy are the main reasons of anti-osteoporosis treatment low efficacy.

In the last decades this problem became increasingly important due to closely related two demographic processes: dramatic increase of elderly and senior people in the population, in particular, women in the postmenopausal period. Approximately in every third woman over 65 years at least one fracture is observed. Femoral fractures lead to decrease of the average life expectancy by 12-15 %.

The aim of osteoporosis pharmacotherapy is to prevent fractures and their consequences, as well as ensure mobility and quality of patient's life. Pharmaceutical preparations should possess the ability to enhance bone formation, inhibit bone resorption, or act on both mechanisms of bone tissue remodeling, as well as calcium homeostasis.

Since 1990s numerous experiments and latter clinical trials appeared and showed that strontium salts taken as bone-stimulating agent have antiresorbtive effect, while strontium ranelate (medical drug based on strontium and ranelic acid) can reduce the risk of fractures in postmenopausal osteoporosis.

Bivalos (strontium ranelate) is an effective drug in treating postmenopausal osteoporosis and preventing the risk of both vertebral and extravertebral fractures. It significantly improves the bone mineral density, has a double effect on bone remodeling by stimulating new bone formation and reducing the rate of bone resorption, and increases the bone strength. Strontium ranelate results in an increase of trabecular bone mass, number of trabecule and their thickness, and improves mechanical properties of bone.

Bivalos is administered in a dose of 2 g (one sachet) once a day. Before administration the sachet content should be dissolved in glass of water to form a homogeneous suspension. It should be taken immediately after preparation.

Bivalos is safe at long-term treatment, does not affect bone mineralization and crystal lattice structure, is well tolerated by patients, easy to use, and provides high level of adherence to treatment.

# PHARMACOTHERAPY OF SALMONELLOSIS

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Today in Ukraine marked a growth of intestinal infections, especially salmonella. This topic is relevant, because the highest share of group of diseases accounted for salmonella. Thus, statistically, children often suffer up to 2 years.

Salmonellosis - an acute infectious disease caused by bacteria of the genus Salmonella and accompanied by symptoms of gastroenteritis and intoxication. The source of infection are often domestic and wild animals, waterfowl, patients and bacteria. Transmitted by the fecal-oral route.

Salmonella gastrointestinal infections usually resolve in 5-7 days and most do not require treatment other than oral fluids. Persons with severe diarrhea may require rehydration with intravenous fluids. Antibiotic therapy can prolong the duration of excretion of non-typhoidal Salmonella and is recommended only for patients with severe illness or those at risk of severe disease or complications, including young infants, older adults and immunocompromised persons. Antibiotic resistance is increasing among some Salmonella bacteria; therefore, susceptibility testing can help guide appropriate therapy. Antibiotic therapy consists of initial preparations (nifuroxazide, ceftriaxone, cefotaxime) and reserve drugs (trimethoprim, ciprofloxacin, chloramphenicol, azithromycin), assisted therapy is divided into enterosorption, with a predominant use of aluminosilicate sorbents (smecta), probiotics drugs that have some kind of normal microorganisms (lineks forte, bifiform) and enzyme (pancreatin, festal).

Emerging drug resistance over the past 20 years has limited the usefulness of these antibiotics. Unfortunately, sensitivity to quinolones has been steadily declining, and these are no longer fool-proof agents for typhoid fever. A growing rate of resistance of nontyphoidal salmonella to nalidixic acid and ceftriaxone has been reported.

Azithromycin is likely to be the preferred empirical treatment, often given together with ceftriaxone, in developed countries where chloramphenicol is usually reserved for life-threatening situations, for which no alternatives are available, and physicians are reluctant to use fluoroquinolones in children and lack easy access to gatifloxacin.

Treatment of salmonella infection in pregnancy is controversial, and antibiotic therapy should be reserved for cases of invasive disease, using amoxicillin or cephalosporin. Non-specific prevention lies in the implementation of veterinary and sanitary and anti-epidemic measures, conduct health education among the population.

Specific prevention involves vaccination.

# PHARMACOTHERAPY OF TUBERCULOSIS

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Tuberculosis (TB) is an infectious disease caused by a pathogen - Mycobacterium tuberculosis, which is characterized by the formation of specific granulomas in various organs and tissues in combination with nonspecific reactions and polymorphic clinical picture, depending on the shape, phase, location and prevalence of pathological process.

The problem of TB disease is very important in our world now, because it's one of the most common diseases. According to statistics, every third person is infected; TB mortality is 20% of the morbidity. There are two forms of TB: pulmonary and extrapulmonary tuberculosis.

The goals of TB treatment are to shorten the clinical course of TB, prevent complications, prevent the development of latency and/or subsequent recurrences, and decrease the likelihood of TB transmission. In patients with latent TB, the goal of therapy is to prevent disease progression. The development of new drugs and methods of treatments will allow treat the latent, active and multidrug-resistant forms of tuberculosis.

Currently TB treatment is equally possible as inpatient and outpatient. Treatment starts with causal treatment of the anti-TB drugs of first line, which are the most effective.

New cases are initially treated with four drugs: isoniazid, rifampin, pyrazinamide, and either ethambutol or streptomycin. After 2 months, they are then treated with a continuation phase of 4 months with isoniazid and rifampin. Patients requiring retreatment should initially receive at least 5 drugs, including isoniazid, rifampin, pyrazinamide, and at least 2 (preferably 3) new drugs to which the patient has not been exposed.

To improve the effectiveness of treatment initially conduct intensive treatment during 2 months of therapy, every day: isoniazid - 5 mg/kg PO, no more than 300 mg for day; rifampicin - 10 mg/kg/day PO or 10 mg/kg PO twice weekly; pyrazinamide - 25 mg/kg PO. According to foreign sources in the intensive phase of treatment also

taking ethambutol - 15 mg/kg, no more than 2g or streptomycin - 25 mg/kg, no more than 2g. Then conduct continuation phase, which lasts for 4 months by taking of isoniazid and rifampicin.

Combined use of antibacterial drugs explained by improvement bactericidal action to reduce the possibility of development of resistance of mycobacteria.

To the convenience of treatment were created the combined drugs, which already contain the necessary doses of isoniazid, rifampicin, ethambutol, pyrazinamide.

Treatment of patients with tuberculosis should be accompanied by a test for sensitivity to drugs. Susceptibilities should be repeated if cultures remain positive after 2 months, even when initial susceptibilities have not revealed any resistance.

When the drugs of first line are not effective, we use drugs of second line: ethionamide or protionamide: every day 15-20mg /kg no more than 1g for day; amikacin, kanamycin or capreomycin daily for 15-20 mg/kg no more than 1 g; cycloserine daily 10-15 mg/kg no more than 1g; ofloxacin or levofloxacin 15-20 mg/kg and 10 mg/kg, respectively; terizidone daily 10-15 mg/kg, no more than 0.9 g; para-aminosalicylic acid daily 150 mg/kg no more than 12g; rifabutin 5 mg/kg 3 times per week; ftivazide daily 1-2g.

The new drugs for the treatment of multidrug-resistant tuberculosis are bedaquiline and delamanid. Bedaquiline are taking for 1-2 weeks for 400 mg per day, then 3-24 weeks for 200 mg 3 times a week. Delamanid are taking for 100 mg twice a day simultaneously with optimized standard regimen.

New drugs can reduce the treatment, but they have a number of side effects. Therefore, their use is possible under certain conditions, proper selection of patients, informed consent, careful monitoring of treatment, choice of treatment regimen and active pharmacovigilance.

Patients diagnosed with active TB should undergo sputum analysis for Mycobacterium tuberculosis weekly until sputum conversion is documented. Monitoring for toxicity includes baseline and periodic liver enzymes, complete blood cell (CBC) count, and serum creatinine.

In the course of studies were systematized principles of therapy TB according to national regulatory documentation and foreign articles.

# ANALYSIS OF THE NEFROPROTECTIVE MECHANISMS

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According to statistics, about 10% of the world's population suffers from chronic kidney diseases, which in most cases lead to disability and death.

The amount of patients who are in need of replacement therapy (hemodialysis, peritoneal dialysis, a kidney transplant), in connection with the development of chronic renal failure is increasing each year. Methods of replacement therapy are expensive and are an economic worldwide problem.

Therefore, prevention of kidney disease, early diagnosis and effective treatment is an urgent medical and social problem.

The basic function of kidneys is excretion of metabolism products, regulation of ion and acid-base balance of the body's internal environment. Therefore, in the pathogenesis of renal disease lie hemodynamics disorders, microcirculation disturbances, water-electrolyte and other metabolic disorders. The main direction in the treatment of chronic kidney disease is to slow the progression of renal failure using drugs with the specific and nonspecific nephroprotective action.

The aim of our work is to analyze the mechanisms of drugs nephroprotective action, which should provide a correction of metabolic processes, while maintaining residual renal function that allows you to delay the onset and development of end-stage renal failure.

One of the important factors contributing to the progression of kidney disease process is oxidative stress, resulting in further endothelial dysfunction and the progression of kidney disease. When reducing efficiency of antioxidant protection its increased the ability of free radicals to inactivate nitric oxide (NO) formation by peroxynitrite, which leads to significant deterioration of renal perfusion and tissue.

As agents that is capable for inhibition of free radicals damaging effects, wide use antioxidant drugs whose actions is to improve the utilization of oxygen and increasing the sustainability of organs and tissues to hypoxia. Unfortunately it is not enough drugs with strong antioxidant and anti-hypoxic action that would apply in nephrology as nephroprotectors.

Thus, given the urgency of the problem, the search for and study of drugs with nephroprotective properties would allow on the one hand to carry out prevention of renal disease, and on the other hand to slow the progression of existing kidney disease.

# ADVANTAGES OF THE CARBOXYTHERAPY

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Carboxytherapy is an innovative medical method of XX and XXI century, minimum invasive, nonaggressive, not demanding anesthesia, safe, available and convenient for the patient.

Carboxytherapy is a simple procedure for receiving beautiful and young skin, improving organism for those who doubt efficiency or safety of Botox and is a disposal method from age changes of a body and organism. Existence of the micromanipulator with adapters for a microscope, a kolposkop and a laparaskop considerably expands CO2 scope, allows exact and safer impact on the pathological center.

Indications to a carboxytherapy is any dissatisfaction with a state of the skin and an organism, it is possible to use it any season.The positive effect is noted within a year.

Carboxytherapy is known for lack of allergic reactions.

Carboxytherapy is already applied by more than 30 years around the world without any complications to therapy of cellulitis, psoriasis, a diabetic ulcer, venous insufficiency, extensions, etc.

Carboxytherapy is actual at any age and at any type of skin. Carboxytherapy is a sparing method for treating diseases of the joints which are especially followed by rigidity, contractures, increase of a muscular tone and frustration of circulation of blood and lymph's. The method allows to forget such diseases of joints as: constraint, pain, muscular weakness. The analgesic effect is reached after the first CO2 injection.

Carboxytherapy, stimulates the immune system and the brain activity, improves work of heart and lungs and it is recommended for the general strengthening of health.

# PRE-MEDICAL AID IN CONDITIONS OF HOSTILITIES

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Providing pre-medical aid on the battlefield is a major key to save the life of the wounded. Analysis of the causes of death soldiers during conduct of hostilities indicates that a significant proportion could be saved with timely and quality provision of pre-medical care. The main causes death of 80-90% wounded were massive blood loss and shock.

In providing of pre-medical aid in hostilities conditionally entails the following steps: providing pre-medical aid in the sector of fire, transportation (moving) the wounded from the battlefield to the shelter sector, aid in shelter sector. In the sector of fire pre-medical aid is provided in the form of self-help and mutual aid. In the sector of fire should only stop life-threatening bleeding, you can stop external bleeding wounds localization in the neck, arms or legs. Transportation of wounded to the shelter sector may different ways by one or more persons. If it is impossible to transport wounded to the shelter sector transfer wounded into position on his stomach. In the sector of shelter wounded should be removed protective elements and check for consciousness. In case of no response you should check the carotid pulse and breathing, examine the wounded from head to foot. In the absence of the carotid pulse and respiration start cardiopulmonary resuscitation. In the presence of external bleeding from wounds limb a tourniquet impose on a limb in case you hasn't been stop the bleeding in the area of firing or during ongoing bleeding. In other cases, to stop bleeding apply a special dressing, or use individual dressing. In the presence of bleeding from the wound of body to stop bleeding perform using hemostatic agents. In the presence of a wounded burns and wounds should impose to the wound tissue. In aid to wounded with penetrating chest wound is necessary to impose occlusion. In the presence of fractures in wounded necessary to limb immobilization using standard or improvised tires.

Thus, providing quality and timely aid on the battlefield - a chance to survive the wounded.

# PERSPECTIVE OF RENAL FAILURE CORRECTION WITH COMPOSITE PHYTOPREPARATIONS

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Chronic renal failure (CRF) is one of the most serious diseases. The number of patients with CRF is growing. Over the last 20 years the number of patients with CRF has increased by 4 times.

The urinary system plays an important role in maintaining homeostasis, the violation of its work leads to reduction or loss of kidney function. This group of diseases characterized by impaired water-salt and protein metabolism, dysuria, violation of excretory kidney function. Degree of filtrative renal function impairment can be estimated by the level of proteinuria, glomerular filtration rate. One of the important markers of pathology is negative change of enzyme activity in urine: increased activity of lactate dehydrogenase, N-acetyl-β-D-glucosaminidase, γ-glutamyl transferase. Changing of these indexes indicates destruction of kidney tissue and violation of the filter.

Based on many years experience of the renal failure studies were designed different models of experimental renal disease. Depending on the required parameters can be modeled on animals and assess the degree of certain drugs effectiveness to change laboratory and biochemical parameters. The varieties of model types give a ways to define drugs effect on the each pathological mechanism.

Specific treatment of renal failure doesn't exist and perspective of medical treatment of CRF is extremely limited (O. Taran, 2003). The aim of conservative therapy patients with CRF is to maintain of residual renal function, reduction of further progression of CRF, making by adequate correction of metabolic disorders.

Due to polisymptomatic manifestations of CRF, patients must input a lot of drugs. It's important to pay attention to the development of side effects of patients with CRF, which will be amplified in time of violation excretion drugs from the body. Therefore, the complexity and efficiency of patient care is a priority renal disease pharmacotherapy. In recent years special attention is paid to the herbal preparation, because it possesses multivalent properties. It effect based on the biologically active substances which is favorable affects on metabolic processes in the kidney tissues and its functional capacity.

# FIRST AID FOR ANAPHYLACTIC SHOCK

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The aim of our study was to investigate of first aid in anaphylactic shock (ASH), which is an immediate type allergic reaction, accompanied by life-threatening clinical manifestations (dramatic decrease in blood pressure, disorders of the central and peripheral nervous systems, respiratory failure, etc.). When parenteral preparations were given al ASH develops immediately after oral - 30-60 minutes.

Most actual causes of anaphylaxis are drug, insect and food allergy.

There are main symptoms typically begin within 15 min of exposure and involve the skin, upper or lower airways, cardiovascular system, or gastrointestinal tract. Symptoms range from mild to severe and include flushing, pruritus, urticaria, sneezing, rhinorrhea, nausea, abdominal cramps, diarrhea, a sense of choking or dyspnea, palpitations, and dizziness.

First aid should begin with the immediate cessation of allergen to the body. Patient should be put on a flat surface (head should be placed below the level of the feet), turn his head to the side, push the lower jaw, and remove removable dentures. Call an ambulance for tel.103 or 112. The primary and most important measure is the introduction of patient pharmacotherapy adrenaline (epinephrine) to control symptoms ASH and high blood pressure. The drug is administered in diluted 1: 1000 (1 mg / ml) at a dose of 0.2-0.5 ml for adults and 0.01 mg per kg of body weight for children, but no more than 0.3 mg dose. Epinephrine injected intramuscularly in the lateral thigh or subcutaneously every 5 minutes. Patients who have stridor and wheezing unresponsive to epinephrine should be given $O_2$. Hypotension often resolves after epinephrine is given. Persistent hypotension can usually be treated with 1 to 2 L (20 to 40 mL/kg in children) of isotonic IV fluids (eg, 0.9% saline). Hypotension refractory to fluids and epinephrine may require vasopressors (eg, dopamine 5 mcg/kg/min).

After that, the patient should be taken to hospital, where he be getting specialized care.

# MODERN PHARMACOTHERAPY OF ATOPIC DERMATITIS

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Atopic dermatitis (AD) is a pruritic disease of unknown origin that usually starts in early infancy, though an adult-onset variant is recognized. In 85% of cases, atopic dermatitis occurs in the first year of life; in 95% of cases, it occurs before age 5 years. The incidence of atopic dermatitis is highest in early infancy and childhood. The disease may have periods of complete remission, particularly in adolescence, and may then recur in early adult life.

Skin care involves the following measures: Hydrating with water, Using soap substitutes rather than regular soap, Taking baths with diluted bleach or colloidal oatmeal, Applying emollients, Wearing wet dressings, Applying coal tar cream or oil. Antihistamines can help relieve pruritus. Options include hydroxyzine 25 mg po tid or qid and diphenhydramine 25 to 50 mg po at bedtime. Low-sedating H1 receptor blockers (such as loratadine 10 mg po once/day, fexofenadine 60 mg po bid or 180 mg po once/day, and cetirizine 5 to 10 mg po once/day) may be useful, although their efficacy has not been defined. Doxepin (a tricyclic antidepressant also with H1 and H2 receptor blocking activity) 25 to 50 mg po at bedtime may also help. Corticosteroids are the mainstay of therapy. Creams or ointments applied twice daily are effective for most patients with mild or moderate disease. Systemic corticosteroids (prednisone 60 mg po once/day for short courses of 7 to 14 days) are indicated for extensive or refractory disease. Systemic immune modulators effective in at least some patients include cyclosporine, interferon gamma, mycophenolate, methotrexate, and azathioprine. Tacrolimus and pimecrolimus are T-cell inhibitors effective for AD. They should be used when patients do not respond to corticosteroids and tar or when corticosteroid adverse effects such as skin atrophy, striae formation, or adrenal suppression is a concern. Tacrolimus or pimecrolimus cream is applied twice daily.

Thus, the modern pharmacotherapy of AD will significantly improve the quality of life of patients.

# PHARMACOTHERAPY OF CHRRONIC HEART FAILURE

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Chronic heart failure (CHF) – a pathological condition in which the heart does not provide the necessary organs and tissues of blood according to their metabolic needs.

According to epidemiological studies of heart failure is 1 in 15 people aged> 75 years and 1 of 7 – aged> 85 years.

Allocate functional class according to the criteria of the New York Heart Association (NYHA): I, II, III, IV FC. Options heart failure: systolic dysfunction of the left ventricle (LV) - left ventricular ejection fraction 45%, with preserved LV systolic function (left ventricular ejection fraction > 45%).

Clinical features of CHF – shortness of breath during physical, tachycardia, fatigue and weakness, nocturia and oliguria, anorexia, weight loss, nausea, swelling of the neck veins, easy, fast, and thread pulse, wheezing, difficulty breathing, ascites, hepatomegaly, pallor. Binding studies in CHF: General studies, complete blood count, urinalysis, ECG 12 leads, echocardiography, radiography of the chest cavity, blood chemistry.

The first-line of the pharmacotherapy in CHF is B-blockers – bisoprolol, carvedilol, metoprolol, nebivolol. They are recommended for all patients with CHF and systolic dysfunction in all functional classes in NYHA. An alternative first-line drug is isosorbide dinitrate, which recommended in combination with hydralazine. Second-line drug therapy for heart failure is angiotensin II receptor antagonists: candesartan, valsartan, irbesartan, losartan, telmisartan and aldosterone antagonists – spironolactone. As an additional CHF pharmacotherapy used cardiac glycosides (digoxin), usually in combination with β-blockers. If signs of fluid retention advisable thiazide or loop diuretics was recommended to use.

General advice for pharmacotherapy of CHF are NYHA I – ACE inhibitors in combination with B-blockers; NYHA II-III – ACE inhibitors in combination with B-blockers and candesartan; NYHA III-IV – ACE inhibitors in combination with B-blockers and spironolactone.

# MODERN PHARMACOTHERAPY OF MIGRAINE

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Migraine is an episodic, often debilitating disorder characterized by attacks of severe headache in association with combinations of neurologic and gastrointestinal symptoms. Migraine most commonly begins during puberty or young adulthood, waxing and waning in frequency and severity over the ensuing years; it often diminishes after age 50.

Pharmacologic agents used for the treatment of migraine can be classified as abortive or prophylactic. Abortive medications include the following: selective serotonin receptor (5-HT1) agonists, Ergot alkaloids, Analgesics, NSAIDs, Combination products, Antimemetics. The choice for an individual patient depends on the severity of the attacks, associated symptoms such as nausea and vomiting, comorbid problems, and the patient's treatment response. Simple analgesics alone or in combination with other compounds have provided relief for mild to moderately severe headaches and sometimes even for severe headaches. Acute treatment is most effective when given within 15 minutes of pain onset and when pain is mild. The 2 categories of migraine-specific oral medications are triptans and ergot alkaloids. The specific ergot alkaloids include ergotamine and dihydroergotamine. The specific triptans include the following: Sumatriptan, Rizatriptan, Zolmitriptan, Naratriptan, Almotriptan, Eletriptan, Frovatriptan. All the triptans are most effective when taken early during a migraine and all may be repeated in 2 hours as needed, with a maximum of 2 doses daily. While different formulations of a specific triptan may be used in the same 24-hour period, only 1 triptan may be used during this time frame. Patients with severe headaches need subcutaneous, intravenous, or oral formulations of an ergot alkaloid or triptan. Prophylactic medications for the treatment of migraine include the following: Antiepileptic drugs, Beta-blockers, Tricyclic antidepressants, Calcium channel blockers, Selective serotonin reuptake inhibitors, Serotonin antagonists, Botulinum toxin. The selection of a preventive medication must take into consideration comorbid conditions and the side-effect profile.

Thus, the modern pharmacotherapy of migraine will significantly improve the quality of life of patients.

# MODERN PHARMACOTHERAPY OF URINARY TRACT INFECTION

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The incidence of urinary tract infections (UTI) is much higher in females during adolescence and childbearing years then in males. The incidence of UTI in men approaches that of women only in males older than 60 years; in men aged 65 years or older, 10% have been found to have bacteriuria, as compared with 20% of women in this age group.

UTI can be divided into upper tract infections, which involve the kidneys (pyelonephritis), and lower tract infections, which involve the bladder (cystitis), urethra (urethritis), and prostate (prostatitis). However, in practice, and particularly in children, differentiating between the sites may be difficult or impossible. Moreover, infection often spreads from one area to the other. Although urethritis and prostatitis are infections that involve the urinary tract, the term UTI usually refers to pyelonephritis and cystitis.

Most cystitis and pyelonephritis are caused by bacteria. The most common nonbacterial pathogens are fungi (usually candidal species), and, less commonly, mycobacteria, viruses, and parasites. Nonbacterial pathogens usually affect patients who are immunocompromised; have diabetes, obstruction, or structural urinary tract abnormalities; or have had recent urinary tract instrumentation. Other than adenoviruses (implicated in hemorrhagic cystitis), viruses have no major contribution to UTI in immunocompetent patients.

All forms of bacterial UTI require antibiotics. Choice of antibiotic should be based on the patient's allergy and adherence history, local resistance patterns (if known), antibiotic availability and cost, and patient and provider tolerance for risk of treatment failure. Propensity for inducing antibiotic resistance should also be considered.

First-line treatment of uncomplicated cystitis is nitrofurantoin 100 mg po bid for 5 days (it is contraindicated if creatinine clearance is < 60 mL/min), trimetoprim/sulfamethoxazole 160/800 mg po bid for 3 days, or fosfomycin 3 g po once. Less desirable choices include a fluoroquinolone or a β-lactam antibiotic. If cystitis recurs within a week or two, a broader spectrum antibiotic (eg, a fluoroquinolone) can be used and the urine should be cultured.

Complicated cystitis should be treated with empiric broad-spectrum antibiotics chosen based on local pathogens and resistance patterns and adjusted based on culture results. Urinary tract abnormalities must also be managed.

For treatment of acute pyelonephritis antibiotics are required. Outpatient treatment with oral antibiotics is possible if all of the following criteria are satisfied: patients are expected to be adherent; patients are immunocompetent; patients have no nausea or vomiting or evidence of volume depletion or septicemia; patients have no factors suggesting complicated UTI. Ciprofloxacin 500 mg po bid for 7 days and levofloxacin 750 mg po once/day for 5 days are 1st-line antibiotics if < 10% of the uropathogens in the community are resistant. A 2nd option is usually trimetoprim/sulfamethoxazole 160/800 mg po bid for 14 days.

First-line antibiotics for parenteral therapy are usually renally-excreted fluoroquinolones such as ciprofloxacin and levofloxacin. Other choices such as ampicillin plus gentamicin, broad-spectrum cephalosporins, aztreonam, β-lactam/β-lactam inhibitor combinations, and imipenem/cilastatin are usually reserved for patients with more complicated pyelonephritis or recent urinary tract instrumentation. Parenteral therapy is continued until defervescence and other signs of clinical improvement occur. In > 80% of patients, improvement occurs within 72 h. Oral therapy can then begin, and the patient can be discharged for the remainder of a 7-to14-day treatment course. Complicated cases require longer courses of IV antibiotics with total duration of 2 to 3 wk and urologic correction of anatomic defects.

Careful asessment of patient and in time started pharmacotherapy of UTI will prevent possible chronisation of disease.

# TARCEVA IS A NEW STANDARD IN LUNG CANCER TREATMENT

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Lung cancer remains a leading cause of human deaths from malignant tumours in the majority of industrialized countries. This is the most common oncology disease, incidence of which steadily increases among both women and men: annually more than 1 million of new lung cancer cases are registered in the world. (Median survival in patients with advanced process was 4-5 months, 1-year survival rate was 10%). But it is also one of the most studied diseases for the moment, which treatment range is constantly updated.

In modern literature there is information about different ways of lung cancer treatment, a targeted therapy is considered to be the most promising one among them. The purpose of the investigation was to study and identify medicines for treatment, achieve a new increased survival rate and improvement of life quality of oncologic patients.

Tarceva (erlotinib) is one of such medicines, which belongs to anticancer agents and is a product of biotechnology. Mechanism of its action lies in direct reversible inhibition of tyrosine kinase of epidermal growth factor receptors $HER_1$/EGFR. On the basis of literature data the patients, who were on advanced stages of lung cancer and which previously did not receive any chemotherapy, took part in one of the investigations. They were randomized into 2 groups: the patients of the first group were prescribed tarceva, patients of the second one – a standard chemotherapy – carboplatin and gemcitabine.

In the course of observation the tarceva medicine confirmed its efficiency as a monotherapy in patients without progression of the disease as a first line of therapy. The medicine significantly increased the overall survival by 42.5%: the median of overall survival in tarceva group was 13.1 months and the 1-year survival reached 31%. Herewith skin rash was the most significant side effect, which is an evidence of sufficiently favourable (in comparison with cytotoxin medicines) profile of the medicine safety. Tarceva therapy is not associated with hepatotoxicity, myelosuppression and neuropathy.

Thus, the advisability of tarceva administration in case of lung cancer does not cause doubt. Basing on the abovementioned data it is possible to assume that tarceva can be an economically viable alternative to platinum-containing schemes of chemotherapy and supposedly is one of the advanced medicines for treatment of patients with lung cancer.

# MODERN PHARMACOTHERAPY OF ACUTE DIARRHEA

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Mortality from acute diarrhea is overall globally declining but remains high. Most estimates have diarrhea as the second cause of childhood mortality, with 18% of the 10.6 million yearly deaths in children younger than age 5 years.

Despite a progressive reduction in global diarrheal disease mortality over the past 2 decades, diarrhea morbidity in published reports from 1990-2000 slightly increased worldwide compared with previous reports. The vast majority of diarrhea-associated infant deaths were reported in 2005-2007, with 86% of deaths occurring among low-birthweight (< 2500 g) infants.

Furthermore, in countries in which the toll of diarrhea is highest, poverty also adds an enormous additional burden, and long-term consequences of the vicious cycle of enteric infections, diarrhea, and malnutrition are devastating.

Viral diarrhea is most common in young children. Rotavirus and adenovirus are particularly prevalent in children younger than 2 years. Astrovirus and norovirus usually infect children younger than 5 years. Yersinia enterocolitis typically infects children younger than 1 year, and the Aeromonas organism is a significant cause of diarrhea in young children.

Pharmacotherapy of dehydration due to diarrhea includes the following:

Minimal or no dehydration: rehydration therapy - not applicable. Replacement of losses: if less than 10 kg body weight - 60-120 mL oral rehydration solution for each diarrhea stool or vomiting episode; if more than 10 kg body weight - 120-140 mL oral rehydration solution for each diarrhea stool or vomiting episode.

Mild-to-moderate dehydration: rehydration therapy - oral rehydration solution (50-100 mL/kg over 3-4 h). Replacement of losses: if less than 10 kg body weight - 60-120 mL oral rehydration solution for each diarrhea stool or vomiting episode; if more than 10 kg body weight - 120-140 mL oral rehydration solution for each diarrhea stool or vomiting episode.

Severe dehydration: rehydration therapy - intravenous lactated Ringer solution or normal saline (20 mL/kg until perfusion and mental status improve), followed by

100 mL/kg oral rehydration solution over 4 hours or 5% dextrose (half normal saline) intravenously at twice maintenance fluid rates. Replacement of losses: if less than 10 kg body weight - 60-120 mL oral rehydration solution for each diarrhea stool or vomiting episode; if more than 10 kg body weight - 120-140 mL oral rehydration solution for each diarrhea stool or vomiting episode. If unable to drink, administer through nasogastric tube or intravenously administer 5% dextrose (one fourth normal saline) with 20 mEq/L potassium chloride.

Not all commercial oral rehydration therapy formulas promote optimal absorption of electrolytes, water, and nutrients. The ideal solution has a low osmolarity (210-250) and a sodium content of 50-60 mmol/L. Administer maintenance fluids plus replacement of losses. Administer small amounts of fluid at frequent intervals to minimize discomfort and vomiting. Oral rehydration is now universally recommended to be completed within 4 hours.

The following probiotics showed benefit in treatment of acute diarrhea in meta-analyses of randomized controlled trials: Lactobacillus GG (I, A) and S boulardii (II, B).

The addition of zinc to oral rehydration solution has been proven effective in children with acute diarrhea in developing countries and is recommended by the World Health Organisation.

At completion of hydration, resumption of feeding is strongly recommended. In fact, many studies convincingly demonstrate that early refeeding hastens recovery. Also, robust evidence suggests that, in the vast majority of episodes of acute diarrhea, refeeding can be accomplished without the use of any special (eg, lactose-free or soy-based) formulas.

Clinical trials found that the vaccines prevented 74-78% of all rotavirus gastroenteritis cases, nearly all severe rotavirus gastroenteritis cases, and nearly all hospitalizations. Rotarix protects against rotavirus gastroenteritis caused by G1, G3, G4, and G9 strains and is administered as a 2-dose series in infants aged 6-24 wk.

With the help of vaccination and early started rehydration therapy it is possible to reduce mortality and to control the morbidity level. Of course there are many other issues such as quality of drinking water in developing countries and its supply to population which sould be improved as well.

# PHARMACOTHERAPY SYSTEMIC SCLEROSIS

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Autoimmune diseases include more than 80 entities that are among the most common and serious human diseases. The frequency of autoimmune disease in the population reaches 8%. Autoimmunnitet forms the basis of a wide range of rheumatic diseases, including rheumatoid arthritis (RA), systemic lupus erythematosus (SLE), systemic sclerosis, systemic vasculitis, and others.

Systemic sclerosis (SS) - a systemic connective tissue disease characterized by progressive fibrosis and widespread vascular pathology of type obliterating microangiopathy, leading to the development of generalized Raynaud's syndrome, fibrotic changes in the skin, lesions of the musculoskeletal system and internal organs.

According to recent studies of pharmacotherapy for the treatment of cutaneous manifestations of SS used immunodepressants (mycophenolate mofetil), antifibrotic agents (D-penicillamine), antimetabolites (methotrexate in combination with folic acid), glucocorticosteroids (GCS). Rational use of these drugs in combination with extracorporeal blood purification methods during an exacerbation, has significantly improved the immediate and long-term prognosis, but in many cases does not allow to control the progression of the disease, the development of life-threatening complications or associated with severe side effects. Relevant is the search for new drugs and the development of schemes for the treatment of systemic sclerosis.

Currently, good results are obtained from the therapy with monoclonal antibodies in lymphocyte blocker - rituximab.

Rituximab - chimeric monoclonal antibody mouse / human, which specifically binds to a transmembrane CD20 antigen and B cells initiate immunological responses that mediate lysis of B-cells. The drug is available under the trade name MabThera / MABTHERA®, F. Hoffmann-La Roche Ltd., Switzerland.

There is no doubt that rituximab is an extremely effective and relatively safe drug for the treatment of severe autoimmune diseases. Its introduction into clinical practice can truly be considered a major achievement of the early 21st century medicine, which not only has important clinical, but also the theoretical value, since it contributes to deciphering the fundamental pathogenesis of human autoimmune diseases. In fact, rituximab is the founder of a new direction in the treatment of autoimmune diseases in humans, based on the modulation of B cell immunity.

# SECTION № 11

# PHARMACOECONOMIC RESEARCH OF MEDICINES

# CONFORMITY ASSESSMENT INPATIENT PHARMACOTHERAPY OF CHRONIC OBSTRUCTIVE PULMONARY DISEASE TO UKRAINIAN ADAPTED CLINICAL GUIDELINE

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According to the WHO, the chronic obstructive pulmonary disease (COPD) is the 4th leading cause of death in the world, killing annually nearly 2.75 million people. The cost of hospitalization is 40-57% of the total direct costs for patients with COPD, therefore the main aim is the treatment of COPD exacerbations, disease progression and mortality. Pharmacotherapy of COPD is of a lifelong nature, and its costs make up a large part of the budget of Ukrainian patients.

The purpose of the study. Analysis of compliance hospital pharmacotherapy of COPD the recommendations of adapted clinical guideline (ACG) 2013.

Materials and methods. Analysis of hospital pharmacotherapy of COPD was performed on the basis of the therapeutic department Dymytrivsk Central Hospital (Donetsk region). Retrospectly 116 letters of medical appointments were studied for conformity assessment to ACG.

Results. 41 trade names (TN) of drugs of the 23 pharmacological groups were assigned for patients. For the treatment of COPD 25 drugs were appointed, for comorbidities states – 16 drugs. More than 40% of total expenditures were spent on anticoagulant direct action heparin, which is not included in the recommendations of ACG.

Dexamethasone (parenteral form) was injected 93 patients, this appointment has no confirmation, because ACG recommends oral systemic glucocorticosteroids (GCS), such as prednisolone at a dose 30-40 mg daily for 10-14 days. According to the recommendations ACG for patients bronchodilators were intended: $\beta_2$-agonists (salbutamol), anticholinergic agents (tiotropiy), inhaled corticosteroids (budesonide) and antibacterials. To prevent side effects of antibacterial agents antihistamines and probiotics were administered for patients.

Conclusion. Analysis of medical appointments demonstrated that in the therapeutic department Dymytrivsk hospital recommendations of ACG were performed in insufficient volume and pharmacotherapy of COPD in this department needs correction.

# ABC-VEN-FREQUENCY ANALYSIS OF TREATMENT OF STABLE ANGINA PATIENT IN HOSPITALS

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Coronary heart disease (CHD) is a narrowing of the small blood vessels that supply blood and oxygen to the heart. CHD is a leader in the structure of morbidity, disability and mortality in all regions of Ukraine for men and women. Patients with CHD should take the following medications: statins, which reduce cholesterol, reduce risk of coronary disease; ACE inhibitors, which treat hypertension and may lower the risk of recurrent myocardial infarction; calcium channel blockers and/or beta-blockers; low dose aspirin. Treatment of patients with coronary artery disease are expensive to pharmacotherapy. Pharmacoeconomic analysis of the cost of drug therapy of CHD is important.

The purpose of the study - to assess the appropriateness of the financial costs of drug therapy in patients with CHD in clinical practice.

Materials and methods. A retrospective analysis of 82 case histories of patients with a diagnosis of CHD, stable angina I-IV, which were treated in a therapeutic department of one of the Kharkiv city hospitals. There were used the frequency, ABC- and the formal VEN-analysis.

The results of the study. The range of drugs in the medical appointment lists consisted of 64 titles. All patients received the drugs recommended by current international standards and protocols for the treatment of these patients. All patients also received another 2-3 medication for the treatment of common diseases (sedatives, vitamins and others). 46.8% of all drugs were expensive foreign drugs. 21% were common medications. Group A included 3 drugs (77% of spending) in group B - 21 drugs (20% of spending) in group C - 33 drugs (3% of the costs). There were 66% drugs category N in group A, 76% drugs category N in group B. On drugs category V has been spent less than 15% of the total amount of money.

Conclusions. Comprehensive drug therapy in patients with coronary heart disease in this hospital comply with the applicable standards of treatment. At the same time, financial resources are used inefficiently. At the same time, financial resources are used inefficiently. It is advisable to review the drug is necessary to form this hospital. It is necessary to reduce the number of expensive foreign medications.

# VEN/FREQUENCY ANALYSES PHARMACOTHERAPY OF PATIENTS WITH CHOLECYSTITIS

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The purpose of the study VEN/frequency analyses medical appointments and evaluation of necessary drugs prescription to patients with cholecystitis in health care facilities (HCF) of Kharkiv.

Materials and methods. Were used Auxiliary types pharmacoeconomic analyses: frequency and VEN-analyses. VEN-analyses was carried out by "formal" sign: the drugs from the National Drug Formulary (NDF) of Ukraine (5th Edition) – had index «V», anather drugs had – the index «N».

Results. The analyses of 160 case histories of patients with cholecystitis aged 26 to 80 years has allowed to identify 83 drugs from 32 pharmacological groups that have been assigned to these patients. The majority of patients were – men 98 and 62 were women. The average number of days of hospitalization was 14. The average number of drugs intended for one patient was 7, that indicates abaut polypharmacy drug therapy, becous the recommended optimal number of drugs 1 patient must not exceed 3-4 drugs.

The undisputed leader of appointments were hepatoprotectors "Thiotriazolin" ("Halychpharm" 2 ml, № 10) – 130 prescriptions, which accounted for 13.7% of the total number of appointments and antispasmodic "Spasmobru" ("Brupharmexport " 2 ml, № 10) – 128 prescriptions, which accounted for 13.5% of total appointments. Among the 10 leaders 6 prescription drugs: Thiotriazolin, Spasmobru, Duspatalin, Dalargin, Ursohol, Fosfohliv used in schemes complex of therapy of patients with a "cholecystitis" diagnosis. Were used is consistent with the data of the clinical standard of medical care (Order of the Ministry of Health of Ukraine No 271 dated 13.06.2005). As a result of formal VEN-analyses a large number of drugs 70.2% belonged to the NDF of Ukraine (5th edition). But 29.8% of drugs were not present in the NDF of Ukraine that requires further correction of medical prescriptions.

Conclusions. 70% of drugs were intended for patients with cholecystitis rationally. Polypharmacy (an average of 7 drugs per patient) and 29.8% of drugs which are not presented in the NDF of Ukraine (5th edition) shows the irrational use of these drugs. Thus, the results of the study can be as a basis for further study of issues related to the rationalization of pharmacotherapy for patients with cholecystitis in this department of HCF of Kharkiv.

# ANALYSIS OF THIOCTIC ACID DRUGS CONSUMPTION IN THE UKRAINIAN PHARMACEUTICAL MARKET

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Introduction. In the treatment of diseases and pathological conditions, which are based on oxidation-antioxidant homeostasis imbalance drugs of thioctic (α-lipoic) acid widely used. Thioctic acid is the first-line treatment of pathogenic diseases that are accompanied by severe neurological symptoms (diabetic and alcoholic polyneuropathy), liver pathology and others. In particular, clinical efficacy and safety of α-lipoic acid in the treatment of diabetic polyneuropathy was confirmed in 9 placebo controlled trials and one meta-analysis.

The purpose of the study is the assessment of thioctic acid drugs consumption in the Ukrainian pharmaceutical market.

Materials and methods. The objective of the study was the data about thioctic acid consumption of a market research analytical system “Pharmstandard”. Consumption of drugs was assessed using ATC/DDD methodology in term of $DDD_S$/1000 inhabitants/day ($DDD_S$/1000/d). This indicator gives an idea of the proportion of the population that receives certain drugs. Consumption of thioctic acid were performed according to the data 2008 - 2012.

Results. 25 thioctic acid trade names were represented in the Ukrainian pharmaceutical market in 2012.

Compared to the data in 2008, in 2012 the consumption of thioctic acid drugs in Ukraine increased by 1.49 times and as 3.36 $DDD_S$/1000/d. Consumption of the drugs "Berlithion" and "Dialipon" was the largest. Consumption of these drugs according to data in 2012 increased by 27.12% and 21.50% compared to data in 2008. In absolute terms the volume of consumption was defined at the level of 0.73 and 0.42 $DDD_S$/1000/d respectively. Consumption of the domestic drugs "Lipoic acid" in 2012 compared to data in 2008 decreased by 99.86%. Their share in absolute terms was 0,000012 $DDD_S$/1000/d. The leader in terms of consumption in 2012 was a drug "Berlithion 600" (Berlin-Chemie, Germany, 600 mg, amp. 24 ml, №5). Volume of consumption increased by 98.50% compared with 2008 in absolute terms was 0,2 $DDD_S$/1000/d.

Conclusions. The analysis of the consumption of thioctic acid drugs in terms $DDD_S$/1000/d in the pharmaceutical market of Ukraine determined growth of its level, about 1.5 times more compared with 2008. It indirectly reflects the growing disease accompanied by severe neurological symptoms.

# FREQUENCY ANALYSIS OF APPOINTING DRUGS FOR PATIENTS WITH LUMBAGO IN HOSPITAL

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Lumbago - a pathological condition characterized by the appearance of pain in the muscles and joints of the lower back. Lumbago is widely spread in people of working age and needs effective treatment. Clinical applications for lumbago treatment include the control of pain.

The aim of this study was to analyze the consumption of drugs for lumbago treatment in hospital.

Materials and methods. Analysis of hospital pharmacotherapy of lumbago was performed on the basis of the therapeutic department of a hospital. For analysis of lumbago hospital pharmacotherapy frequency analysis were used.

Results. Frequency analysis assesses the dominant pharmacological groups of therapy. As a result of frequency analysis by pharmacological groups was found, that the dominant trends in the treatment of patients lumbago were: anti-inflammatory, analgesic and vitamin therapy.

Anti-inflammatory therapy was performed with the use of these drugs from such pharmacological groups: M01A-antiinflammatory and antirheumatic agents, the appointments of which were amounted 22.7% of total appointments. These drugs 196.4% of patients received, for one patient is prescribed more than one drug from this group. The appointments of miorelaxants (M03B) accounted 7.4% of total appointments. 64.2% of patients used these drugs. Vitamins (A11D) amounted 6.6% of the total appointments. Vitamins were prescribed to 57.1% of patients. Appointments of local anesthetics (N01B) constituted 5.7% of total appointments. Anesthetics were assigned 50% of patients. Corticosteroids (H02A) for systematic use were assigned 46.4% of patients, it was 5.3% of the total appointments.

Conclusion. Comparing the prevailing trends of pharmacotherapy with those defined by current clinical protocol to provide medical care to patients with lumbago was found, that in general these trends were the same. Unjustified may have been a significant number of vitamins appointments. Efficacy of vitamins in reducing pain in patients with lumbago needs confirmation.

# ANALYSIS OF DRUGS RANGE FOR ANTIHELICOBACTER THERAPY OF GASTRIC AND DUODENUM ULCERS ON THE PHARMACEUTICAL MARKET IN UKRAINE

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**The aim of research** – to analyze the drugs range for antihelicobacter therapy of gastric and duodenum ulcers on the pharmaceutical market in Ukraine.

**Materials and methods.** Structural, logical, comparative and marketing methods were used.

The drugs range for antihelicobacter therapy of gastric and duodenum ulcers (proton pump inhibitors, antibacterial drugs, antagonists of histamine $H_2$-receptor, bismuth drugs) on the pharmaceutical market in Ukraine was determined by using a system of market research "Pharmstandard" of company "Morion" (November, 2014).

**Results of research.** In the period of study 5 international non-proprietary names of proton pump inhibitors (omeprazole, pantoprazole, lansoprazole, rabeprazole, esomeprazole), 2 international non-proprietary names of antagonists of histamine $H_2$-receptor (ranitidine, famotidine), 6 international non-proprietary names of antibacterial drugs (amoxicillin, clarithromycin, levofloxacin, metronidazole, tetracycline, tinidazole) and 1 international non-proprietary name of bismuth drugs (bismuth subcitrate) were presented on Ukrainian pharmaceutical market.

Quantity of their trade names (TN) was, respectively, 91 TN, 27 TN, 138 TN and 6 TN.

The share of drugs of domestic production was 36% (95 drugs).

Number of the offers of imported drugs exceeds the offers of domestic manufacturing companies on the pharmaceutical market almost 3 times.

Drugs for antihelicobacter therapy of gastric and duodenum ulcers were presented in different medicine's form: tablets, capsules, injection, powders for preparation of suspensions and solutions for injection.

The largest number among them were the drugs in the medicine's form - tablets and capsules (78% - 205 drugs).

**Conclusion.** The drugs range for antihelicobacter therapy of gastric and duodenum ulcers was in a wide range on the pharmaceutical market in Ukraine.

This fact allows the doctor to choose the drugs based on its efficacy and safety, as well as the individual patient and the disease severity level.

# VEN/FREQUENCY ANALYSES OF PATIENTS WITH STEATOHEPATITIS PHARMACOTHERAPY

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The purpose of the study. VEN/frequency analyses medical appointments and evaluation of necessary drugs prescription to patients with steatohepatitis in health care facilities (HCF) of Kharkiv.

Materials and methods. Were used Auxiliary types pharmacoeconomic analyses: frequency and VEN-analyses. VEN-analyses was carried out by "formal" sign: the drugs from the National Drug Formulary (NDF) of Ukraine (5th Edition) – had index «V», anather drugs had – the index «N».

The obtained results. The analyses of 55 case histories of patients with steatohepatitis aged 26 to 80 years has allowed to determine the 74 drugs that were assigned to these patients. The majority of patients were – men 32 and 23 were women. The average term of patient's staying in the department was 14 days. The average of prescriptions per 1 patient were 10 drugs, that indicates the presence of polypharmacy, drug therapy, becous the recommended optimal number of drugs 1 patient must not exceed 3-4 drugs.

The undisputed leader of appointments was hepatoprotectors "Tiotriazolin" - 39% of the total number of appointments and "Ursohol" - 26% of total appointments. Most of the 10 top leaders ("Spasmobru", "Thiotriazolin", "Ursohol", "Berlithion", "Fosfohliv", "Creon", "Dalargin", "Espa-lipon", "Panhrol", "Geptral") were used in schemes of complex therapy of patients with a diagnosis steatohepatitis this confirmins rationality of appointments pharmacotherapy in HCF of Kharkiv. As a result of formal VEN-analyses of a large number of drugs were included in the NDF of Ukraine (5th edition), because these drugs were classified in group V (vital). They made most of the medical appointments - 74.3%, but 25.7% of drugs were not included in the NDF of Ukraine, so it is necessary to optimize the assignment of non-essential drug, which can not exceed 10% of the intended drugs.

Conclusions. About 75% of drugs intended for patients with steatohepatitis Can we consider reasonable, but set polypharmacy and a significant amount of drugs (25.7%), in the absent in the NDF Ukraine opposes their use. Thus, the results can be as a basis for further study of rational pharmacotherapy of patients with steatohepatitis in this department HCF.

# COMPARATIVE PHARMACOLOGICAL AND ECONOMIC ASSESSMENT OF EFFICIENCY OF IMMUNE-MODULATORY AND ANTIBACTERIAL THERAPY OF EXTRA HOSPITAL PNEUMONIA

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Questions of optimization of antibacterial therapy of extra hospital pneumonia in the conditions of the state allocations remain an actual problem of applied medicine with different age groups.

Objective of this research was the assessment of clinic and economic efficiency of antibacterial therapy and immune-correction of extra hospital pneumonia at residents of Shymkent in the Republic of Kazakhstan.

It is conducted for an assessment of expediency of inclusion of the immuno-supporting drugs in therapy of extra hospital pneumonia by retrospective and prospective research of a state of health of 534 sick miscellaneous of age by extra hospital pneumonia with a favorable outcome.

Economic efficiency of therapy by medicine was determined by method of an assessment of "efficiency/expenses", by number of additional consultations of the doctor, quantity of cases of recurrence of a disease.

Patients were divided into 2 groups:

1. group receiving standard treatment by antibacterial preparations;
2. the group receiving immune-supporting preparations in a complex with antibacterial preparations.

Each group included patients of different age groups, and medium-weight degree of a course of a disease of extra hospital pneumonia widely meets in category of adults, i.e. efficient people.

The analysis of frequency of purposes of antibacterial preparations in the first group showed that the leading place in antibacterial therapy is taken by amino-pentsilin, in particular the penicillin protected.The second place is taken cephalosporin, especially by 3 generations, macro-leads and further fluorine-hinolon and other groups of antibiotics.At the same time efficiency mono - antibacterial therapy fluctuated within 64% of cases, in the others needed repeated antibacterial appointments, applications of 2 and more antibacterial preparations in the scheme of treatment of extra hospital pneumonia.

Inclusion in treatment of extra hospital pneumonia of immune-correction authentically lowered indicators of time of treatment and recovery a little, more than twice reduced quantity of cases of recurrence of a disease, more than reduced quantity of cases of repeated consultation of the doctor, cases of application of two and more antibacterial preparations and replacement of an antibacterial preparation in comparison with the first group four times.

Assessment of economic factor medicine cost at inclusion the immune-supporting of preparations in our case showed increase in an expense on treatment on average by 28,5% of average expenses in standard therapy, and clinical efficiency of immune-modulatory therapy increased on average by 13,4%.

The comparative pharmacological and economic analysis of therapy by medicine of extra hospital pneumonia showed that inclusion the immune-supporting of preparations in antibacterial therapy at extra hospital pneumonia increases efficiency of the carried-out therapy.

Growth of costs of immune-modulatory preparations on the one hand reduces quantity of cases of repeated prescriptions of antibiotics, reduces quantity of cases of resistance to antibacterial preparations that eventually will cut expenses on elimination of undesirable actions from drugs.

# THE DEFINITION OF AVAILABILITY OF ANTIHISTAMINIC DRUGS FOR UKRAINIAN PATIENTS

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In recent years there is trend to a significant increase in the frequency of allergic pathology worldwide. According to the data of World Health Organization (WHO) various allergic symptoms and diseases recorded in 7-30% of cases of all diseases. According to statistics, in Ukraine approximately 1.5% of the population has been diagnosed an allergy. However, the actual figures are much higher – up to 25% of population or about 10 million people, so determining the availability of antihistaminic drugs (AHDs) for Ukrainian patients is a priority.

The aim of the study was to determine the availability AHDs for Ukrainian patients in 2014.

Materials and methods. To determine the availability of AHDs for patients were calculated ratio of the adequacy of solvency (Ca.s.) and the availability coefficient (D) of drugs in 2013-2014.

Results. In 2013 in accordance with the calculated Ca.s., weekly costs for patient treatment with AHDs were from 0.05% - 6.37% of the average wage, and in 2014 - from 0.03% to 6.73%. In 2013-2014 the trade names (TNs) AERIUS® (syrup 0.5 mg/ml vials. 60 ml, Switzerland), TELFAST (tablets 180 mg № 10 and 30 mg № 10, France) were least accessible for patients, because the costs in 2014 ranged from 5.23% to 6.73% of the average wage. Although specified by the high ratio of the adequacy of solvency AHDs were available.

The coefficients of availability (D) showed that the availability of AHDs for patients in 2014 decreased in comparison with the year 2013: only 25 TNs of 105 drugs, which were presents in the market in 2014, were available for patients, in 2013 77 TN from 121 drugs were available. In 2013 the TNs of desloratadine, and in 2014 the TNs of fexofenadine became more available.

Conclusion. The ratio of the adequacy of solvency and the coefficients of availability showed that many AHDs for the treatment of allergic diseases were not available for patients. In comparison with 2013 availability of AHDs in 2014 sharply decreased, but Ukrainian patients can afford to continue treatment with AHDs, because the maximum costs for AHDs were 6,73% of average monthly salary.

# COST ANALYSIS ON PHARMACOTHERAPY OF GASTROESOPHAGEAL REFLUX DISEASE

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**The aim of research** – to determine the cost of the use of proton pump inhibitors for the treatment of non-erosive form of gastroesophageal reflux disease.

**Materials and methods.** Objects of study - drugs of proton pump inhibitors (omeprazole, pantoprazole, lansoprazole, rabeprazole, esomeprazole) in tablets or capsules that were present in the pharmaceutical market of Ukraine in 2014.

Cost analysis on the use of these drugs for the treatment of a patient with non-erosive form of gastroesophageal reflux disease was performed with the daily doses of drugs: omeprazole - 20 mg, pantoprazole - 40 mg, rabeprazole - 20 mg, lansoprozol - 30 mg, esomeprazole - 40 mg. The course of treatment lasted 4 weeks. The currency ratio of UAH to dollar (USA) on 28.11.14 p. was 14.96:1.

The proton pump inhibitors range on the pharmaceutical market in Ukraine was determined by using a system of market research "Pharmstandard" of company "Morion" (November, 2014).

The average weighted price of their packings was determined by using electronic database "Compendium OnLine» (November, 2014).

For determining the range of costs for the use of proton pump inhibitors their trade names with minimum and maximum cost for a course of gastroesophageal reflux disease pharmacotherapy in one patient were determined.

**Results of research.** The range of costs on the use of proton pump inhibitors for pharmacotherapy of non-erosive form of gastroesophageal reflux disease was the following: for omeprazole – 0.99-15.18$, pantoprazole – 5.18-47.91$, lansoprazole – 6.29-12.76 $, rabeprazole – 3.18-96.46$, esomeprazole – 13.70-56.17$. It was wide enough for many proton pump inhibitors This is due to a significant difference in the price of their packings, with a lot of generics in Ukrainian pharmaceutical market and with its different medicine's form.

**Conclusions.** The cost of proton pump inhibitors on the use for pharmacotherapy of non-erosive form of gastroesophageal reflux disease can be quite high. Therefore, to apply for choice of proton pump inhibitor for disease treatment it is appropriate to use the results of pharmacoeconomic studies. This will allow to optimize cost of the payer (state, insurance companies and patients) for the treatment of gastroesophageal reflux disease.

# PHARMACOECONOMIC ASPECTS OF HYPERTENSION TREATMENT IN HOSPITAL

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In Ukraine the prevalence of arterial hypertension (AH) among cardiovascular diseases is 46.8%, almost 32% of adults have high blood pressure. The primary goal of antihypertensive treatment is to prevent clinical complications and not simply to lower elevated blood pressure. A significant proportion (60%) of the costs of treating cardiovascular diseases are the costs related to the medical treatment of patients. Pharmacoeconomic evaluation of treatment of hypertension and rationale for the selection of a medicinal product (MP) in order to optimize costs is relevant today.

The aim of this study was to analyze the consumption of antihypertensive drugs in hospital.

Materials and methods. Analysis of hospital pharmacotherapy of AH was performed on the basis of the therapeutic department Railroad Hospital of Poltava region. For analysis of AH hospital pharmacotherapy ABC -, VEN - and frequency analyses were used.

Results. The total number of prescribed drugs were 127 trade names (TNs). As a result of ABC-analysis showed that group A consists of 10 drugs, total cost of which amounted to 108398.26 USD, or 79.91% of the total costs for pharmaco-therapy. In the group B 27 drugs were included, the total cost of which amounted 20 579.16 USD, or 15.17%. The group C consists of 90 drugs related total cost of which amounted 6670.01 USD, or 4.92%. To vital drugs (category V), which are presented in clinical standard, 73 (57.48%) drugs were included, in the group non-essential (category N) 54 (42.52%) drugs were included. In the group A the majority 109 (85.83%) of prescribed drugs were included, 18 drugs (14.17%) were included in the group B. The frequency assignments leaders were: sodium chloride - 275 appointments, thiotriazolin – 111 appointments, metamax – 84 appointments, tivortyn and cardiomagnil 76 and 51 appointments respectively.

Conclusion. Comparison of results AVC-, VEN- and frequency analyses of prescriptions to the patients with arterial hypertension showed that majority of funds were spent on essential drugs (category V), which were accounted the majority of appointments.

# REAL USE OF ORAL HYPOGLYCEMIC AGENTS BY PATIENTS WITH TYPE 2 DIABETES MELLITUS IN UKRAINE

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Introduction. Diabetes mellitus type 2 is a medical and social problem because of its high prevalence and incidence, the individual disease burden of patients due to macro- and microvascular complications. The aims of pharmacotherapy in diabetes are to achieve good glycemic control. Reflection of the real pharmacotherapy of type 2 diabetes mellitus is the data on the amount and structure of consumption of oral hypoglycemic agents (OHAs).

Materials and methods. The objective of the study was the data on consumption of A10V group - hypoglycemic drugs for oral administration, of a market research analytical system "Pharmstandard". Consumption of drugs was assessed using ATC/DDD methodology in terms of $DDD_S$/1000 inhabitants/day ($DDD_S$/1000/d). Analysis were performed according to the 2013 data.

Results. According to the 2013 data in the structure of OHAs consumption a significant proportion (98.95%) of the total amount belongs to 2 groups - sulphonylurea derivatives (73.84%) and biguanides (25%), and only 1.16% relates to thiazolidinediones (TDs), dipeptidyl peptidase-4 inhibitors (DPP-4), combination drugs (CDs) and other oral hypoglycemic agents group (OOHAs group). Analysis of the range of the most consumed 2 groups of OHAs in the Ukrainian pharmaceutical market has shown that according to the 2013 data biguanides (metformin) are presented by 11 trade names (TNs). Among TNs the leaders in terms of consumption are siofor (Berlin-Chemie/Menarini Group, Germany), glucophage (Takeda, Japan) and diaformin (Farmak OJSC,Ukraine).The amount of their consumption was 1.44; 0.51 and 0.50 $DDD_S$/1000/d, respectively. In 2013 sulphonylurea derivatives are presented by 4 INN - glibenclamide, gliquidone, gliclazide and glimepiride with the level of consumption in 2013 2.09; 0.61; 3.01 and 2.48 $DDD_S$/1000/d, respectively, and 21 TNs.

Conclusions. In the structure of consumption of OHAs in Ukraine according to the data in 2013 98.95% of the total amount belongs to 2 groups - sulphonylurea derivatives (73.84%) and biguanides (25.11%). Among sulphonylurea derivatives identified significant consumption of II generation - glipizide, gliclazide and glibenclamide. Defined by inadequate intake drug of III generation – glimepiride.

# ANALYSIS OF EVIDENCE ABOUT CLINICAL EFFECTIVENESS OF VITAMINS $B_6$, $B_{12}$ AND FOLIC ACID FOR CARDIOVASCULAR DISEASES TREATMENT

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Today cardiovascular disease is one of the leaders in the structure of all diseases. In Ukraine, the number of patients suffering from cardiovascular disease is estimated at 25 million. The feasibility of use of vitamins for the prevention and treatment of cardiovascular complications is open. In epide-miologic studies, elevated homocysteine is linked to ischemic heart disease and stroke. A meta-analysis of prospective observational studies showed that a 25% lower homocysteine level was associated with an 11% lower ischemic heart disease risk and a 19% lower stroke risk. Homocysteine-lowering therapy with vitamins $B_6$, $B_{12}$ and folic acid (FC) for the prevention and treatment of cardiovascular complications is widely covered.

The aim of this study was to find and analyze evidence of clinical efficacy of vitamins $B_6$, $B_{12}$ and FC for the treatment of cardiovascular diseases.

Subject and methods - search for evidence of the clinical efficacy of vitamins $B_6$, $B_{12}$ and FC for the treatment of cardiovascular disease in the Internet site: www.trialresultscenter.org.

Results. As a result of analytical search on the Internet 16 original clinical studies were found. In these studies the effectiveness of B vitamins in the pharmacotherapy of cardiovascular diseases was studied, but only in four clinical studies the effectiveness of the combination of three vitamins $B_6$, $B_{12}$ and FC was studied. Only in one of these studies the ability of homocysteine-lowering therapy with folic acid (2 mg) and vitamins $B_{12}$ (0.5 mg) and $B_6$ (25 mg) in a single tablet in patients with recent stroke or TIA (within the past seven months) lower the risk of cardiovascular events (relative risk 0.91, 95% CI 0.82-1.0) was found. The results of two other clinical studies have not confirmed the high efficassy of vitamins $B_6$, $B_{12}$ and FC in the prevention of cardiovascular complications - stroke and myocardial infarction. Only one clinical study found that the incidence of the combined endpoint (cardiovascular events) was significantly lower in patients treated with vitamins, compared with a group of patients with initially low levels of vitamin $B_{12}$.

Conclusion. Homocysteine-lowering therapy with vitamins $B_6$, $B_{12}$ and FC improves prognosis in patients with CVD with initially low levels of vitamin $B_{12}$ in the blood.

# SECTION № 12

# MANAGEMENT AND MARKETING IN PHARMACY

# RESEARCH OF EFFICIENCY OF ASSORTMENT FORMING AT THE PHARMACY

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Assortment policy is a system of measures to determine a set of product groups, the most desired for successful activities and to ensure the economic efficiency of the enterprise as a whole. Assortment policy establishes a link between the demands of the market, on the one hand, and the intentions and capabilities of the firm on the other. Task of assortment policy is in any given moment the goods produced by the company meets best the needs of consumers both quality features and quantitative volumes. The presence of wide assortment allows to satisfy the needs of different segments, to prevent the emergence of competitors, to provide price range and stimulate of leaders.

Expanding the assortment of pharmaceutical products in the pharmacy is a key success factor for pharmacy retailers. However, every pharmacy has to choose a policy of resource allocation: to buy a large batch of cheap drug, or just a few expensive packages.

The purpose of our research is to estimate assortment policy of the homeopathic pharmacy and formulating recommendations about increase of its efficiency.

The breadth, depth and stability of pharmacy assortment drugs have been analyzed. The largest assortment of the pharmacy is in such pharmacotherapeutical groups of medicines as NSAID, analgesics, antipyretic; cardio-vascular and drugs affecting the respiratory system.

A study (using questionnaires) influence of consumer behavior to management by assortment policy of the pharmacy have been carried out. It was revealed that most of consumers of homeopathic medicines are women (75%), about 40% of purchases make people age from 31 to 40 years, 80% are people who take homeopathic remedies for the purpose of adjuvant therapy, 70% of consumers are choosing homeopathic herbal, solid dosage forms have greater demand among consumers (83%). 45% of consumers prefer foreign manufacturers of homeopathic medicines, advertising has a strong influence on the choice of consumers (60%). When buying homeopathic remedies most important criteria for consumer are safety 60%, efficiency (22%), price (13%) and brand recognition (5%).

# INVESTIGATION OF THE STRUCTURE AND IMPORTANCE OF MARKETING TASKS OF PHARMACIES' NETWORKS

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The process of integration and consolidation taking place in the pharmaceutical market in accordance with the current trends of world globalization, contribute to the dynamic development and dissemination of pharmacies' networks. Establishing modern models of economic relations subjects' retail segment of the pharmaceutical market is accompanied by changes in marketing approaches to management of the pharmacy. Achieving functional goals and high financial and economic indicators for pharmacies' networks might adapts their marketing activities to the objective process of forming market space, quality tasks of social responsibility to consumers of drugs and society in general. Today marketing tasks pharmacies' networks are closely related with common tasks of pharmacies as a healthcare institution and play an important role in the process of socio-economic activities. In terms of commercialization of pharmaceutical business, increased competition and the simultaneous implementation of the principles of Good Pharmaceutical Practice pharmacies' networks should focus their efforts not only on profit but also the performance of social functions important for the entire population. Addressing marketing tasks pharmacies' networks at the appropriate level serves as an indicator of the effectiveness of their marketing activities and provide professional pharmaceutical care.

The aim of this work is to study the structure and importance of marketing tasks pharmacies' networks. The study was conducted using the method of expert opinion. According to the results survey found that heads of pharmacies' networks rated highest scores marketing tasks associated with analysis and planning assortment policy, analysis of activity of competitors and market research.

There are different ways of formation of pharmacies' networks. For the retail segment of the pharmaceutical market in recent years is typical process of creating pharmacies' networks in the wholesale or manufacturing plants, whose main goal is to promote their goods directly to the retail network, thus bypassing the secondary distribution network. There is also a way to create a network by combining individual pharmacies into a single network structure, but the approach is different efficiency is primarily due to the fact that in the suggested model is very difficult to attract large investments. Combining pharmacies can occur on a franchise when pharmaceutical companies began working on a contract basis under a single brand name network, part of which it was included. Choose how expanding network business depends on the policy of the network of the region, which plans to enter the network structure, level of development of the pharmaceutical services, the availability of powerful local networks of competitors and commitment of individual pharmacies operate under well-known brand without losing its own legal.

# PECULIARITIES OF SUPPLY AND CONSUMPTION OF STATINS IN UKRAINE

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Statins are a class of drugs used to lower cholesterol levels by inhibiting the enzyme HMG-CoA reductase. The best-selling statin in the world is atorvastatin. In 2003 it became the best-selling pharmaceutical in history. Launched 1997, Pfizer Inc.'s Lipitor became the best-selling satin drug just three years after its debut. It went on to become the best-selling drug in the history of pharmaceuticals. Despite losing patent protection and a growing generic market, Lipitor (which lost patent protection in late 2011), together with Merck's Zocor (whose patent expired in 2006), still accounts for 57% in USA of the 264 million cholesterol prescription pot.

At the retail pharmaceutical market of Ukraine in 2015 are registered Simvastatin (36 foreign and 4 domestic drugs), Lovastatin (1 domestic drug), Pravastatin (1 foreign drug), Fluvastatin (1 foreign drug), Atorvastatin (69 foreign and 11 domestic drugs) and Rosuvastatin (70 foreign and 2 domestic drugs). Thus, the maximum number of registered statins belongs to Atorvastatin, and Rosuvastatin subgroups (80 drugs and 72 drugs respectively).

To analyse market share and consumption of statins we used the audit data of the pharmaceutical market of the system «Pharmstandart» of the company «Morion». In 2013 at the Ukrainian pharmaceutical market were sold around 3 million of packs of lipid modifying agents amounting to 225.8 million UAH.

The market share of statins among all lipid modifying agents at the Ukrainian pharmaceutical market is 73% in volume terms and 82% in monetary terms. The largest volume of sales in physical terms as well as in monetary terms belongs to atorvastatin. Annual volume of sales of atorvastatin is around 1.4 million packs to the amount of 122.6 million UAH. At the atorvastatin segment there is original drug Liprimar (known worldwide as Lipitor) and 79 generic drugs. Original drug Liprimar takes only 2.69% of atorvastatin segment in physical terms and 10.45% in monetary terms.

Market share of foreign atorvastatin drugs is 80.52% in physical terms and 85.4% in monetary terms. The leading positions among atorvastatin in Ukraine according sales in value terms belong to generic Europe companies KRKA, Slovenia (45,12%) and Zentiva, Czech Republic (12,33%).

# FORMATION OF CLIENTS' LOYALTY AS A COMPONENT OF THE ENTERPRISE EFFICIENCY

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Task of the pharmaceutical organizations at the present stage of development of economy is not only receiving profit, but, first of all - performance of social function on providing the population with medicines, qualitative and available at the price. At present, the pharmaceutical market is characterized by strong competition, which led to a positive change in the activities of pharmaceutical companies: implementation of marketing information, market research, market management of medicines, the introduction of new advertising projects, expansion of services aimed at ensuring the loyalty of consumers, and others.

Materials and methods: content analysis of scientific literature.

In today's economy, the center of all marketing activities of the enterprise is transferred from the product to the buyer. Valuable assets are long-term relationships with customers. Some researchers believe that the effect of loyalty is a more powerful factor in the success of the enterprise than even the market share or the volume and cost structure. In their opinion, areas of activity that require high intelligence and professionalism (insurance, banking, publishing) are most sensitive to the effect of loyalty. This should include the field of medicinal products.

When Ukraine's transition to a market economy, a large number of firms offering similar medicines with the same consumer characteristics, quality and selling price. High level of competition in the pharmaceutical market necessitates companies to fight for a client in every way possible, as soon as it will help them to survive in the competition.

Today, with the unfolding crisis, the problem of customer loyalty becomes even more relevant and drugstores are no exception. Pharmacies are looking for clients and finding are making great efforts to attract them, that is trying to provide them with quality service, the convenience at the pharmacy, and wish to maintain a friendly attitude. Customer Loyalty for pharmaceutical institutions is now becoming one of the main objectives of management for any pharmacy.

Thus, marketing loyalty is a mechanism for the formation of stable and long-term client assets. In terms of market saturation competently developed loyalty program gives the company a sustainable competitive advantage and guarantee long-term existence.

# SCIENTIFICALLY METHODICAL AND PRACTICAL JUSTIFICATION OF APPROACHES TO THE ESTIMATION OF BRANDS OF DRUGS

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With the rapid movement of market processes, appearance of new needs of consumers, the emergence of a significant number of substitute and analogue drugs, saturation of the market and increased competition, pharmaceutical companies more often have to fight for market position through their direct products – drugs. Pharmaceutical manufacturers are interested in converting their drugs in bestsellers.

We are accustomed in this case to use the term "brand". We faced the task to determine which of the drugs to treat hypertension brands are, and what characteristics they should have. As you know, companies do not create leaders – consumers create them. The real leader is one whom consumers find the leader. In the pharmaceutical industry it is expressed through both a commitment to a particular manufacturer and commitment to a specific drug. Arterial hypertension remains one of the most important medical and social problems and the leading risk factor for myocardial infarction and stroke. According to the forecast, by 2020 cardiovascular diseases will prevail over infectious diseases as the leading cause of death and disability. The prevalence of hypertension, which is the main risk factor for cardiovascular mortality in Ukraine, exceeds 40%.

Our researches are directed on analysis and theoretical and practical substantiation of the components to assess the brand of drugs for the treatment of hypertension and determine factors influencing the choice of consumers.

We explored the domestic market of antihypertensive medications and analyzed approaches, methods and specific techniques used in evaluating brands. We have identified the key indicators that characterize the brand value of medications as well as qualitative and quantitative indicators drugs. We conducted a survey on the assessment of antihypertensive drugs by consumers, pharmacists and doctors.

Of course, the most important characteristics that affect the evaluation of the brand are its prevalence, trust and recognition by consumers of products that are sold under a particular trade mark. In the final case, all these characteristics determine the volume of sales, the company's profits and the value of the brand. In many cases the value of brand may dominate the value of all tangible assets of the company and be a powerful tool in competing for the consumer.

During research of quantitative characteristics of the brands of drugs we were based on both general indicators and specific indicators of drugs.

The first of these quantitative indicators is the level of spontaneous knowledge. The minimum level of spontaneous knowledge will be to 30%. The higher the level of spontaneous knowledge, the higher the probability that consumer will choose this drug at the pharmacy. Indicators of spontaneous knowledge for strong brands are 60-70%, for very strong brands they are 80-90%.

The second important factor is the level of brand identification among other categories. The minimum level is the same – 30%. Advertising is responsible for this indicator. The more is reminding consumers about the product, the higher is the rate.

The third indicator in quantitative evaluation of the brand is the level of consumption that is directly associated with spontaneous knowledge. Thus, if the level of spontaneous knowledge is 30%, the minimum level of consumption of the brand should be 20%.

The last fourth indicator lies in the fact that the consumer is able to explain the difference between the medicinal products among others. Not only from the standpoint of rational preferences, but also by emotional feelings.

We have selected to the list qualitative indicators of antihypertensive drugs such indicators: efficiency, quality, safety, availability, duration of action, level of trust, prestige of manufacturer prevalence in pharmacy chains, convenience receiving, packaging design and others.

The study was carried out using a specially designed questionnaire for consumers, pharmacists and doctors. Results of the questionnaire allowed establishing the degree of importance of each of the characteristics which evaluated drug, its trademark and brand transition boundaries.

When processing parameters, were taken into account not only the subjective opinions of consumers, but the main objective factors that have a direct impact on brand perception. Among them there are recognition level, value, the term of presence in the market, presence in the retail points of sale and others.

Thus, the degree of recognition of the studied antihypertensive drugs by consumers was: Enap – 100%, Fosicard – 53%, Amlodopine-Zdorovje – 100% Lerkamen – 75%, Renitek – 88%, Atenobene – 93%, and others.

Due to the results, pharmaceutical companies receive the answer to the question: "What to do next and what brand strength indicators should be developed depending on the purpose and capabilities of the company."

# MARKETING RESEARCH OF MEDICINES MARKET FOR MIOCARDIAL INFARCTION TREATMENT

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Cardiovascular diseases (CVD) of population are the most topical medical and social-economical problem both for domestic public health and for society generally. According to the data of State Statistics Committee, the substantial increase of illness with cardiovascular pathology has been noted in Ukraine recently.

The aim of our research is investigation of medicines which have the largest frequency of prescriptions, within the Miocardial Infarction treatment (MI) and to conduct an analysis of drugs for MI treatment.

For the research tasks fulfillment the ABC analysis was conducted, VEN – analysis of drugs for MI treatment, a cost for medicamentous treatment was calculated.

On mortality rate of population from CVD, Ukraine is the first country among European countries. For long time, acute forms of the ischemic cardio disease of hold a leading position in the general structure of CVD and mortality. Despite significant achievements of the last years in the field of diagnostics and treatment, in Ukraine the tendency is evident that patients with such diseases are younger, trend of unfavorable course of disease and, as a result, increase of early disability of working-age individuals.

In the world practice, more frequently the methods of clinical and economical analysis are used with the aim of effective models development of pharmaceutical supply and rationalization of medicines' consumption.

Thus, the analysis of drugs prescriptions frequency according to medicinal forms, determines that the leading position in terms of prescriptions frequency from the total numbers of prescriptions occupied 56,98 % of liquid medicinal forms (solutions).

# RATIONALE OF APPROACHES TO ESTIMATION OF QUALITY OF ENTERPRISE MARKETING ACTIVITY

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The problem of estimation of marketing of the company is connected with the necessity of choosing priority strategic and tactical direction when planning marketing activities. Thus, the purpose of our research is to study approaches to assessing and improving the quality of the marketing of the company.

According to the scientific literature the approaches to the assessment of the marketing of the company have been study. In particular, the components for evaluating the effectiveness of various marketing activities have been selected: implementation of marketing strategies; marketing management system; logistics activities of the company, relationships with partners, functioning of marketing information systems and implementation of different marketing activities.

Another area of research is the development of approaches to estimation the achievement of marketing objectives, based on the allocation of such categories as customers, suppliers, competitors, financial indicators.

It was found that development of such Target-indicators that assess to estimate the approach set marketing goals is important for companies. As Target-indicator for consumers is proposed to use: volume of the target segment and its characteristics; degree of customer satisfaction; loyalty to the company; models of consumer behavior; brand perception by consumers; priority of the brand for consumers compared to competitors' products; awareness of consumers; volume of purchases undertaken by consumers; the cost and probability of acquiring of competitors' products by customers. Financial indicators include revenue, income, profits, including profits from new customers, the average level of discounts, expenses, their structure, the cost of attracting new customers, marketing expenses etc.

For the category of "supplier" it is appropriate to use such indicators as the effectiveness of relationships with suppliers; clarity of the conditions of cooperation; the quality of supply. It is advisable to estimate competitors by indicators such as market share; positioning strategy; existing barriers to entry; cost structure and pricing etc.

Use of the following parameters allows making reasonable decisions about the quality of implementation of marketing activities and adaptation of the enterprises to requirements and needs of the market.

# ANALYSIS OF MAIN ADAPTIVE MEASURES FOR PHARMACEUTICAL ENTERPRISES

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Today for increasing the competitiveness Iraq**'s** pharmaceutical enterprises is appropriate implementation of new technologies to pharmaceutical companies, modernization of production by the rules of GMP; improvement of the legal base area; transition to advanced technologies and quality standards in the Iraqi pharmaceutical industry; of scientific advances and innovations in practice pharmaceutical manufacturers; the development and implementation of measures to promote products promotion Iraqi pharmaceutical manufacturers, active opposition to the spread of counterfeit goods and illegal drugs, implementing and defending the principles of free competition, protect the interests of the Iraqi pharmaceutical industry in the legislature, executive and judiciary power.

The aim of this work is to analyze the main adaptive measures for Iraq's pharmaceutical enterprises.

For solving this aim market research was conducted by us using method expert estimations.

Thus the main adaptive measures for Iraq's pharmaceutical enterprises are: changing assortment policy of the company, the implementation an effective pricing policy, the search for new distribution channels, development and implementation of effective marketing strategy, participation in conventions, congresses, conferences, seminars, workshops and develop and implement a strategic program of pharmaceutical enterprises. The lowest commonly used were the following adaptive events: information and communication staff, insurance against the risks of changes in the external environment and creation MIS software and marketing analysis, respectively, creation information systems needed to control all possible changes in the external environment and creating CRM-system.

Recent data show a very low level of information technology for pharmaceutical enterprises.

Thus, the received results on this stage of research allow doing a conclusion that the management by the changes is inalienable part of successful activity of production pharmaceutical enterprises. The management by the changes helps to avoid such negative effects and factors, as decline of productivity, resistance to the changes from personnel, exception of workers from a labour process, professional exhaustion, dismission of workers by their own desire, conflicts between workers, slow introduction of changes, deviation from work, division of personnel on «we» and «they». Thus, after analyzing the major changes taking place in the external environment, there is a need to develop models of adaptive control for pharmaceutical companies, which made us on the example of Iraq's pharmaceutical enterprise.

# DEVELOPMENT OF THE DOMESTIC PHARMACEUTICAL INDUSTRY

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It is known that the pharmaceutical industry is one of the most socially important spheres of activities in any country. However, often imported drugs are characterized by their significantly higher prices, particularly for cancer patients. Accordingly, there are tasked to ensure domestic consumption of drugs is due to the national pharmaceutical production by Government to President of the Republic of Kazakhstan Nursultan Nazarbayev. So, in 2010 approved a program for the development of the pharmaceutical industry of Kazakhstan for 2010-2014, the main tasks which indicated issues of supplying the population with medicines produced domestically. At the same time, analysis of the development of the national production of drugs in the pharmaceutical market of Kazakhstan is a prerequisite for the implementation of this program.

It should be emphasized that the process control system of drug provision of the population, mainly based on market analysis of the pharmaceutical market in the country. We conducted an analysis and found that the amount of funds allocated to the health system of the Republic of Kazakhstan from the state budget in the period from 2005 to 2013 increased significantly. So if the 2005 budget was only 131, then in 2013 it was already 738,7mlrd. tenge.

According to information received from the information source "Farm exports" on the situation in the retail pharmaceutical market in the CIS, Kazakhstan is one of three countries that make up 80% of the retail pharmaceutical market in the CIS.

At the moment, the number of objects pharmaceutical services operating in the territory of the Republic of Kazakhstan in 2013, is 10,987, of which:

- The number of pharmaceutical production - 110;
- The number of retail drugs - 8133;
- The number of objects that implement the drugs through medical facilities - 549;
- The number of drug stores - 1660;
- The number of objects wholesale medical products devices and medical equipment –535.

At the same time, in 2013 71% of drugs in the Republic of Kazakhstan accounted for the largest pharmaceutical factory- JSC "Chempharm.

Thus, for the sustainable development of the pharmaceutical industry of the Republic of Kazakhstan should provide new best management practices based on market research of these processes for the harmonious development and other pharmaceutical companies.

In this regard, the issue of improving the efficiency of maintenance of the population of the Republic of Kazakhstan drugs domestic production is relevant and important in the current social and economical situation.

The aim of our studies is to develop methodological approaches to system development of domestic medicines in the Republic of Kazakhstan.

The objectives of the study include:

1. Definition of the situation on the pharmaceutical market in the CIS countries and abroad, the rate of the volume of the pharmaceutical industry;
2. Conduct market analysis import-changeable ability of domestic products;
3. The dynamics of drug consumption in the pharmaceutical market of Kazakhstan for 2008-2013;
4. For a discussion of the characteristics and classification of the availability of drugs;
5. Minimizing the cost of state procurement of drugs and medical devices, SPMFP
6. Development of guidelines for the creation and justification of organizational and functional marketing strategies of domestic drugs.

The objects of study will serve as:

- The need for medicines of domestic production,
- Domestic pharmaceutical enterprises of the Republic of Kazakhstan;
- Pharmacy and medical institutions of the Republic of Kazakhstan.

In this paper we will apply the following methods:

- Systems analysis;
- Marketing analysis.
- Method of expert evaluations.

The subject of the study are:

- Regulatory and legislative acts in the field of drug treatment;
- Statistics of the RK and the MEAS;
- The results of sociological research doctors and patients.

As a result of our research, we obtain new data that will determine the novelty of the research:

1. There will be first conducted comprehensive studies of domestic drugs, in order to determine their competitiveness for import substitution;

2. For the purpose of import will be developed organizational and functional diversification of the system of promotion in the market of domestic medicines and will be given its scientific justification.

In conclusion, it should be emphasized that the study of the pharmaceutical industry on the example of Kazakhstan JSC Chempharm, will solve the issues related to the promotion of domestic medicines and provision of the Republic of Kazakhstan to the fullest extent.

# USING OF RESULTS OF MARKETING RESEARCH IN CUSTOMER LOYALTY DEVELOPMENT SYSTEM

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Upcoming trend in development of pharmaceutical business, which is accompanied by new customer acquisition and extra profit earning, is improvement of pharmaceutical assortment based on appending of parapharmaceutical products, usage of loyalty programs, focused at enhancement of consumer interaction, decision taken is based on results of marketing research. At present loyalty programs in pharmaceutical business at macro level, meso level and micro level are widely integrated. At micro level pharmacy institutions use programs of loyalty of employees to company and the company's to customers loyalty programs. According to statistics loyal customers can increase the profit of 25 to 85%. Thus, the problems of elaboration and maintaining of loyalty require investigation and resolution.

In this regard we implemented a research to develop methodological approach to the evaluation of loyalty of curative cosmetics consumers based on results of marketing research. Consequently was created a methodology that helps to evaluate the association between customer satisfaction, derived in grades as a result of marketing researches, and customer loyalty to manufacturer’s trademark.

It was found that segment of conservative customers, who kept loyalty to trademark, was 37,3%, segment of customers who occasionally agreed to try a new good of different trademark was 46,8%. Enquiry results and calculations of average values of satisfaction and importance of showings say that following parameters best of all satisfy consumer’s requirements: hypoallergenicity (91,1%), the price of products (87,0%), efficiency (86,7%), product quality (83,3%). Thus, the integral indicator of customer satisfaction with therapeutic cosmetics, calculated on the basis of loyalty, is 51,3% versus 84,9%, calculated using the average value of the average ratings of satisfaction and importance. This means that customer satisfaction with the most important attributes of product and marketing indicators of activities will enable the company to rely on 51,3% of secondary purchases.

Thus, it has been found that to increase loyalty it is necessary to specify criteria of evaluation of customer allegiance, methodologies and frequency of analysis of customers database and develop procedures that will control relationships with customers. Implementation of components for establishment of loyalty control process will allow the company attract a number of loyal customers, gain a competitive edge at the market, and improve pharmacy’s income level.

# RESEARCH OF MERCHANDISING RULES USAGE IN THE PHARMACY

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The current marketing situation that exists on the modern pharmaceutical market has makes it difficult for the pharmacies to stand out with the exclusive assortment or pricing. An important way to keep existing loyal customers and attract new ones is creating an image of pharmacies by arranging comforting conditions for making the purchase. The key tools in this process are methods of sales promotion, including merchandising.

At present, the increased the amount of pharmacies contributes to the increased competition in the pharmaceutical market. The product range has grown considerably (dietary supplements, homeopathy, valeopharmacological drugs) and increased almost three times over the past 60 years, and in most cases by introducing a range of drugs analogues of different manufacturers. Thus, the amount of medicines offered in the pharmacy exceeds the demand. Pharmacies have to make considerable efforts to maintain competitiveness and maximize their earnings. Merchandising techniques, among other tools, may help maximize the turnover without needing to change pharmacy topography.

The aim of the study was to examine the usage of merchandising tools and methods in pharmacies. During the research the factors that influence the choice of drugs were studied. By analyzing the data obtained using the survey the dependence between the usage of methods and rules of merchandising and the turnover rates at the pharmacy was discovered.

It is proved that the prompt implementation of merchandising helps to increase the total revenue pharmacies, increase rates of turnover, help create a steady demand for a particular product, and makes it possible to attract new customers. Thus we can conclude that the usage of the merchandising methods and techniques allows to significantly improve the key performance indicators of the pharmacy.

# PHARMACEUTICAL MARKET OF THE UNITED ARAB EMIRATES

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Pharmaceutical market of the United Arab Emirates (UAE) ranks second place behind Saudi Arabia with regard to of investments attracted to the Middle East, and through the development of free trade zones, which contributes to good prospects for growth. Medical tourism, direct instructions regulators and increased spending in the health sector will be the key factors in the development of the pharmaceutical market based on the recent study of the pharmaceutical industry of the UAE and current trends of its development.

Pharmaceutical market of the United Arab Emirates estimated at $ 2.4 billion. In 2013, and predict that it will reach $ 3.7 billion. With increasing 5.3 % CAGR (Compound Annnual Growth Rate) in 2020. Medical equipment market estimated at 2008 in the amount of 600.2 million dollars and 733.3 million dollars in 2013. We estimate that in 2020 it cost will be $ 978.9 million dollars with increasing 4.2 % CAGR compared with those in 2014. Positive trends can stimulate an increase in health insurance coverage and public initiatives to improve health care in the healthcare market of the UAE.

UAE market also receive additional benefits through the creation of free zones, concerning the development of the health sector. There are biotech area Dubai Biotechnology and Research Park Research Park (DuBiotech), which stimulates the creation of global players in the pharmaceutical market to build regional centers in the country. Companies that are in the territory DuBiotech, get 100% exemption from payment corporate and individual tax guarantees for 50 years. Expenditure on R&D segment is minor in comparison with other countries, which means that new drugs imported at high prices. Projects such as DuBiotech are meant to help restore the disturbed balance.

Key players in the pharmaceutical market in the UAE are Julphar, Neopharma, Pfizer, GlaxoSmithKline and Novartis, in the medical equipment market is Medtronic, Siemens Healthcare, F. Hoffmann-La Roche, Abbott Laboratories and Boston Scientific Corporation. An important role in the growth of the pharmaceutical market in the UAE will play medical tourism. Dubai plans to receive $ 20 million in 2020. Wealthy customers are willing to travel around the world in search of the best hospitals and medical care. In addition, just Dubai Health Care City will provide a platform for increased medical tourism and a significant increase in profits.

# ANALYSIS OF THE APPLICATION OF MERCHANDISING TO INCREASE THE VOLUME OF IMPULSE PURCHASES AT THE PHARMACY

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Competitiveness of each company depends on effectiveness the marketing approaches, new technologies, competently performed assortment policy, selected staff, satisfaction of customer needs. Under these conditions, it is important to identify and maximum to use of any reserves increase revenue and attracting customers to the pharmacy, not forgetting about the interests of the consumers and the ethical side of the point. One of these reserves is unplanned purchases, which are according to different estimates up to 75% of the total volume of sales in pharmacies. This is especially important due to the increased assortment of OTC medicines that are impulsive demand.

The aim of our research is the analysis of using of merchandising to increase the volume of unplanned purchases at the pharmacy.

A survey of visitors of pharmacies has been carried out. The vast majority of visitors recognize the tendency to make impulse purchases (over 75%). The main factors influencing impulse purchases are: advices of pharmacists (45%) and the location of the relevant goods on showcases (30%).

As for the types of goods of impulsive demand, the main groups are cosmetics, vitamins, immune stimulants, supplements and herbal teas.

The most important factors that influence the choice of the pharmacy visitors recognize: professional quality of pharmaceutical specialist (2,6 points), the price level (2,1), the location of the pharmacy (1,7) and schedule (1,6), the presence of a medical consultant (1,7), ease of finding a product (1,9), a wide assortment (1,8) and preliminary offers.

Also it was found that for expensive medicines the impact on the buyer by changing the display of goods is inefficient, due to, the difficulty of making decision according to the price of the medicine and the prevalence of rational motives over emotional during the process of buying. It was revealed that for the well-known medicines the effect of merchandising is smaller, which may be due to the fact that information about the medicine has already reached the target audience and number of new customers responding to the competent display of goods and presentation of medicines is less.

# IMPROVEMENT OF THE MANAGEMENT SYSTEM IN THE ENTERPRISEWITH "BROKEN WINDOWS THEORY"

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The purpose of this article is the use of "Broken windows theory" in management, productivity – enhancing.

Broken windows theory formulated in 1982 by two criminologist. Its essence is that the active struggle with the slightest violation of the order (like graffiti) reduces the level of crime in the area, because it shows the population of the principled position of the authorities. Ignoring minor offenses authors compare with broken windows in the house – it is a signal for causing further destruction. If one broken window left unglazed, soon will kill the rest of the glass in the building, and the quarter in which it is building pro – hlestnet wave of crime and chaos. Many experts have ridiculed this approach, but New York City Mayor Rudolph Giuliani broken windows theory is based his new policy of zero tolerance for any offense. He started with washing graffiti subway cars – and soon he was able to revive the city. From minor problems grow large, but on the other hand, the complex also includes changes in the situation of small decisions.

The theory of "broken windows" works well as personnel. If one person begins to violate discipline and others see that it is easy to get away with it, soon almost all of your staff will be late, leave jobs before they are and generally wander aimlessly around the office, simulating rough activity. The manager must adhere to a policy of zero tolerance for "broken glass" in his organization. No trifles. Nothing can be left unattended. Mainly zero tolerance should apply to the staff. When an employee harms us, it becomes a kind of "broken window", so it is important to notice the "broken windows" team, because they suffer from the productivity of the entire staff. To avoid the "broken windows" and do not give your business to move into the category of second-class, Naladte clear chain of command staff. Monitoring is an integral part and one of the functions of the management process is the constant and systematic monitoring of processes and facilities for compliance with their behavior and state policy management system of the organization and current legislation. The most accurate value for the concepts of "management" and "control" defined the famous master of management P. Drucker: "If we express the basic idea of these concepts is extremely compressed, the control – this measurement and information, and control - is first of all the action. Thus, the purpose of monitoring is to identify what is happening and to control - ensuring that the work performed consistent with the original plans, so "control" provides information on the basis of which the "management", that is to perform the necessary actions."

Using this theory will help to figure out who violate discipline of employees, working time efficiently administering, and be able to evaluate how it affects the work of colleagues.

# PROBLEM SOLVING AND DECISION MAKING

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Much of what managers do is solve problems and make decisions. Decision-making is a key role of a manager and leader. Some managers find this to be one of the most difficult tasks to perform. They have a fear of failure, and procrastinate mainly because they have a lack of a structured approach. One of two things usually happens, they either put off making the decision in the hopes that someone else will bail them out, or even worse, make a decision using a knee jerk reaction.

It is best to think of making a decision, as drawing a line between two points. If you can't draw a straight line between the two points, then that decision should most likely be rejected. When the line goes off into tangents, there might not be a realistic link between the proposed action and outcome.

New managers often try to solve problems and make decisions by reacting to them before they fully understand all of the possible factors. They feel that the quickness of a decision is more important than the long-term outcome. There are times when a quick decision is needed, such as dealing with a violent act in the workplace. However, most decisions are not needed immediately and you do in fact have the time to make the right decision. That is the key, making the right decision. Just be careful to not let decisions accumulate, or else you will have a backlog of both small and complex decisions to make. You need to find the perfect balance of knowing when to make quick and easy decisions on the fly, and when to take time with the complex decisions. Define the problem or need before you make the decision. Ask yourself, and others if needed, the following who, what, when, where, how and why type of questions. In lesson 9 we will discuss cost-benefit and task management tools, however, here are 12 steps to follow to use as a guideline when making important decisions:

1. Who should make the decision? First of all, you might be looking at a problem or need that is not your decision to make. Be sure you are not stepping on anyone's toes, even though your heart is in the right place. If you are the one to make the decision, go to the next step.

2. What makes you think there is a problem, or why the need? Before you can start to make any decisions, you need to be absolutely clear the problem or need is valid. Make sure you consider those who will be affected by the decision. Talk to

some key staff members to make sure you and your staff fully understands the nature of the problem or need. You want people who will speak up, are efficient, take necessary risks, have somewhat opposing views, and are strongly motivated. There are times when it seems like the problem or need comes at you like "the sky is falling," but when you take the time to truly investigate the problem or need, you might find it is overly exaggerated. This happens quite often as emotions take over logic. For instance, is it one person complaining about a particular situation or does everyone feels the same way? Is there a common complaint from your customers or just one or two disgruntled people who will never be happy? Is there a common trend or is it just speculation? Do you really need to invest in a new database or can you work with what you've got? Dig deep to find if there is a true problem, and then start on finding ways to improve. You don't want to fix something that is not broke. If you indeed suspect there is a problem, follow steps 3 through 12.

3. Where is the problem or need? Is it internal or external? Is it in your department or somewhere else? Is it only in certain areas of your network? Is it one employee or the whole group? You need to know where the problem or need lies before you can begin to make the right decision to fix or buy.

4. When is it happening or needed? Is it certain parts of the day? Is it when there is over usage? Is it when shifts overlap? Is it always at the end of the month? Is it every time there is a new software release? By pinpointing when the problem happens, it helps greatly in detecting the root cause of the issue.

5. What is causing the problem or need? Is the problem process related? A lack of training? Old and slow computers causing longer handle times, which in turn is affecting customer satisfaction? Are there not enough employees to handle the amount of calls? Is it a design or engineering flaw? Is it quality control issues? You need to get with key staff members to truly determine the root cause of the issue. Determining you have a problem is useless if you, or another department, cannot find the cause.

6. How complex is the problem or need? The more complex the problem or need, the deeper you will have to dig. Don't be afraid to go back to the drawing board until you are fully confident with the choices you have made.

7. What is the urgency and how should you prioritize? Some problems are more important than others. You would not want to work on a complex minor issue when you have an easy major issue that should be dealt with immediately.

# SALES ACTIVITIES OF PHARMACEUTICAL ENTERPRISE

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Sales activities must be organized in accordance with variable needs of the market and capacities of an enterprise itself. Solution of a problem of improvement of sales policy management is an actual issue for all participants of a system of sales promotion of products to the end consumers. Therefore, it is necessary to enhance quality and promptness of administrative tasks' approving to improve sales policy of pharmaceutical enterprises for providing population with medicines in sufficient quantity and owners' profit maximization.

The goals of this research was investigation of marketing decisions related to an enterprise's sales policy making and key factors ascertaining for pharmaceutical enterprise's success in distribution.

As informative backgrounds for the research, the data of financial report of the pharmaceutical enterprise «Chemist's «Interhospital»» were used.

During the research, the methods were applied as follows: Delphi approach (for marketing risks' evaluation in distribution, estimation of sales capacity level of enterprises etc.) and systematic analysis (within marketing research of enterprise for conception argumentation of sales management strategic marketing).

While implementing works, marketing decisions of sales policy of the enterprise were analyzed and the factors of pharmaceutical enterprise's success were ascertained.

Sales system applied by the enterprise is one of the factors of product's competitiveness. Therefore pharmaceutical enterprise should design an accurate sales policy. In competitive climate, manufacturing and non-manufacturing enterprises should have an effective marketing strategy of sales management.

Based on the analysis that has been conducted, the following outcomes were made: the marketing activities of enterprise are at the very low level, there is a decline in economic efficiency of marketing sales strategic management of the enterprise. Thus, the enterprise requires service improvement, establishing program of patients' loyalty rise, essential services introducing, and enlarging assortment of medicines.

**VEN-ANALIZ ASSORTMENT OF ANTIDEPRESSANTS**

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Today in Ukraine there is an emergency situation, thus anxiety and depressive disorders are the most common (70%) forms of nonpsychotic depression conditions. Majority of them are difficult for cure.

From the medical point of view military conflict is a traumatic event, the consequences of which can be quite different and devastating. The spectrum of these effects varies from relatively mild to severe depression.

Today, it is essential to know how the fighting affected the mental health of residents from areas of military conflict. Much of mental disorders due to trauma are being formed in time from several weeks to several months after the events. That's why leading psychiatrists of Ukraine (I.V. Linskiy, V.N. Kuzminov, L.F. Shestopalova, Ye.G. Grinevich etc.) recently conducted studies on the issue.

As a result of the military conflict residents of the eastern regions of Ukraine forced to move to other cities of the zone ATO. The migrants tend to have increased anxiety. Therefore there is a need to explore the local population to find adequate corrections of these states.

The aim of the study was VEN-analysis of the range of antidepressants.

Methods: pharmacoeconomic, VEN-analysis.

Results. VEN-analysis is a directive segmentation "necessity" range. It is used in medicine and pharmacy in a parallel with ABC-analysis to determine the feasibility of using the funds for medicines (drugs). This analysis of drugs in accordance with international practice, is divided into vital (V), essential (E) and secondary (N). VEN-analysis allows us to evaluate which category is dominated by drug use. The group V has the drugs within the National List of Essential medicines and medical purposes. Group E consists of drugs that are available in the State logbook drugs, and group N has all other drugs not included in the groups V and E.

Of the 55 drugs under the international non-proprietary name (INN) in group V INN there are 47 drugs (88.5%) and in group N there are 8 INN drugs (14.5%).

Conclusions. Results of VEN analysis of antidepressants have shown that essential drugs of V constitute 88.5% share of sales. Only 8 of the 55 drugs was not included in the State FORM LS 4th edition. Hence, physicians preferred drugs recommended by national standards applicable by Ministry of Health Protection of Ukraine. These results can be used in pharmacoeconomic evaluation of neurotic anxiety pharmacotherapy.

# ANALYSIS OF FACTORS CONTRIBUTING TO THE CONSUMPTION OF HEPATOTROPIC DRUGS

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A group of drugs with hepatotropic activity as it has been shown in numerous studies of domestic specialists' sheets is often enough appointed by Ukrainian doctors. Foreign branded drugs Essenciale (produced by French company Sanofi) and Karsil (produced by Bulgarian company Sopharma) traditionally are among the top 20 best-selling drugs in Ukraine.

The aim of this paper is to analyse causes of consumption of hepatotropic drugs in Ukraine. In our study we used desk research (content-analysis and analysis of documents).

Causes of consumption of hepatotropic drugs can be divided into two main groups: objective and subjective ones. Morbidity and mortality from liver disease in spite of the progress in the prevention and treatment of many diseases, exhibits a strong tendency to increase. The most common types of pathology of hepatobiliary system include acute and chronic viral hepatitis, toxic and medicinal defeat, alcoholic disease of liver and nonalcoholic steatohepatitis.

In addition to objective reasons for the application of hepatotropic drugs, there are many subjective reasons. Firstly, a large number of scientific papers devoted to the use of a class of hepatotropic drugs. A conflict of interest may arise in the financing of research or publication by the pharmaceutical companies. Number of scientific publications on the use of hepatotropic drugs with pathologies unrelated to the main indications is growing.

Secondly, the advertising of drugs in the media influences the final consumers. According to the data of market research of analytical system «PharmXplorer» / «Pharmstandard» of the company «Proxima Research», in 2014 the brand Essenciale took a first place in the top ten drugs leaders in expenditure on television advertising. The sales volume of television advertising of the drug was 157.1 million UAH for about 22 thousand displays of advertising. Among other subjective reasons for using hepatotropic drugs we can identify subjectivity of medical appointment, a high level of self-medication among the population and the use of hepatotropic drugs off-label.

Our further research will be focused on the study of consumers' behavior and consumers' attitudes to the class of hepatotropic drugs.

# ANALYZE OF PHARMACEUTICAL INDUSTRY IN EUROPE

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Medicine is for people, not for profits. A monopolistic position, medical innovation, patent protection, and an increasing number of patients worldwide allow the pharma companies to make billions of USD every year but medicine made is for people, not for profits. In the face of crisis, few industries are profitable and well-functioning, but there are some that still keep on generating benefits and offering work places. The pharmaceutical industry is one of the most profitable sectors on our globe, and considered the most lucrative after-market weapons. Total global spending on medicines will exceed one trillion USD in 2014 and reach almost $1.2 trillion in 2017. By 2017, the global spending on medicines will have almost doubled the spending in 2007. Economically stable countries implemented two to seven policy changes each, whereas less stable countries implemented 10 to 22 each. Of the 88 policy changes identified, 33 occurred in 2010 and 40 in 2011. They involved changing out-of-pocket payments for patients in 16 cases, price mark-up schemes in 13 and price cuts in 11. Sales volumes increased moderately in all countries except Greece and Portugal, which experienced slight declines after economic crisis in 2009. Sales values decreased in both groups of countries, but fell more in less stable countries. Less economically stable countries implemented more pharmaceutical policy changes during the recession than economically stable countries. Unexpectedly, pharmaceutical sales volumes increased in almost all countries, whereas sales values declined, especially in less stable countries.

We argues that the decisive factors are institutions and resources, which in turn govern global economics. Institutions are the rules of the game – both formal and informal. Now, formal constraints include laws, regulations, and rules. Informal limitations are norms, cultures, and ethics, which can be continuously divided into normative and cognitive supportive pillars. Referring to the resource-based view, we suggests using the SWOT (strengths – weaknesses – opportunities – treats), but even more the VRIO framework (value – rarity – imitability – organization) when evaluating the companies. This idea is especially valuable when applied to international business. When going abroad, familiar rules of the game are often not available. To capture the hearts, minds, and wallets of customers in other markets, companies need to pay attention to the rules of the game there, especially unwritten informal ones.

# ANALYSIS OF MONITORING ADVERSE EVENTS SYSTEMS IN DIFFERENT COUNTRIES OF THE WORLD

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In the course of international studies have shown that millions of patients suffering from severe and sometimes irreversible complications of drug therapy. Ongoing monitoring of the drugs safety allows to evaluate the risk to benefit and to make decision about further medical use of the drug. Given the consequences of drugs adverse reactions monitoring system have been developed, the most popular and effective of which is the spontaneous reporting system, which is the basis of pharmacovigilance in all countries.

The purpose of our research is to analyze the systems for monitoring adverse events in Ukraine and other countries.

Monitoring of drug adverse reactions can be carried out by various methods. Particular preference is given for one of them, depending on the specifics of the region for control and research purposes. Post-marketing clinical trials, active monitoring of the hospitals and the method of spontaneous reports are the most universal methods. There is also quite effective methods include prescription monitoring, literary meta-analyzes, the analysis of individual cases described in the literature, etc. Approaches to pharmacovigilance have been identified and recommended by the World Health Organization (WHO). WHO also has been proposed classification mechanisms of adverse effects, designed specifically for the system of spontaneous messages.

The principles the foreign organizations for monitoring of adverse reactions have been analyzed: Danish Health and Medicines Authority (Denmark), Adverse Event Reporting System (USA), Drug Reaction Reporting System (Australia), Centre for Adverse Reactions Monitoring (New Zealand), MedEffect (Canada), Pharmaceuticals and Medical Devices Agency (Japan).

There is also an international system for monitoring of drugs adverse reactions (An international system for monitoring adverse reactions to drugs). WHO Headquarters is responsible for policy and center of the WHO for international monitoring of medicines in Upsala (Uppsala Monitoring Centre, Sweden) has operational responsibility for the program.

The monitoring system of adverse reactions operates in Ukraine since 1996 and it is harmonized according to international approaches to pharmacovigilance.

# THE STUDY OF CONSUMER BEHAVIOR OF PHARMACY VISITORS

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Consumer behavior is an action that individuals take during purchase, and consumption of goods and services with the purpose of satisfaction their needs and desires. A buy is a step that leads to the purchase, and include the purchase or order of goods. The main task of the pharmacy institution is satisfaction of population needs in high-quality and effective medicines. It requires special knowledge about the purchasing preferences of visitors of pharmacies, their behavior and motivation when making decisions about buying medicines. Therefore, the study of consumer behavior can improve the quality of customer service and the efficiency of the pharmacy.

The purpose of our research is study the features of consumer behavior of consumers of OTC medicines.

We use research methods: content analysis, questionnaire, comparative analysis, grouping, and statistical analysis. Based on the literature data, we have studied the existing classification of consumer behavior. Depending on the classification of the characteristic it is possible to allocate the following classifications. Depending on the decision to purchase are: 1) Planned purchase (buyer pre-plans his/her shopping basket and the amount of money spent). 2) Unplanned or spontaneous purchase, which is characterized by behavior that can be influenced using the merchandising tools and various factors of price incentives. In accordance with the results of our research, which was conducted on a range of pharmacies of Kharkiv and Vinnytsia regions, it was found that in most cases, visitors of pharmacies carry out pre-planned purchases (69%).

Depending on the level of price sensitivity of buyers of pharmaceutical products they can be divided into the following categories: economic, personal, ethical, apathetic. According to the results of our study it was revealed that economy buyers is dominated at pharmacies, willing to buy nasal drugs at prices from 20 UAH up to 50 UAH.

Depending on the level of emotional sensitivity the following types of customers are distinguished: shy; good-natured; uncommunicative; aggressive; self-confident. Studies have shown that the pharmacy appeal mostly good-natured (42%) and aggressive buyers (35%).

Thus, pharmacists it is advisable to take into account different types of consumer behaviour that will improve the quality of their service, and as a result, to improve the efficiency of the enterprise.

# MARKETING RESEARCH OF CONSUMER ATTITUDES TO PHARMACEUTICAL ENTERPRISES PRODUCTS

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Consumers are always a subject of a special attention of a manufacturer. Success of the company depends on a consumer choice. The research covers a number of consumer trends, consumer attitude to the company; research of a consumer attitudes to certain brands of goods; research of a customer satisfaction; research of consumer loyalty to a brand; research of the intentions of a consumers; research of decision-making process while purchasing, and its behavior during and after the purchase; research the motivations of consumers; market segmentation by consumer groups.

The aim of the study is to determine the place of the "Lekhim-Kharkiv" enterprise in the market and consumer attitudes toward drugs of this brand.

In this paper, survey in the form of a questionnaire was selected as the main method of the marketing research. This survey was performed while investigation of a consumer attitudes to drug "Prostatilen" the manufacturer "Lekhim-Kharkiv". First, the survey found that 60% of respondents use drugs factory "Lekhim-Kharkiv". 55% answered that they rate very well the brand "Lekhim".

Then it was found that 28% of consumers use "Protatylen" of the manufacturer. According to the study, 56% of consumers believe the price of the drug makes it available. 26% of consumers responded they frequently purchase the drug. The growing number of Internet users emerge that 87% of respondents discovered the drug via the Internet. There is a positive attitude to the drug "Prostatilen", because 89% of respondents would recommend the drug to their friends.

The study found that 50% of consumers believe that "Lekhim" drugs have the high quality. It was also found that 57% of consumers are satisfied with the effect of this drug. 57% of respondents like the design. People mostly under the age of 40 years participated in the survey. It was found that the drug is bought by consumers with income from about 2000 - 3000 UAH. Therefore, this drug is available to the public.

Based on the results of the study, it was found that the company-manufacturer "Lekhim-Kharkiv" is one of the leading domestic manufacturers and their products are in great demand. In order not to lose market share of the trademark "Lekhim" should attract new customers and to improve packaging design.

# PROBLEMS OF INNOVATION DEVELOPMENT IN UKRAINE

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Solving the problems of the national economy as a whole economic structure depends on the performance of each company. Of particular importance for the development of self-regulation and economic system has an innovative 'activities.

Research on the development of innovative Ukraine show that in recent years the level of innovation activity of enterprises significantly reduced. The main problems that hinder innovation in Ukraine, there are several. First - a flawed system of normative guidance and government support. The long period of innovative legislation of Ukraine was characterized by a certain fragmentation and inconsistency. Today, Ukraine has a number of laws and regulations issued by the Cabinet of Ministers of Ukraine and more than 100 acts of departmental character that regulate innovation activity. However, most of the mechanisms of state financial support and tax incentives provided by these acts can not be used in full. The lack of a systematic approach and unified scientific-technological and innovation policy is not offset by an increase in the number of legislative and regulatory acts, numerous amendments to them. Providing support innovative entrepreneurship should be the next step in the innovation system. As part of this trend should create a favorable investment climate and mechanisms and incentives to increase interest in innovation, namely to ensure stable regulation and promotion of innovative development of all sectors of the economy and protect the interests of innovation.

Among the ways external promotion of innovative activities based on the experience of foreign countries are the following: tax breaks, partial or full reimbursement to the state for development of innovation, participation in special government assistance programs of innovation.

Thus, the modernization of the Ukrainian economy based on innovation development has provided comprehensive use of all available instruments of economic policy and prevent conflict between their influences and addressing strategic and operational objectives. Under these conditions, innovation strategy such as that by definition will help increase the profitability of domestic enterprises can be a real space for multifaceted cooperation between state and business.

# SOME SUCCESS RECIPES OF PHARMACY EMPLOYEES

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One of the main branches of pharmaceutical deontology considers the relationship of pharmacy workers with customers. A modern customer is divided into two categories: price-sensitive and sensitive to the quality of goods and services.

For price-sensitive customers rationalism, aimed at a lower price is important. For "Traditionalists" the main thing is proven, long-known medications that have proven to be successful. For "Saving customers" the crucial thing is a low price.

For sensitive to the quality of goods and services visitors the guarantee of product quality and counterfeit protection, comfort with the purchase. You can attract such a visitor by some original design of your pharmacy, the correct computation and professional advice of the staff. For "innovators" everything new is important, but it must be of very high quality, reliable and aimed at the preservation of health. "Upward" focus more on the prestige of the product than on its quality and reliability.

All these categories of pharmacy customers have special temperament and manner of behavior. Therefore, the pharmacist has a challenge - to be able to cope with the emotions of a man who stands on the other side of the counter. Here are the main group of customers: “A sure customer” knows exactly what he needs. He asks questions only about the issue, insists on his opinion and relies on his taste. “ A know-it-all” thinks he knows better about the product than you. But he can argue actively with you, demonstrating his knowledge. A pharmacist needs to listen to his customer’s comments, but to defend his own position. “A talkative customer” is always happy and literally dancing with joy. The task of the pharmacist is to try to direct the flow of his words in your professional direction: to learn about the disturbing problem and to choose the necessary drug. The so-called “knight at the crossroads” is quite a difficult customer, who can not make the right choice. With this visitor be patient but persistent; clearly define his preferences, show the benefits that he will receive, taking the decision to buy now. “ A positive thinker” is generally positive. He's interested in the product and in the information that you can provide. Communication with this customer is probably the most constructive: the questions relate clearly to the subject, his objections are always reasonable, he listens and makes quick decisions.

Conclusion: despite the commercialization of relations in pharmacies, we can not forget that the task of the pharmacy staff is providing high-quality, effective and affordable medicines. Be an assistant in recovery of all your customers!

# MARKETING RESEARCH OF THE PHARMACEUTICAL COMPANY

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In the modern conditions the demand in accurate and adequate information on the processes taking place in some markets is increasing from the business entities. This is due to the fact that for occupation a competitive position in the market, maintaining or expanding market segment a complex solution of the functioning adequacy is extremely important in the current economic environment.

The main aim of the study is performing the market research and analysis of the company «Scientific and Production Pharmaceutical Company "AIM" to determine its level of competitiveness.

In this paper we used the following methods: questionnaire, expert evaluations, SWOT-analysis, forecasting method. The process of organizing and conducting marketing researches in the company is analyzed; the major problems encountered during its implementation are identified.

In the study, consumers were asked to evaluate the importance of the drug features of the “Prostatofit” made by “Scientific and production of pharmaceutical company “AIM” (efficiency, safety, price, design of the package, the type of dosage form, usability, rationality dosage form, dosage itself, manufacturer, awareness of the product). The degree of an importance of the attributes was evaluated as follows: a sign is crucial for consumers when purchasing a product - 3 points; important - 2; a small value- 1; not important - 0.

Results of the study indicates that consumers primarily pay attention to the price (13.5% of respondents), efficiency (13.1%) and security (12.1%) of the drug "Prostatofit".

Also consumer attitudes to catalog LLC "AIM" and competitors were studied by analyzing consumer awareness about them. It is discovered that "AIM" takes sixth place for awareness and has 4.6% of the votes.

The survey showed that the company produces high quality medicines at affordable prices and is in demand among its target audience.

The results of the SWOT-analysis showed that the studied pharmaceutical company has a number of strengths and opportunities in the pharmaceutical market. It can be offered specific strategies to increase position of this features and opportunities only if consider and limit the impact of weaknesses and threats that will provide the company a competitive advantages.

# ESSENCE AND IMPORTANCE OF THE CONCEPT OF RELATIONSHIP MARKETING

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The objective of our research is to reveal the essence of the new approach to the marketing management, based on formation and retaining the loyalty of customers, employees and partners of the organization.

Materials and methods: content analysis of scientific literature about relationship marketing, comparative analysis.

A new approach to marketing management, focused on formation of long-term mutually beneficial relationships with key partners and customers in the market of goods and services is relationship marketing. The basic idea of relationship marketing is that the main object of marketing management is relations (communication) with customers and other stakeholders in the process of sale.

Relationship marketing is sometimes called network marketing, interaction marketing, partnership marketing, loyalty marketing, etc. Keeping of existing customers is the purpose of relationship marketing. In the scientific literature, the concept of relationship marketing is treated differently. Kotler said that relationship marketing is the practice of formation of long-term mutually beneficial relationships with key partners to interact in the market customers, suppliers, distributors, in order to establish a long-term privileged relationship. The end result of relationship marketing is the formation of a unique asset of the company, named the marketing interaction system. Marketing interaction system involves the enterprise itself and all other stakeholders in the work of groups of consumers, employees, suppliers, distributors, retailers, scientists, advertising agencies, and all those with whom the company has established mutually beneficial business relationship. Grënroos, Webster and other leading experts in the field of marketing relationship considered marketing as a result of the ongoing development of marketing that reflects its current status, as the next step after the concept of socially-oriented marketing.

Thus, the implementation of the concept of relationship marketing allows us to provide quality customer service and individual approach based on the preference and trust. Therefore, the concept of relationship marketing is attractive for the pharmaceutical enterprises, which produce socially significant products and are focused on ensuring the public health.

# FIVE REASONS WHY TIME MANAGEMENT IS IMPOTENT

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Time management is the act or process of planning and exercising conscious control over the amount of time spent on specific activities, especially to increase effectiveness or productivity. To take the first step in effective time management you need to know yourself. As we grow older it is easy to lose track of the things that really matter to us in life. It is amazing that we can let this happen to us, but it happens all too easily.

We've all heard the saying "time is money", and that phrase is essentially true. Unfortunately, time doesn't always equal money though. Time is continually passing but that doesn't mean you are continually making money, this depends on how you manage your time and what you do with it. Here are 5 reasons time management is important:

1. Time is limited. Everyone gets the same amount of time each day, and it's limited, therefore it's important to make the most of your time if you ever want to be more than average at the workplace.

2. Accomplish more with less effort. By taking control of your time, you're able to stay focused on the task at hand. This leads to higher efficiency since you never lose momentum. Imagine running a mile where you stop every 5 seconds, this would cause you to become exhausted very quickly and take much longer to complete the run.

3. Make better decisions. There are many choices in life and often-times we're faced with many choices to choose from at the same time. When you practice good time management, you have more time to breathe; this allows you to determine which choices are the best to make.

When you feel pressed for time and have to make a decision, you're more likely to jump to conclusions and not fully consider the different options; this leads to poor decision making.

4. Be more successful. Time management is the key to success; it allows you to take control of your life rather than follow the flow of others. You accomplish more, you make better decisions, and you work more efficiently; this leads to a more successful life.

5. Learn more. When you control your time and work more efficiently, you're able to learn more and increase your experience faster. There's a reason some students graduate earlier than others, so imagine implementing time management throughout your entire career. You'll not only stand out from the rest, but you'll gain experience must faster and be able to move up in life a lot sooner.

## SECTION № 13

## SOCIO-ECONOMIC RESEARCH IN PHARMACY

# INTRODUCTION OF PROJECT MANAGEMENT IN PRACTICE OF PHARMACEUTICAL ENTERPRISES

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**Relevance of research**. The increase of number and cost of projects results in the necessity of introduction of methods of project management for activity of pharmaceutical enterprises of Ukraine. The necessary condition of successful implementation of projects is a presence of effective control system by projects.

**The purpose of the study** is to create a model of process project management in the conditions of pharmaceutical production.

**Materials and methods**. Base materials of research are standards of project management (A Guide to the Project Management Body of Knowledge – PMBOK®, Practice Standard for Work Breakdown Structures). Methods: analysis, process approach.

**Results**. With the purpose of adaptation of experience of project management to the terms of pharmacy in the scientific work outlined the stages of forming of corporate standard of management of projects, certainly aggregate of templates of documents of projects with the grant of general description essence of basic from them.

A model of process of initiation of innovative project is offered in the conditions of pharmaceutical production, which takes into account successive implementation of nine subprocesses of initiation of project (with pointing of documents of entrances and initial and performers of subprocesses). Also a model of process of planning of project is developed, including implementation to twenty two subprocesses of planning of project. A process model of implementation of innovative project is offered in the conditions of pharmaceutical production, including realization of seven subprocesses of implementation of project. Also a process model of close project is offered in the conditions of pharmaceutical production. The model includes realization of three subprocesses with pointing of incoming and outgoing documents and executors of subprocesses. The model examines subprocesses: decision-making about close project, contracts closure, finishing treatment of project documents.

Within the framework of implementation of process of planning of project the Work Breakdown Structure, the schedule, the diagram of Gantt, the budget of project curve are built.

**Conclusions**. The offered models of process of project management allow more effectively to co-ordinate the actions of participants of project.

# IMPROVED ENTERPRISE MANAGEMENT COSTS

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**The relevance of the study**: Since today's world is rapidly changing and improving, especially enterprise management system and all of its systems and components. Management System rapidly stepping forward, so production system does not stand still, need constant improvement of existing and new use of their systems in order to go with the times.

**Objective:** Determination of the optimal cost management systems that meet modern requirements.

In this paper we have identified a number of advanced systems management costs for zrivnnya them with classical systems to improve and ix possible use in combination in order to meet the requirements. For nahlyadnosti we compare klassychni and advanced systems in order to see their strengths and weaknesses.

Basic modern management costs:

1.Oschadlyve production (Leanmanufacturing). *Essence:* production company philosophy aimed at continuous removal of all types of losses, increase flexibility, prevent deviation from the standards. Based on three elements: the specific tools and techniques, performance management system and culture of continuous improvement. *Effect:* The annual cost reduction in the amount of 3.7% (in most cases achieved significant short-term effect), increased product quality, increased productivity. *Problems:* The contradiction existing accounting system. Inventories - that withdraws money from circulation and slows down the order to the customer. Restructuring of production lines, rearrangement of existing equipment, which requires significant investment costs.

2.Kayzen-kostinh (KaizenCosting). *Essence:* Cost reduction tool that managers use to achieve the required level of cost and ensure the profitability of. *Effect:* Skillful use allows one to significantly reduce the cost of production stages - 5%. *Problems:* Employees are found under great pressure from the system that makes possible to reduce all costs. The period during which the set objectives may not coincide with the period of development of new techniques employees.

3.AVS - control (Activity-based costing). *Essence*: Indirect overhead costs attributed to the product as they appear in the implementation of the relevant business - a process rather than localized on the types of products after the production process. *Effect:* Full transition on ABC - technology can reduce costs by at least 8%. *Problems:* Significant time spent on introduction of technology in large enterprises. Thorough transfer pricing mechanisms. (*Table*)

This comparison shows the main differences between the systems, as well as current requirements are very high, and the need to base, standard systems use more

flexible in combination and in unison standards in order to increase their competitive advantage and gain new ones.

Table - Comparative characteristics of traditional and advanced system management costs businesses

| Criterion Compare | Traditional cost management | Improved cost management |
|---|---|---|
| Goal | cost reduction | - Reduce costs while maintaining production levels;<br>- An increase in production costs at a constant level;<br>- Reducing costs by increasing production volumes |
| Stakeholders | cost analysis conducted in the interests of only one group of business actors - managers. Without attention are the interests of shareholders - shareholders and strategic investors | analysis takes into account the interests of all participants of business: shareholders, strategic investors, managers |
| Horizon analysis | costs are analyzed only at a certain stage of the life cycle of the product | analyzed all stages of the product life cycle |
| Methods of analysis | limited analysis - the traditional analysis of operating costs typically associated with the use of one or two circuits: "standard" or "direct" costing | костинг методика аналізу allows simultaneous use of many known methods of calculation of costs that selects the best of them as the base |
| The depth factor analysis | Company establish that rejection, but the reasons of cost increases | analysis reveals the reasons for rejection costs |
| The degree of influence on the results | on the results of the analysis can not draw conclusions on measures to be taken at the level of production units in order to reduce costs | on the results of the analysis of measures to reduce costs ranked by efficiency |
| Possibility of simulation and operational risks | analysis does not provide a comprehensive assessment of risks deviation of operating costs, and as a result, can not predict in advance the possible measures to neutralize them | neutralization allows not only to assess operational risks, but at the same time develop measures to neutralize them |
| Taking into account the involvement of staff | this issue attention is paid to | allows for any strategic decision to develop an effective system of personnel motivation |
| Preliminary calculation of the efficiency of system implementation | not carried out | conducted |

# FEATURES OF PHARMACEUTICAL PROVISION FOR RURAL POPULATION IN THE WORLD PRACTICE

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At present, the problems of the pharmaceutical supply of the population, who live in remote areas of the countryside, exist in many countries worldwide and are solved at both national and regional levels, depending on the socio-cultural and economic levers of the country development. Therefore, analysis of the experience of European countries serves a decisive factor in the development of approaches and mechanisms to improve the efficiency of the pharmaceutical supply of the population in remote rural areas of Ukraine.

The aim of our study was to analyze the organization of the pharmaceutical provision of the rural population, taking into account the features of the world practice. We have used systematic and logical and comparative methods of analysis.

According to the analysis of domestic experience in the organization of the pharmaceutical provision in rural areas, the most pressing problematic issues have been established which include:

• insufficient infrastructure of the pharmaceutical supply of the population due to the low economic efficiency of pharmacies opening compared to urban pharmacies;

• prevalence of people with low incomes in rural areas;

• large remoteness of areas and low territorial access of the population to pharmaceutical institutions;

• low staffing of pharmaceutical institutions with pharmaceutical staff and insufficient level of specialists training.

In comparison with domestic practice in the developed countries of Europe there is virtually no correlation between the development of pharmaceutical infrastructure and the level of pharmaceutical provision of residents with drugs in remote rural areas. So, in some European countries, which include *the United Kingdom, Slovenia, Finland, Belgium, Ireland, Australia* and others doctors have the right to sell medicines to patients that in a certain way solves the problems of the pharmaceutical provision in the case of an insufficient number of pharmaceutical institutions in rural areas.

According to the WHO part of commodity circulation, which is provided by doctors in the retail trade of pharmaceutical market in the country varies from 1%

(Belgium, Ireland) to 20% (the Netherlands), while trade turnover of directly hospital pharmacies is from 10% in *France* and up to 30% in *Greece*. For example, in the UK around 4000 doctors (about 12% of the total number of general practitioners) have the right to sell drugs to their patients. In *Slovenia* product range is supported by local pharmacies and general practitioners dispense medicines only in those settlements that are located more than 10 kilometers away from the nearest pharmacy. In *Finland*, in rural areas with low population density, dispensing of medicines is done by means of postal offices and departments in grocery stores. Thus, the current system is considered non-perfect, namely the number of such units to provide the population with drugs gradually decreases due to the establishment of new pharmacies.

In *Denmark*, the problem of rural population pharmaceutical provision is solved by structural units of pharmacies (satellite-pharmacies and specially equipped kiosks) that are permitted only in the countryside, because hospital-type pharmacies and doctors are forbidden to engage in dispensing to the public. In *Spain* and *Canada*, the number of pharmacies is regulated by legislation based on the number of inhabitants served by one pharmacy. At the same time in *Australia*, because of geographical features, there is a serious imbalance of pharmaceutical institutions in rural areas, which is solved correspondingly by the general practitioners who receive from the government permission to dispense drugs to the public. In addition, the problem of rural population pharmaceutical provision in European countries is solved by the introduction of logistic forms in the pharmaceutical provision, namely through online pharmacies postal delivery of drugs or special courier service delivery. It is necessary to indicate that these logistic forms are in great demand among the population.

Considering the above, in the world practice the problem of availability of pharmaceutical provision to rural and hard to reach areas with low population density in the absence of pharmacies is solved by the implementation of medicines through:

- structural units of pharmacies;
- family practice physicians;
- post offices, shops in rural areas, online pharmacies and courier delivery.

Thus, taking into account international experience and the need to fulfill the social function of rural pharmacies, as the major in pharmaceutical provision, a promising way to increase the efficiency of the latter in Ukraine is, in our opinion, the introduction of mechanisms for liberalization of opening and commercial operation of pharmaceutical institutions in rural areas, as well as the creation of rural family health clinics, in which staff the position of a pharmacist or pharmacy technician is assumed.

# ASSESSMENT OF PROMISING DIRECTIONS OF FORMATION OF PHARMACEUTICAL MANUFACTURERS' PRODUCT PORTFOLIO

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The dynamic development of the global pharmaceutical market encourages producers of all countries to strengthen their competitive advantage by adapting to the requirements of the target markets. According to analyst firm, sales of medicines in the pharmaceutical market of Ukraine in 2014 in monetary terms increased by 14.5% with a decrease in real terms by 12.2%, which is different from the respective figures of the previous years. Given the characteristics of changes in macroeconomic indicators and regulatory transformations in the pharmaceutical field, modification the direction of the formation of commodity producers of medicines policy becomes relevant to fully meet changed demand among consumers.

The purpose of our work was analysis of the Ukrainian pharmaceutical market and determination promising areas for forming product range of pharmaceutical companies. Information market research analytical system used in the analysis, the methods of marketing analysis, comparative and mathematical methods used as research methods.

The main factors influencing the formation of assortment policy directions companies highlighted on the results of our analysis of the trends in the development of the Ukrainian pharmaceutical market. It is possible to carry the following factors to external: the dynamics of disease, consumption medicines, the market capacity of products selected by pharmacological groups, the ratio of market share among manufacturers and competitors, the ratio of prices in the market segments, particularly the positioning of manufacturers and their products, pharmacoeconomic indicators use of medicines. Internal factors are based primarily on the logistics of the production process in accordance with international standards, research and

development capabilities of the enterprise, ready for the introduction of new production technologies and management personnel.

Given the morbidity statistics and trends of the market segments medicines analysis on the example of the following pharmacological groups held in the next phase of our research: Nonsteroidal anti-inflammatory medicine, antibacterials, medicines for peptic ulcer and gastro-oesophageal reflux disease, hypolipidemic medicines, histamine antagonist medicines. According to the group of medicines analyzed the following parameters: the number of trademarks Ukrainian and foreign production, a variety of dosage forms, dynamic presence in the market in volume and value terms, the prospects of the use of sub-groups and individual medicines analyzed groups. The obtained results of the research are possible to identify medicines that are most promising in terms of therapeutic efficacy and competitiveness in today's pharmaceutical market.

Thus, in a segment medicines for peptic ulcer and gastro-oesophageal reflux disease the subgroups of ranitidine, famotidine, omeprazole, pantoprazole, lansoprazole, omeprazole and esomeprazole were considered. According to the analysis of these indicators, pantoprazole, rabeprazole and esomeprazole are the most promising from a therapeutic point. However, a more detailed mathematical analysis of the dynamics of the indicators with the use of simulation showed that the medicines group rabeprazole are the most promising for inclusion in the product range manufacturers.

In that way, the current conditions of the market analysis of trends in the formation of the product portfolio of pharmaceutical manufacturers it is necessary to use an integrated approach to the analysis of the competitive environment, given the marketing and pharmacoeconomic application features medicines. Considering that the modern Ukrainian market is almost 65% in value and only 30% in terms of foreign production of medicines, the search for new promising directions of development through the revision and expansion of product range is relevant for Ukrainian producers. Based on the conducted research disease trends and market development, pharmaceutical manufacturers can implement promising medicines into production and to keep improving positions in the pharmaceutical market.

# PECULIARITIES OF LABOUR RESOURCES MANAGEMENT AT ESTABLISHMENTS OF PHARMACEUTICAL BRANCH

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At this time pharmaceutical branch is defined as dynamically developed and therefore requires a great number of qualified employees. Activity in this area demands a set of features: from education at the beginning and till labour contracts at the end. Thus, at the present moment this topic is a quite relevant issue.

The aim of the work is analysis of peculiarities of labour resources management and features of working conditions for pharmaceutical professionals, research of fields which require pharmaceutical control from a side of society and individuals.

We have analyzed the materials of the Code of Laws in the labour; the Standards of pharmacy service quality (joint instructions of FIP/WHO on GPP); the Code of Ethics for pharmacists of Ukraine. During the research the method of systematic analysis was used.

According to the research's results, we have estimated the problem of pharmaceutical staff employment and features of their work. The forming and development of exchange relations connects with substantial changes in labour service, work force movement, and significant excess of supply over demand that specifies existence of such category as a labour market.

A qualified employee of pharmaceutical branch should observe such ethical norms as: to be respectful towards every patient from positions of personal service, to possess psychological communication skills to achieve trust and mutual understanding with patient; to act straightforwardly, honestly and fear, do not use patients' lack of familiarity and uninformedness on medicines and medical products for personal or establishment's advantages, do not apply pressure to patients to get it.

Thus, there are roles expected to involve pharmacists or control over them from a side of society and people for which benefit pharmacists work: manufacturing, formulation, preservation, safety, expansion, application, delivery of goods for medical use; ensuring of effective medicamental therapy; assistance and improvement of professional activity; contribution to the effectiveness improvement of the system of medical aid and public health.

# ANALYSIS OF THE PHARMACEUTICAL PROVIDING EXPENSES OF THE PREGNANT WOMEN AND AND IN DELIVERY IN THE CONDITION OF MEDICAL INSURANCE

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Childbirth - is a complex multistep physiological process that terminates pregnancy and is accompanied by birth. The correctness of delivery of birthchild largely reflects on the outcomes for both the mother and the fetus.

It has been proven long ago that the majority of complications developing during pregnancy can be prevented by correct preparing, namely by the minimazation of shortfall of vitamins, examination, diagnosis of possible disease states and their correction.

Analysis of the literature, statistical data from the Ministry of Health of Ukraine showed that timely diagnosis, correct preparation and management of pregnancy allows to birth the baby, while not sacrificing baby's or mother's own health.

The goal of our research is to determine the cost of pharmaceutical providing of the women during pregnancy and childbirth for the rational use of medicines.

To implement this goal the following tasks delivery were defined:

• to analyze and summarize the literature on the costs of pregnancy and childbirth as abroad and in Ukraine;

• to conduct the survey women have been registered in counseling maternity centers of the Kharkiv in order to determine the actual cost items;

• to calculate solvency of adequacy ratio of average labor cost for the citizens of Ukraine, Germany and the USA.

Data analysis and literature survey on the total cost of women during pregnancy and childbirth in Ukraine and abroad show that Ukraine accounted for a larger percentage of other costs are almost 70% of the total cost, and abroad in average direct and indirect costs are almost identical for under normal childbirth as they related as 45% to 55%, and cesarean section 52% to 48% (respectively);

The calculation of the solvency adequacy ratio average cost of childbirth showed that more affordable value for German citizens (average ratio - 3), then the U.S. (3.7) and slightly worse than the citizens of Ukraine (almost 4). But the quality of services have been provided differentiated significantly .

Conducted studies have shown that complex of training programs for childbirth and the use of drugs in pregnancy and childbirth are not rational and do not fully meet the actual requirements of women.

# IMPROVEMENT CALENDAR VACCINATION BY COMBINED VACCINES IN KAZAKHSTAN

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Vaccination is a cost-effective means of prevention and control of infectious diseases. Their widespread use has allowed to take control of diseases such as diphtheria, tetanus, pertussis, polio, and infections caused by Haemophilus influenzae type b.

To date, the knowledge of the application, effectiveness and safety of vaccines needed for the modern doctor in any specialty. The doctor must be able to objectively answer the questions of their application, creating a positive attitude towards vaccination of the population, and promoting the most comprehensive coverage of vaccination, which is essential for health, epidemiological well-being and economic stability of the country.

Global Plan of Action for vaccines (GPAV) was approved by 194 countries - members of the World Health Assembly in May 2012 for the implementation of the concept of the Decade of Vaccines by providing universal access to immunization. GPAV task is to improve health through dissemination of 2020 and beyond, comprehensive benefits of immunization to all people, regardless of where they were born, their social status and inhabited.

By GPAV end of the decade can be prevented from 24.6 to 25.8 million deaths and billions of dollars to get further through productivity growth. In addition, immunization will make a huge contribution to the reduction of mortality in children under 5 years by two-thirds.

Existing immunization programs should be strengthened by increasing the population's commitment to immunization, timeliness of vaccination, as well as improving the safety and efficacy of vaccines.

The advantages of combination vaccines are to reduce the number of required injections and a concomitant decrease in episodes of pain experienced by children.

This article provides an overview of the vaccination calendar in the Republic of Kazakhstan (RK).

As part of the immunization schedule of RK use a combination vaccine AbKDS +Hib+HBV+IPV (hexavalent) and AbKDS+Hib+IPV (pentavalent).

First applied at 2 and 4 months of age in the second 3 and 18 months. This allows for the full course of immunization against infections such as whooping cough, diphtheria, tetanus, hepatitis B, Hib, polio.

Also, the advantage of these vaccines is that they comprised acellular pertussis component which reduces the risk of the expected reactions in postinfluenzae period.

Before the advent of combination vaccines, children received oral polio drops. Now, with the introduction of a multi-component vaccine the child is protected against polio, replacement of oral polio vaccine to inactivated negates the risk of serious vaccine reactions, as vaccine-associated polio.

Used in the calendar combination vaccines are produced in the form of single-dose syringes, which guarantees the correct dosage reduces the risk of possible errors during the vaccination, and also leads to savings in logistics costs and the amount of storage of vaccines.

Thus, if in other countries of Central Asia, a child under the age of 6 years, gets about 18 injections during vaccination, the Republic of Kazakhstan due to a combination vaccine he received 13 injections.

Currently, the data were combined vaccine for more than 10 clinical studies, c involving about 5000 subjects who received at least one dose of vaccine.

A very important component vaccine is safe. Safety assessment in the primary vaccination was carried out in eight studies in which about 15 000 doses of vaccine have been assigned more than 4,500 children. Comparisons of the safety of vaccines containing whole cell pertussis-the obtained results proved that the combined vaccine reactogenicity is lower than that of whole-cell pertussis vaccines-as swelling at the site of injection in the case we studied vaccine was observed at 35% less, temperature rise of 20% less than using the whole-cell pertussis vaccine.

There is a lot of experience on the use of combination vaccines in many European countries, such as Belgium, Germany, Hungary, Czech Republic, Italy, Spain and others.

Accordingly, the use of these vaccines to reduce the number of injections needed for immunization, as well as provide increased commitment to vaccination and reduce the number of pediatric infectious diseases.

In view of the increasing number of manufacturers of modern multicomponent vaccines, it is expected that such a vaccine will become more readily available, and is also likely that in the coming years will be made available all the more complex multi-component vaccine.

# AN ANALYSIS OF MICROECONOMIC LEVEL OF PHARMACEUTICAL INDUSTRY IS FOR OPENING OF PHARMACY

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The analysis of literary, statistical data, standard and legal documents showed that for today in Ukraine availability of the population to the main medicines both physical and economic doesn't conform to national requirements.

Main objectives of the national medicinal policy are: availability of medicines, their quality and rational application.

Therefore the purpose of our researches was:

To carry out the analysis of conditions of a microeconomic level of pharmaceutical branch for opening drugstore.

To implement this goal the following tasks delivery were defined:

– to analyze and generalize data of literature on the basic principles of the organization of medicines provision in microeconomics system;

– to carry out the analysis of license conditions of implementation of the economic activity connected with retail sales of medicines in the territory of Ukraine;

– to carry out a choice of a location of a drugstore and the analysis of possible conditions for goal implementation;

– to carry out questioning of pharmacists in Kharkov for the purpose of definition of expenses articles which future drugstore in accordance to will have license conditions of pharmaceutical activity in Ukraine;

– to carry out the analysis of the calculated main indicators of trade and financial activity of future drugstore in order to forecast the point of profitability.

The objects of research were healthcare institutions of Ukraine in Kharkov which provide the population, necessary medicines and products of medical appointment.

The subject of research was a process of opening of pharmaceutical enterprise in order to improve the availability of providing the qualitative pharmaceutical help for the population.

One of the criteria which influences on the availability of medicines is the number of inhabitants served by one pharmaceutical establishment. An average figures show flat across Ukraine 2193 persons served by one pharmaceutical institution.

Then we continued the calculation of average sales of one pharmaceutical institution during the year which we need for definition of the main indicators of trade and financial activity and definition of a point of profitability became the following stage of our researches. For Ukraine this average value is nearly 1 million 730 thousands UAH a year.

Hi order increase in an indicator of commodity sale turnover of the future drugstore we carried out questioning of customers. In the questionnaire a number of questions which defined factors influencing increase in this indicator were set. The

analysis of questioning showed that different factors influences on commodity turnover of a drugstore: qualification of the personnel, the drugstore location, the range of the drugstore, the open presentation for parapharmaceutical goods, opportunity to get primary medical advice and the help (to measure pressure, level of blood sugar, etc.).

Carrying out questioning of 10 drugstores of Kharkov for the purpose of definition of their primary and monthly articles of expenses was the following stage of our researches. So for one pharmaceutical institution that will work in accordance with general practice on tax accounting with apartment purchase were the expenses 741 thousand 800 UAH. The sum of average monthly expenses on one pharmaceutical institution will make 32 thousand 200 UAH.

The analysis of the profitability was carried out at constant level of trading imposing and the sums of expenses showed that drugstore opening with profitability in 1,3% isn't perspective. Because the net profit will make about 1040 UAH, and primary expenses counted by us make earlier 742,5 thousand UAH. It means that primary expenses will be blocked more than in 58 years. With profitability in 5% in 12 years, from 6-8% respectively in 9,5 and 7 years, but the point of an extremum is the best of all with profitability in 12% will come in 3,5 years.

The following stage of our researches carried out calculations of the same indicators, but for pharmaceutical institutions with the simplified tax system (the 2nd group: to 10 workers with commodity turnover to 1 million UAH). For this group of businessmen average monthly expenses could be from 14 to 32 thousand 300 UAH. In our questioned group they made approximately from 16 thousand to 20 thousand UAH.

The analysis of the calculations of profitability that we have carried out and a profitability point for a pharmaceutical institution which works at a uniform tax showed that the net profit will make nearly 4800 UAH, and primary expenses will decrease to 735 thousand UAH. It means that primary expenses will return in 12 years, and profitability will make 6%-7%.

As a results of research we come to the conclusions:

1 . The analysis of number of pharmaceutical institutions and the population in Ukraine showed that 2160 persons are served by one pharmaceutical institution.

2 . The results of calculations of average sales of one pharmaceutical institution that it makes 1729,1 thousand UAH In Ukraine a year.

3 . The analysis of results of questioning of 10 drugstores of Kharkov showed that average prime expenses counting on one pharmaceutical institution make 624500 UAH. Average monthly expenses counting on one pharmaceutical institution which works in accordance with general tax practice, make 32300 UAH, and on the simplified system from 16 to 20 thousand UAH.

4 . The analysis of the calculations of a point of profitability carried out by us showed that with profitability in 12% the point of an extremum will come in 3,5 years, and for pharmaceutical institution which works at a uniform tax and income in day doesn't exceed on the average 5100 UAH primary expenses will be blocked in 12 years, and profitability will make 6%-7%.

# RESEARCH OF INCIDENCE AND PREVALENCE RATE OF DIGESTIVE DISEASES AMONG THE UKRAINIAN POPULATION

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Today in Ukraine gastrointestinal diseases occupy the third place in the structure of chronic morbidity of the Ukrainian population, fifth place - in the structure of causes of hospitalization and death, seventh and eighth - in the structure of the initial transfer to disability and temporary disability respectively. In addition, diseases of the digestive system are serious problem in Ukraine, as in most cases are chronic diseases.

Continuous and relapsing flow of disease is accompanied by a significant decrease in quality of life that determines diseases of the digestive system as important medical and social problem and makes it necessary to search for new directions of improving prevention and treatment of these diseases.

On the basis of the above mentioned, the aim of our study was a retrospective analysis of prevalence and morbidity rate of diseases of the digestive system of the population of different age groups in Ukraine.

The results of analysis of the dynamics of morbidity rate of diseases of the digestive system of the Ukrainian population show its decrease in all age groups. Thus, over the period reduction in the incidence rate ranged from -17.73% in the age group 0 to 6 years to 7 to 14 years -3.03%, with an average rate of decline in Ukraine 7.4%. However, it should be noted that infant morbidity has the highest compared with older age groups (table. 1).

*Table 1*

**Dynamics of incidence rate of diseases of the digestive system in the population by age groups in Ukraine, 2009-2013 (per 100000 people of the corresponding age)**

| Age group | | Year | | | | | 2013/2009 (%) |
|---|---|---|---|---|---|---|---|
| | | 2009 | 2010 | 2011 | 2012 | 2013 | |
| 0-6 years | incidence | 5064.2 | 4937.9 | 4576.3 | 4324.7 | 4166.4 | -17.73 |
| | prevalence | 7734.0 | 7404.5 | 7075.8 | 6733.8 | 6417.3 | -17.02 |
| 7-14 years | incidence | 5779.1 | 5710.6 | 5684.3 | 5641.1 | 5604.1 | -3.03 |
| | prevalence | 18778.2 | 18515.3 | 18291.4 | 17981.7 | 17851.4 | -4.94 |

| | | | | | | | |
|---|---|---|---|---|---|---|---|
| **15-17 years** | incidence | 5456.2 | 5248.9 | 5313.4 | 5325.3 | 5148.6 | -5.64 |
| | prevalence | 21037.1 | 20935.1 | 20744.1 | 20603.6 | 20418.3 | -2.94 |
| **above the age of 18, including:** | incidence | 4923.9 | 4864.9 | 4778.6 | 4674.7 | 4557.7 | -7.44 |
| | prevalence | 36598.6 | 36625.1 | 37129.8 | 37571.6 | 37575.6 | 2.67 |
| **working-age** | incidence | 2673.6 | 2617.6 | 2567.1 | 2530.2 | 2468.0 | -7.69 |
| | prevalence | 15677.8 | 15791.5 | 15822.6 | 15918.7 | 15852.0 | 1.11 |
| **persons older than working-age** | incidence | 2455.0 | 2444.6 | 2442.3 | 2371.0 | 2336.8 | -4.81 |
| | prevalence | 26246.3 | 26678.6 | 26853.2 | 26985.6 | 27097.9 | 3.24 |

According to Table 1, during the analyzed period the prevalence rate of diseases of the digestive system among people of working age increased from 15677.8 cases per 100000 of corresponding population in 2009 to 15852.0 cases in 2013 (growth rate - 1.11%) and among population in older age groups – from 26246.3 to 27 097.9 cases respectively (growth rate - 3.24%) with a decrease of this index in children aged 0-6 years from 7734.0 6 to 417.3 cases (rate reduction - 17.02%).

The analysis shows that the prevalence rate of diseases of the digestive system gradual increases with the years - from 7734.0 cases per 100000 of corresponding population in the age group 0-6 years to 36598.6 in people aged 18 years and older.

Another concern is the fact that a significant number of patients with gastroenterological pathology is in the working-age group of the population, prevalence of which in 2013 totaled 15852 cases per 100000 of corresponding population.

Thus, the analysis of the dynamics of the incidence and prevalence rate of diseases of the digestive system among the age groups revealed diverse trends, including decrease in incidence in all age groups, which ranged from -17.73% in the age group 0-6 years to -3.03% in age group 7-14 years with an average rate of decrease in Ukraine by 7.4%. However, over the period observed increase in prevalence among HOT those of working age and older age groups (1.11% and 24% respectively) while reducing the rate of children aged 0-6 years (-17.02%) .

However, during the analyzed period increase in prevalence rate of diseases of the digestive system among working age and older age groups (by 1.11% and 24% respectively) with decreasing rate of children aged 0-6 years (-17.02%) is observed.

# THE ANALYSIS OF IMMUNIZATION COVERAGE IN UKRAINE AND IN WHO EUROPEAN-REGION COUNTRIES

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Vaccination is deservedly considered the most significant achievement of medicine in the last two centuries, because it showed the most significant medical intervention effects on human health by eliminating of certain particularly dangerous infectious diseases. Today thanks to modern vaccines that can simultaneously create immunity against several infections it has become much easier to prevent the emergence of infectious diseases and their spread.

According to the National immunisation schedule in Ukraine routine vaccination against tuberculosis, measles, rubella, hepatitis B, pertussis, tetanus, mumps, diphtheria, poliomyelitis and Haemophilus influenza type B is carried.

Recommendations of the World Health Organization (WHO) established immunization coverage, at which an enough level of population immunity is created and only sporadic occurrences of diseases are provided and which should be 95%. However, a much lower rate of immunization coverage for certain infectious nosologies, especially in recent years, is observed, because of low government funding and the lack of vaccines in clinics to perform routine vaccinations in required terms in Ukraine.

Based on the above, the purpose of our research was to analyze the level of immunization in Ukraine and to compare the indicators with European.

Based on the results of the immunization coverage's analysis of children under 1 year, which are considered the most susceptible to infectious diseases, it was found that in Ukraine since 2010 this rate has been decreased. For some infections it was less than 50%, which is a critical indicator. Particularly difficult situation remained in 2013, when recommended level of immunization coverage of 95% has not been reached for any infection.

If we trace the dynamics of European indicators of immunization coverage, it can be argued that in most infections they are in line with recommendations of WHO. Only against Haemophilus influenza type B and hepatitis B immunization coverages are high enough – 83% and 81% respectively, but not considered by WHO experts as critical indicators (Table 1).

*Table 1*

**Comparative analysis of immunization coverage of children under 1 year in Ukraine and in WHO European-region countries during 2009-2013, %**

| Year | Ukraine | | | | | | WHO European-region countries | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|
| | Tuberculosis | Poliomyelitis | Measles, mumps, rubella | Haemophilus influenza type B | Hepatitis B | Pertussis, diphtheria, tetanus | Tuberculosis | Poliomyelitis | Measles, mumps, rubella | Haemophilus influenza type B | Hepatitis B | Pertussis, diphtheria, tetanus |
| 2009 | 96 | 74 | 75 | 66 | 68 | 71 | 94 | 95 | 94 | 72 | 77 | 95 |
| 2010 | 92 | 57 | 56 | 51 | 48 | 52 | 95 | 95 | 93 | 74 | 78 | 94 |
| 2011 | 90 | 58 | 67 | 26 | 21 | 50 | 94 | 95 | 94 | 77 | 78 | 94 |
| 2012 | 95 | 74 | 79 | 83 | 46 | 76 | 95 | 96 | 95 | 83 | 79 | 96 |
| 2013 | 80 | 62 | 39 | 39 | 24 | 60 | 95 | 96 | 95 | 83 | 81 | 96 |

Thus, a sufficiently high level of immunization coverage in Ukraine until 2009 contributed to the achievement of a high level of population immunity, which allowed for some time to inhibit the growth and spread of infectious diseases, controlled by routine immunization.

However, the sharp decline in immunization coverage, especially in 2013, threatens of sudden infectious disease outbreaks and its uncontrollable spread. Too acutely this applies to such diseases as measles and rubella, characterized by extremely highly contagious and quick spread, and immunization coverage of which in 2013 was, unfortunately, very low (39%).

Thus with a view to create and support well-being of epidemic situation in Ukraine, in our opinion, the first step is to ensure sufficient immunization coverage recommended by WHO and The National Program on Immunization, at the level of not less than 95%, which is possible only if we completely ensure the needs of healthcare facilities in medicinal immunological products for routine vaccination and their uninterrupted and rhythmic delivery in regions.

# PROFESSIONAL BURNOUT SYNDROME EMPLOYEES OF PHARMACEUTICAL PRODUCTION

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Introduction. In modern conditions is urgent need to study occupational health as the ability of the individual to maintain and enhance protective, regulatory and compensatory mechanisms that ensure the effectiveness, efficiency and personal development of the employee in all conditions and at all stages of professional activity.

The necessity of studying this subject for pharmaceutical professionals is that in Ukraine the issue of professional health remains little developed. Belonging to the professions "subject-to-subject" type, which include the activities of pharmaceutical professionals, takes place in conditions of high socio-psychological demands, emotional depth, considerable mental and emotional stress, causing severe nervous tension, and sometimes even stress.

In real conditions of professional activity personality pharmaceutical worker is subject to constant pressure from stressful circumstances - the nature of the organization of labour, psychological pressure from patients and their relatives, colleagues, and administration. This places high demands to their professional health requires special control and health monitoring pharmaceutical workers, which largely depends on the efficiency and quality of their work.

The purpose of the study. The purpose of the study was to conduct a statistical analysis, identifying the level of professional burnout syndrome among pharmacists and pharmacists, as well as developing recommendations for the prevention of its occurrence.

Materials and methods research. To address this goal survey was conducted and used mathematical-statistical methods of data processing using spreadsheet Microsoft Office Excel 2007. The methodology included conducting a survey using a questionnaire consisting of 22 questions. As a result of processing of the responses received, according to the table of levels of burnout, we determined the level of burnout among employees of pharmacies. This table includes three indicators: emotional exhaustion, depersonalization and reduced personal relationships. The study involved 50 pharmacists and pharmacists of various networks of pharmacies Ukraine. It was formed three groups of respondents, depending on seniority. So the number of respondents, the experience of which amounted to less than 5 years - 15 people (30%); 25 people (50%) had experience from 5 to 10 years and 10 people (20%) - with experience of over 10 years.

The results of the research. The analysis found that in the first group of 9 people (18%) with low levels of burnout and 6 (12%) with an average level of burnout. In the second group of 15 people (30%) with an average level of burnout and 10 people (20%) with a high level of burnout. In the third group all 10 people (20%) with a high level of burnout, which is represented in Fig.1.

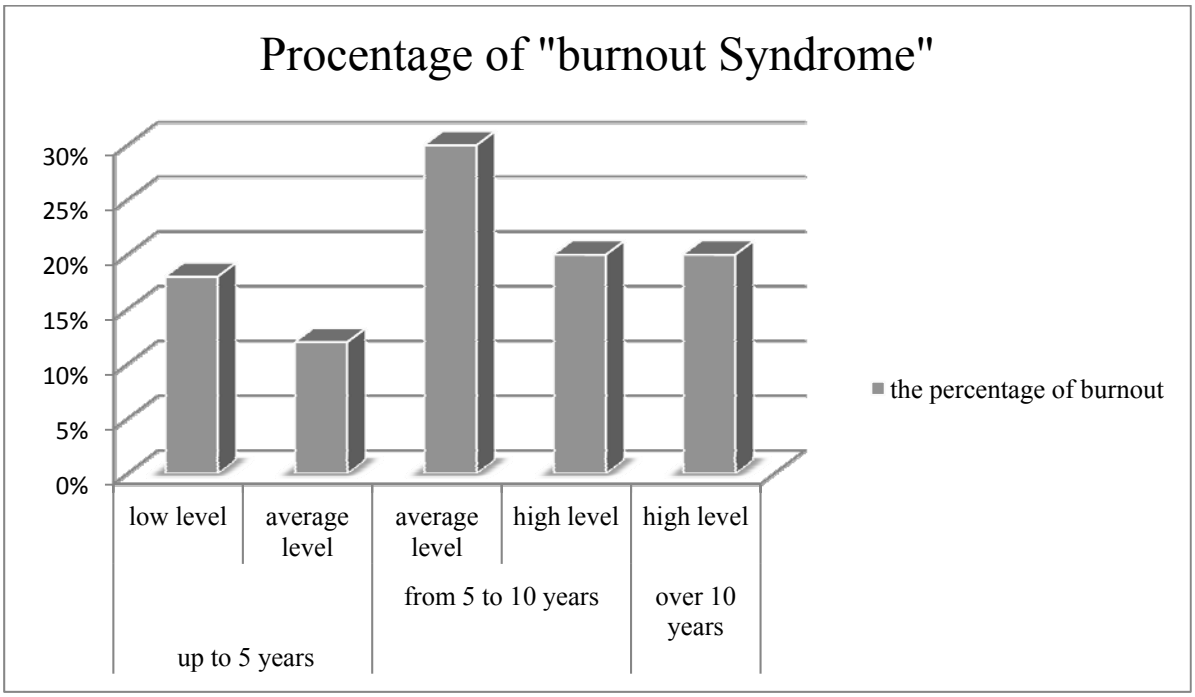


Fig.1. The burnout syndrome in pharmaceutical workers (%)

Study of psychological characteristics of professional health pharmaceutical workers showed that specialists are characterized by low level of adaptation, possible borderline mental status and long-term functional impairment,they conflict and have low neuro-mental sustainability. There was a high level of resourcesthe, which suggests that they are fairly balanced life achievements and disappointments, there is quite a high adaptive capacity and low level of stress vulnerability. Also pharmacists have a low level of optimism, which means that employees do not believe in their own strength, expect failure, try to avoid contact with other people, and are closed at their inner world. With an average level of activity they are quite energetic and cheerful, but there is a lack of self-confidence and the average level of anxiety.

The conclusions. Thus, on the basis of the obtained results was developed theoretical model for the prevention of the development of the burnout syndrome, as well as management risk factors and their correction. The use of the model in practice in drugstores and other enterprises of the pharmaceutical industry will increase productivity of pharmaceutical workers and improve their own financial and economic indicators.

# RESEARCH OF MEDICATIONS CONSUMPTION USED FOR TREATMENT OF ISCHEMIC STROKE ACCORDING TO THE RESULTS OF ABC-ANALYSIS

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Ischemic stroke is one of the most acute medical and social problems that cause significant economic losses to society due to high mortality, significant disability and social exclusion of patients. In terms of hard deficit of funds that occurs in the Ukrainian health care system, the issue of effective, economic and efficient treatment of stroke becomes an important social value.

On the basis of the above mentioned, the aim of our study was to conduct clinical and economic analysis of the actual medical prescription for patients with ischemic stroke in Ukraine.

We conducted a retrospective analysis of the data from the medical records of 581 patients with acute ischemic stroke who received treatment between 2007 and 2012 at a specialized hospital in Kharkiv.

According to the patient record studied, we have determined that the total amount of medical prescriptions was 6280 medications. The analyzed nomenclature of prescribed by doctor medications represented 198 international nonproprietary name from 11 pharmacotherapy groups, which is 322 by the trade names of medications. In order to generalize the obtained statistical data on the use of medications in a specialized hospital we calculated the average medical prescription for the treatment of one patient with ischemic stroke, which were 11 prescribed medicines.

The analysis showed that medications of pharmacotherapy group N «Nervous system» occupy 25.38% of all medical prescription. Among the pharmacological subgroup of anatomical main group N the largest number of prescribed medicines accounts for the subgroup “Psychostimulants” (936 prescribed medicines or 14,90% of the total prescriptions), which is represented 8 international nonproprietary name. It should be noted that the leader for the number of prescribed medicines among this subgroup by the trade names takes *Ceraxon* (Ferrer Therapeutics Inc., Spain), represented 28.77% of the total number of prescribed psychostimulants medicines. Also, doctors appointed quite often such medications as *Cavinton* (24.17%) and *Piracetam* (19.25%).

The next stage of our research that we carried out was ABC-analysis, which consists in dividing medications into three categories (A, B, C) from being the most valuable items to being the least valuable ones, basing its ratings on the following rules:

- A-items are medications which annual consumption value is the highest; the top 70-80% of the annual consumption value typically accounts for only 10-20% of total inventory items;
- B-items are the interclass items, with a medium consumption value; those 15-25% of annual consumption value typically accounts for 30% of total inventory items;
- C-items are, on the contrary, items with the lowest consumption value; the lower 5% of the annual consumption value typically accounts for 50% of total inventory items.

The analysis showed that the class A includes both costly drugs and those drugs that have the greatest rates prescriptions, which is represented 21 international nonproprietary name (10.61% prescribed medicines). In total medications consumption the proportion of this class of medicines was 79.98% of the costs.

The class B included 42 international nonproprietary name of medications (21.21%), and group C consisted of 135 international nonproprietary name (68.18%). Thus, we can say that more than half of the medicines used by doctors, accounted for only 5.12% of all costs associated with the pharmaceutical provision of patients with ischemic stroke. The proportion of consumption of medications from class B was 14.89%.

It was established that the cost of pharmacological subgroup "Psychostimulants" is 244 825.79 UAH (37.16% of total costs). In class A the proportion of the cost of mentioned pharmacological subgroup is 45.46% of the total consumption value, in class B - 5.39% in class C is - 0.02%.

Thus, the results of the frequency analysis of medical prescriptions, that we carried out, has shown that medications of pharmacotherapy group N «Nervous system» occupy 1 594 prescription (25.38% of total prescriptions). It should be noted that among this group of medications by the trade names quiet often was appointed such medicines as *Ceraxon*, *Cavinton* and *Piracetam*.

The ABC/frequency analysis of medical prescription showed that the class A (the most valuable items) included 21 international nonproprietary name of medications (10.61% of all prescribed medicines), accounts for 79.98% of the total consumption value.

# MAJOR ISSUES OF BUSINESS ETHICS IN PHARMACY AND WAYS FOR SOLUTION

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With growth of pharmaceutical establishments of private property, its holders, and also with development of entrepreneurship based on private ownership, a need of main principles creation of business ethics arises. Without applying of ethic principles in pharmaceutical business, it is impossible to ensure stable forward movement of establishments to the best results of activities. That is exactly why it is important to determine actions required in order to business operations would be grounded on invariable moral standards.

Taking into consideration the pharmaceutical industry expansion, the aim of this research is study of major issues with adherence of business ethics in pharmacy and ways for these issues solution.

As theoretical and methodological foundation for the research, the scientific works of domestic and international authors in business ethics issues were used. The methods of systematic analysis, monitoring, logical generalization etc. were applied during the research.

It was established while analyzing that the major reasons of this problem is absence of ethical traditions and standards of pharmaceutical business operations in Ukraine. In this context, it is necessary to apply a system of measures designed to improve a situation in the field. That is demanded by increasingly severe competitive environment, which influence the domestic economy is tinged with.

The main ways to solve problems in pharmaceutical business ethical practices are the following: announcing the total fight with mass media involved against public and political societies with any facts of corruption, bribery or damaging to an enterpriser by state employee's illegal actions; interpersonal relations are built on basis of moral Christian ethical norms; simplification to the minimum of the procedure of enterprises' establishing and operations, and private business performing; displacing of the State from economical field as an absolutely ineffective system of business dealing. Under these conditions, it is possible to create principles for business activity on the backgrounds of ethical norms.

Thus, under current conditions of economy management the ethics of pharmaceutical business operations is crucially important. The further development and improvement of economic system is impossible without attraction of progressive economical ideas and principles of ethical business activity.

# SCIENTIFIC-METHODICAL APPROACH TO MODELING IN EPIDEMIC DEVELOPMENT

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Throughout the history of humanity time to time epidemics and pandemics were observed in multiple territories. They lead to mass illness, a large number of deaths and serious social upheavals. In modern conditions the society concerned that new viruses may appear and begin to spread more and more with significant pandemic potential.

In this case the main task of the state is to save the lives of citizens, reducing the impact on public health by the pandemic and to minimize disruption of public services. That is why, research on the occurrence of epidemic process in the population is important.

The aim of this study is to construct a model of an epidemic process and followed her approbation.

During the occurrence of epidemic complications, failures in the health care are observed, especially when the number of affected people become extremely large. In such cases, the possibility of available forces and means to combat disease are limited and it exists risk of development of critical scenarios. Therefore, conducting leading research in analysis and forecasting of possible epidemic scenarios is an important stage of research, that allows early to assess the extent and impact of the epidemic, and usually they are carried out with the use of mathematical and computer modeling of epidemic processes.

SIR-models are the highest prevalence to simulate epidemic processes. This involves, that initially the patient is in the «Susceptible» group, in the case of disease, he can move in the «Infected» group, and after a certain time they passes «Removed» group. In this case, the susceptible person is in contact with an infected person, who can give an infection him with chance $\beta$. Every infected person carries contacts $c$ per unit time, respectively, the percentage contact, that during time the infection is carried out, is in contact with $c * \beta$. Usually the population is presented, as susceptible patients and infected as well as those who recovered and have immune, therefore it is necessary to take into account in the model. Another important aspect of the modeling process is the speed of recovery, which requires the addition of this parameter in the model, after that it can be considered final.

For the formation model, we used a computer simulation program Vensim, which created a "container" for the states (Susceptible, Infected, Removed) and Ways to "movement." In the system Vensim this tool is called "stream» (contamination – infection, recovery – convalescence). Also this model includes parameters (number of contacts, chance of infection with a single contact and duration of the disease) and formulas. As a result the model building we obtained its flowchart (Fig. 1).

To check of working capacity model we introduce to the initial values. Given that the example is the Kharkiv, the model includes the following statistics: the population of 1.5 mil. people, that is the number of susceptible persons. Another condition is that the number infected is stuffed with a person, the number of contacts per day is 5, the probability of infection – 0.1 (10%) and recovery time – 10 days.

As a result of the use of the model we have established the number of susceptible, infected and removed persons, which makes it possible to predict the development of the epidemic process (Fig. 2).

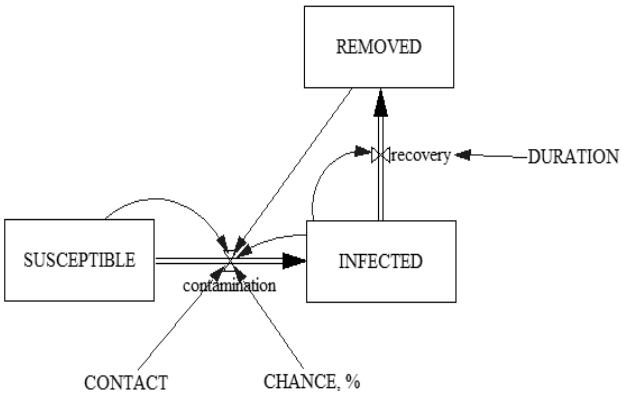


Fig.1. SIR-epidemic model

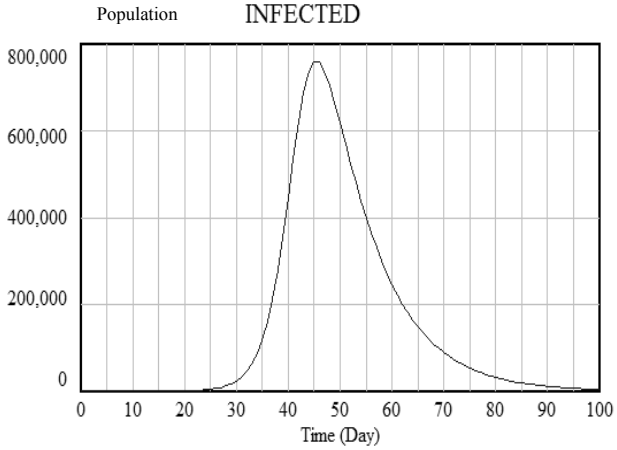


Fig. 2. The results of the analysis of the number of infected people in the base model SIR-model

Conclusions: Due to the construction of a computer model of the epidemic process we obtain graph the number of infected persons. In accordance with the graph, present epidemic is of limited duration. In this, a significant increase in the number of infected people is observed on day 35 from the appearance infection, and the maximum number of infected is observed on the 45th day and it includes759 351 people, followed by the number of infected people is reduced to a complete cessation of identifying new cases.

# RESEARCH OF THE CURRENT STATE OF SOCIAL RESPONSIBILITY IN PHARMACEUTICAL BRANCH

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The phenomenon of social responsibility (SR) is widespread in many countries of the world, especially in the economically developed ones. Studying of a current state of SR of the domestic and foreign pharmaceutical companies which are presented in the market of Ukraine became **the aim** of our research.

**Materials and methods of the research.** We investigated the data of the Center "Development of Corporate Social Responsibility" about the assessment of pharmaceutical companies' websites taking into account the level of disclosure of information about CSR, and also the data of scientific and popular scientific references concerning activity which it was possible to call socially responsible. When carrying out the research we used statistical, logical, comparative and marketing methods of the analysis.

**Results of the research.** A concept of SR in Ukraine and abroad are treated differently: representatives of foreign companies that have positioned their activities as socially responsible, adhere to the norms of civil society, show care of material welfare of their employees, effectively dispose of resources, stimulate and support innovations. Representatives of the Ukrainian companies, even the most developed in this direction perceive their role more narrowly and limiting it to the payment of taxes, implementation of the obligations established by laws before employees and before the state, and also charity.

The center "Development of CSR" in 2012 carried out an assessment of web-sites of 20 greatest Ukraine's pharmaceutical companies about the level of information's disclosure of CSR on the methodology of the Index of the transparency developed by the Beyond Business Company (Israel). On the basis of the results of the sites' assessment, it is possible to note that the level of publicizing of activity in the main spheres of SR is quite low, and some spheres generally remained unsolved. Also, information on the management and financial activity of the companies is quite closed.

Commenting on the results of the Index of transparency and the accountability it was noted that only 6 companies from 20 ("The Arterium Corporation", "Actavis Ukraine", "Bayer Ukraine", "GlaxoSmithKline Ukraine", "Darnitsa", Pharmaceutical firm "Nykomed Ukraine ") have the separate section devoted to CSR on the web-site.

The companies "Novartis Ukraine", "KRKA Ukraine", Pharmaceutical firm "Interchem" and "OmegaPharma Ukraine" have no personal web-sites of their own at all. Lighting its policy takes only 3 companies that represent the policy work with staff: "Actavis Ukraine", "The Arterium Corporation" and "Nycomed Ukraine". On

activities to promote and support territorial communities only 5 companies and they are: "The Arterium Corporation", Pharmaceutical firm "Darnitsa", "Nycomed Ukraine", "Sanofi Ukraine", "GlaxoSmithKline Ukraine" work in this direction. Measures for environmental protection describe only two companies: "Bayer Ukraine" and "The Arterium Corporation". It should also be noted that non-financial report provided only "The Arterium Corporation".

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Regarding the activities of development and support of territorial communities, we've got only 5 companies: "The Arterium Corporation", Pharmaceutical firm "Darnitsa", "Nycomed Ukraine", "Sanofi Ukraine", "GlaxoSmithKline Ukraine" work in this direction. Measures for environmental protection is described by only two companies: "Bayer Ukraine" and "The Arterium Corporation". It should also be noted that non-financial report is provided by single corporation – "The Arterium Corporation".

Based on the assessment of Web-sites, the leader of the transparency index among pharmaceutical companies became "The Arterium Corporation" with the level of disclosure 45%. Among the top three the Pharmaceutical companies "Darnitsa" and "Nycomed Ukraine" (both have a level of disclosure of about 13.5%).

It should be noted that two years in a row (2013, 2014) the "Abbott Company" was the leader of this branch according to the Dow Jones Sustainability Index (DJSI) – one of the most authoritative ratings in the sphere of CSR and continuous development, taking the top position in the sector "equipment and services in the field of health care". The total number of points scored by the company (83) was significantly higher than the average score on branch (41). It is noteworthy that "Abbott Company" does not have its own web-site in Ukraine and was not analyzed by the Centre "Development of CSR", which indicates the absence of stimulating factors to the coverage of the SR of the company at the state level.

**Conclusions.** By the results of the research it is possible to draw a conclusion that in Ukraine the unsatisfactory level of SR of the pharmaceutical companies, both domestic, and foreign has revealed that in our opinion, it's inadmissible, especially considering a social orientation of pharmaceutical branch.

Considering that the companies of known international brands with the developed KSR-strategy ("Abbott Company", "Novartis Ukraine", "OmegaPharma Ukraine") have no web-sites in Ukraine, it is possible to claim that introduction of SR in pharmaceutical branch of health care in Ukraine happens quite slow.

One of the most important arguments in the favor of need to implement SR in the practice of pharmaceutical companies is that SR is a factor in improving the competitiveness of enterprises and at the same time an effective strategy for the growth of welfare and achieve sustainable development.

# MARKETING RESEARCH MARKET SEGMENTS ANTICANCER DRUGS USED IN TREATMENT OF CHRONIC LEUKEMIA

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The pharmaceutical market (PM) is one of the strategic sector not only for the economy but also for social development of all countries. In today's PM definition is presented as a complex multilevel structure, which crossed financial, scientific, social, economic, medical and pharmaceutical, ethical and other interests of society and the state. The dominant trends of PM in any country, regardless of the system of health and social protection of the population of the state have a direct impact on the organization of medical care and drug provision by any group of patients. Of particular importance is the question of the availability of medication to patients with various types of chronic leukemia.

According to the National Cancer Institute in Ukraine leukemia is a major cause of mortality in patients with malignant pathology in patients of all ages, leukemia also took first place in the structure of diseases lymphoid and hematopoietic tissues of humans and mortality is about the percentage of the total mortality in all countries of the world. Pharmaceutical provide patients with leukemia in Ukraine made centrally through the budget of different levels within the framework of the state program "Oncology", which is authorized for 2016. The dynamics of the market, as well as on the sales performance is influenced by many factors. However, despite the devaluation of the currency, economic crisis and the fall of solvency consumers emergence of new domestic and imported products is important.

The experience of the EU, efficiency implementation mechanisms external reference pricing and reimbursement mechanisms for cost effective use of medicines depends on the actions of a complex of factors, the study has significant social and economic importance.

First of all, one of the research areas at this stage is a marketing analysis of existing market range of pharmaceuticals products (PP) used in the treatment of chronic leukemia.

Also, the results of market research PM can be used in the formation of a rational structure of procurement of drugs recommended for the treatment of chronic leukemia.

The object of the study were selected clinical data protocols such as chemotherapy, which is fixed by the MOH of Ukraine in "Hematology" also used by the State Expert Center MOH Ukraine. In addition, the research materials of State form (SF) medications 6 release by section 13 "Hematology PP 19"; PP for the treatment of malignant tumors "data state registration of drugs that are on the official website of state and Analysis Center of the Ministry of Health of Ukraine. We also used historical, logical, comparative, statistical methods and market analysis.

At the previous stage of research was necessary to determine segment PP used in chemotherapy with chronic lymphoid leukemia CLL and chronic myeloid leukemia CML. The analysis schemes chemotherapy CML and CLL was formed

sample preparations, which included 15 names of drugs by international non-proprietary name (INN). In the treatment of CLL is recommended INN for such drugs as: fludarabine - (ATC code - L01B B05; anti-neoplastic agents, purine analogues structural); chlorambucil - (ATC code - L01AA02; anti-neoplastic agents, alkyluyuchi compounds); prednisolone - (ATC code - N02AV06, simple preparations of corticosteroids for systemic use); cyclophosphamide - (ATC code - L01AA0; anti-neoplastic agents, alkylating compounds); vincristine - (ATC code - L01C A02; vegetable alkaloids and other drugs of natural origin, vinca alkaloids and their analogues); rituximab - (ATC code - L01X C02 monoclonal antibodies); methylprednisolone - (ATC code - N02AV04, simple preparations of corticosteroids for systemic use); cladribine - (ATC code - L01BB04 structural analogs of purines); alemtuzumab - (ATC code - L01X C04 monoclonal antibodies).

In the treatment of CML is recommended to use these drugs name medications: imatinib - (ATC code - L01XX28 other anti-neoplastic drugs); hidroksykarbamid - (ATC code - L01XX05 other anti-neoplastic drugs); interferon-alpha - (ATC code - L03A B05, adjuvants); nilotynib - (ATC code - L01XE08 protein kinase inhibitors); dazatynib - (ATC code - L01X E06 protein kinase inhibitors); cytarabine - (ATC code - L01B C01 structural analogs of pyrimidine).

Further, according to the registration of drugs was determined that in the treatment of chronic leukemia 85 items available anticancer drugs (AD) a trade name (TN). Thus, the group L01A - alkylating compounds 9 (10.58%) PP, including 2 (2.35%) domestic production; group L01B - antimetabolites 16 (18.8%) private foreign names; the group L01C - vegetable alkaloids and other drugs of natural origin included 5 (5.88%) foreign agents; group L01D - Cytotoxic antibiotics and related drugs represented only 8 (9.41%) PP items, including 1 (1.17%) domestic production of the drug; in the group L01X - Other anti-neoplastic agents 21 (24.70%) name drugs foreign; a group L03A - Immunostimulators 14 (16.52%) PP items, including 5 (5.91%) of domestic drugs.

The results of the analysis of a significant portion of the PP, used in the treatment of chronic leukemia refers to imported products.Thus, according to a study, it was found that in the treatment of CLL and CML using three groups (of 7) namely the: L01B -Antymetabolity; L01C - vegetable alkaloids and other drugs of natural origin; L01X - other anti-neoplastic agents; which is one hundred percent made up of foreign-made products.Thus, it more urgent introduction of a national program import PP, and the need to attract significant investment, primarily for the purpose of logistic conversion hematologic domestic service.

Thus, under the unstable situation in the foreign exchange market, shortage of resources in the national health care system and the unstable socio-economic situation in society, acquire special importance of research aimed at the development of ways to increase the efficiency of pharmaceutical providing patients with socially dangerous diseases and those that the need for health indicators available pharmaceutical care. One aspect of solving this problem is the introduction of social and economic cost reimbursement mechanisms consumption of medicines, regardless of social status and income levels.

# TRENDS OF DISTRIBUTION DRUGS IN UKRAINE AND IN ALL THE WORLD

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**Introduction.** In the world and in Ukraine since the end of the 20th century, there are processes of dynamic development of the distribution system of medicines (drugs). During the years of independence of Ukraine's pharmaceutical market is constantly being an improved, new quality assessment system drug. For the licensing conditions wholesale sales drugs becomes mandatory for good practice GDP and GSP.

**Materials and methods.** Used statistics on the number of distributors in Ukraine and other countries, as well as international rules «Guidelines of November 5, 2013 on Good Distribution Practice of Medicinal Products for human use (2013 / C 343/01) and Guidelines "Drugs. Good practice distribution. CT-N Ministry of Health 42-1.0:2014". The study used methods of system analysis for organizing, summarizing and forecasting the distribution of drugs in Ukraine compared with other countries.

**Results of research.** Since 1999 in Ukraine there is a tendency to reduce the number of distributors. Thus, according to the 2005 wholesale sales of drugs in 1184 were involved entities, in 2010 their number decreased almost twice and reached 623 companies. According to 2014, the country has operated 440 wholesale companies (70.6% of the data for 2010). According to experts, currently about 5-6 national distributors control over 85% of the wholesale market in Ukraine. This global trend in development of wholesale level distribution network. For example, in the US for the past 30 years has seen a reduction of wholesale pharmaceutical companies from 150 to 50. In France, there are only 6 powerful distributors in the UK - 9, Germany - 13, Spain - 58, Italy - 85. Disproportionate nature of the wholesale and retail segments of the domestic pharmaceutical market shows that in Ukraine on a wholesale company accounts for around 45 pharmacies, as for example in the EU is almost an order of magnitude more - 390-450.

**Conclusions.** Equipped with modern trends in the development of the system of distribution of drugs in the world: reducing the number of suppliers, improving the quality of their work, a high level of pharmaceutical service, prompt delivery of drugs and their wide range of products.

# REGULATIONS OF REALIZATION OF THE UTILIZATION AND EXTERMINATION OF THE LOW-QUALITY REMEDIES

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The aim of our research is to find out how utilization and extermination of the low-quality remedies (LQR) is held. We used the descriptive method for that.

LQR are remedies (R) whose quality doesn't satisfy the requirements of normative documents. They are R which had expired; R which were withdrawn from the commerce; unregistered R; R which were under mechanical, chemical, physical, biological or other influence, which makes their further usage impossible; R whose previously unknown harmful characteristic or serious side-effects were discovered. LQR, including those, which are expired and those, which cannot be utilized are to be exterminated. Procedure of extermination: institution files an application to the Narcotics Control Board to get the permission for the extermination of the LQR, which contain narcotics, psychotropic substances and precursors. Application is to be submitted with the R analyses report.

For the extermination of the LQR these methods are used: encapsulation; inertisation, high-temperature incineration, water dilution and discharging to the municipal manifold. The encapsulation method is the process of LQR conversion into monolith in isolated bulk using astringents. The inertisation method – is the process of LQR conversion into monolith using astringents with further decomposition and dispersion. The high-temperature incineration – is the usage of kilns of cement-producing industrial enterprises, carbonic thermoelectric power stations and foundries. The water dilution and discharging to the municipal manifold is carried out by the dilution of remedies with water using the ratio 1:200 with the next gradual discharging to the municipal manifold. To exterminate the LQR, in the form of solid products (powders, capsules, granules, injection powders), semisolid products (creams, lotions, gels, suppositories) encapsulation, inertisation, high-temperature incineration methods are used. To exterminate the liquid LQR (solutions, suspensions, syrups) water dilution and discharging to the municipal manifold method is used.Responsibility for labour protection and accident prevention during utilization is laid onto the manager of the institution providing utilization (extermination).

To draw a conclusion we can say that such methods as the encapsulation; inertisation, high-temperature incineration, water dilution and discharging to the municipal manifold are used to exterminate LQR.

# CLINICAL AND ECONOMIC ANALYSIS OF PHARMACEUTICAL PROVIDING PATIENTS WITH GLAUCOMA

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Modern trend of rapid development of medications market and the emergence of new treatment regimens on the one hand, and the growing number of ophthalmic patients on the other, determines the need for rational choice of drugs. To determine the possibility of further improving the quality of medical and pharmaceutical care using clinical and economic analysis (QEA).

The aim of our study was to conduct QEA with use retrospective, systematic, logical, frequency, and ABC- and VEN- analysis methods.

The retrospective analysis of 422 patients hospital records, who were treated in the polyclinic department of the regional clinical hospital in Kharkiv in 2012-2014., shows that the total number of medical appointments was 764. It is established that doctors had used 26 medicines of trade names or 12 preparations for the international nonproprietary name (INN).

As a result of the ABC analysis revealed that the group A (most expensive) included 9 medicines for brand name. In total volume of medicine consumption proportion of this group of medicines is 79.82% of the costs. Revealed, that 8 of 9 drugs of this group - is costly foreign medications. Group B (medium expenses) represented 11 drugs. On their acquisition spends 17.60% of the total consumption. The group C (least expensive) formed 25 medicines, which spent 5.10% of the total amount of expenses for all antiglaucoma medicines. The results of VEN-analysis found that the structure of medical appointments antiglaucoma medicines 46.16% owned preparations category E (essential). At medicines category V (essential) and N (minor, unimportant) accounted for 26.92% of the total range of antiglaucoma medicines.

In the implementation of the consolidated ABC / VEN-analysis found that the most expensive by INN in pharmacotherapy of glaucoma medications is with the status of A / E - tafluprost (18.53% of the cost), latanoprost (14.46% of the cost), combined drug on the basis of timolol (13.85% of the cost), brynzolamid (9.60% of costs), and betaxolol (3.68% of costs).

Thus, we can conclude about the inadequate of rational expenditure financial resources and the need for complex organizational, economic and pharmacoeconomical researches efficiency of use medicines in order to form the necessary steps to improve the pharmaceutical providing patients with glaucoma.

# ANALYSIS OF PRESENCE AND DYNAMICS PRICES OF MEDICINES FOR DIABETES TYPE II TO THE PHARMACY KHARKIV

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According to international estimates, every 13-15 years the number of diabetics doubled. A similar trend is observed in Ukraine - the incidence rate increased from 115.6 (1993) to 292.4 (2012) to 100 thousand population. The situation is complicated by the fact that patients with type II diabetes, hypertension observed in 2 times more likely than patients who did not suffer from diabetes. In the structure of general morbidity pathology of endocrine organs and tissues is sixth place. Thus every third person with endocrine disease diabetes because research pharmaceutical providing patients with type II diabetes is important.

The aim of the study was to analyze the range of medicines for the treatment of type II diabetes in pharmacies m. Kharkiv serving patients with diabetes mellitus.

The analysis found that of the 36 items antidiabetic drugs (drugs), imported drugs occupy 70%, including 32%, of German, Austria / France 17%, other countries occupy a total of 21% of its pharmacies.

Analysis of drugs for pharmacological groups showed that the largest share of the range are bihuanidy- mono-drugs and combinations of drugs from other groups (50% range). The second mistsi- sulfonylureas 42%, DPP- 4 inhibitors were 6% and 3% range mehlitynidy- drugs.

Analysis of the range of drugs for the INN found that the pharmacy is dominated by drugs metformin - mono preparations and in combination with drugs other groups (50% of drugs), drugs based on glimepiride occupy 25% range, medicinal products based on other materials (gliclazide, glibenclamide, repaglinide, saksahliptynu, sitahliptynu) occupy a total of 25%.

As a result of price changes analazu drugs to treat diabetes domestic and foreign production during the period July 2014 - March 2015 found that in the group of sulfonylureas price Diapiryd tab. 4 mg №30 (Ukraine) increased in the period July-October 2% in October-January to 1%, and from January to March by 13%. The

price of Amaril tab. 4 mg №30 (Germany) in the period July-January increased by 2% and in January-March an increase of 23%.

In group biguanide + sulfonylureas price Hlyukovans tab. 500 mg / 5 mg №30 (France / Austria) increased in the period July-October by 19% in October-January by 13%, and from January to March by 10%. The price of Hlibofor tab. 500 mg / 5 mg №60 (Ukraine) in the period July-January increased by 14% in October-January decreased by 4% and in January-March increased again by 10%.

Among the drugs of biguanide price Siofor tab. 1000 mg №30 (Germany) during July-October fell by 3%, and in October and January remained unchanged, and in the period January-March increased by 33%. The price of Diaformin SR tab. 1000 mg №60 (Ukraine) during July-October increased by 10% in October-January it increased by another 16% in the period January-March increased by only 4%.

In the group of drugs which include PPP-4 inhibitors represented in Ukraine only imported drugs, the price Yanumet tab. 50/1000 mg №56 (- Puerto Rico / Switzerland) in July-October grew by 8% in the period October-January remained unchanged, and in January-March rose very sharply - 4 times. The price of Onhliza tab. 5 mg №30 (USA) in July-October increased by 14%. Price Yanuviya tab. 100mg №28 (Italy) during July-October was unchanged and the subsequent period from November to January Onhliza tab. 5 mg №30 (USA) Yanuviya tab. 100mg №28 (Italy) was not available in pharmacies Kharkiv.

Conclusion. Pharmacies m. Kharkiv attended medicines for the treatment of diabetes mellitus type II Ukrainian (30%) and imported, including drugs manufactured in Germany is the largest segment of 32%

Established that over the period the greatest increase in prices of medicines for the treatment of type II diabetes was observed in January-March 2015 on imported drugs, due to the fast growth rate of foreign currencies to the local currency. The largest growth rates in pharmacological groups are: a group of drugs which include PPP-4 inhibitors (Yanumet tab. 50/1000 mg №56 (Puerto Rico / Switzerland) - the price increased 4 times, the group biguanide price Siofor tab. 1000 mg №30 (Germany) to 33% in the group of sulfonylureas Amaril Table. 4 mg №30 (Germany) to 23%.

# RESEARCH OF FOREIGN EXPERIENCE OF THE INTRODUCTION OF MEDICAL INSURANCE: PROBLEMS AND PROSPECTS.

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Introduction of obligatory medical insurance (OMI) in Ukraine is a serious step in reformation of the whole system of health protection. For successful realization of this project development and introduction of modern strategy that can be based on foreign experience of medical insurance are necessary.

According to the WHL estimation nowadays in Ukraine only 3% of GDP is allocated on health protection, and only insignificant part of them, near 5% is paid from the funds of voluntarily medical insurance, and 80% of consumptions is on payments of population.

Therefore the aim of our research is analysis of foreign experience of introduction of the OMI system with determination of problem questions and directions of improvement of this system.

The system analytical method of analysis has been used in research, in particular, grouping and generalization of data. The analysis of foreign experience of the OMI system introduction has been carried out in the case of six countries such as: Estonia, Poland, Japan, Finland, Switzerland, and Germany. It was stipulated by their different geographical, political and socio-economic features. Thus, Estonia and Poland initially had a number of similar with Ukraine macroeconomic factors of influence on the health protection system.

Therefore results of our research have shown that the main positive results of OMI introduction foreign countries are:

- improvement of the quality of rendered services in health protection;
- increase of population lifespan;

- reduction of health protection establishments funding from state;
- increase of access to the doctors of different narrow specialties.

Thus, along with positive tendencies, there are negative consequences, namely:

- rise in medical services and medications prices;
- reduction of amount of functioning health protection establishments;
- difficulties in procedure of getting the directions to narrow specialists;
- durable period of hospitalization expectation;
- the population is poorly informed about the rules of work of the OMI system and it's separate subjects;
- increase of the obligatory tax from the salary of working citizens.

Taking into account the presence of the critical phenomena in native health protection, which on the estimations of specialists, consists of the low level of financing of medicine and pharmacy, low level of profits of population, mistrust of population to the insurance companies, insufficient technological level of equipment of medical establishments; insufficient amount of skilled specialists, and presence of corrupted constituent it is possible to make conclusion, that introduction of the OMI system will bring not only positive changes in a home health protection and social sphere on the whole but also some negative tendencies.

Therefore, in our opinion, the improvement of organizational structure of native health protection is the main problem that must be solved in Ukraine nowadays for subsequent introduction of the OMI system. The principles of social justice and financial practicability must be fixed on basis of this improvement, that will provide more effective introduction of OMI, taking into account the features of organization of the health protection system in Ukraine, and also national features of country.

# THE LEGAL BASIS OF PHARMACY

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Pharmacy is a sub-sector of healthcare that connects the health and chemical sciences. Its major role is distributing pharmaceutical drugs in an organized and regulated manner.

Though the number of pharmacy applications represents more roles such as supplying medicine, it also includes the more contemporary services related to health care, such as reviewing medical drugs for safety and effectiveness, clinical services and providing drug information.

Pharmacists are licensed professionals that oversee the process of the delivery of pharmaceutical drugs, both over-the-counter and prescription, to patients and the general public. The primary aim of this profession is to provide patients with a means of accessing FDA approved drugs and other general supplements and medication.

In order to practice pharmacy business must comply with the rules of trade drugs (Regulations: Laws of Ukraine «On Medicines», «Fundamentals of the Ukrainian legislation on health care», Order of the Ministry of Health «On approval of the license terms of economic activities for the production of pharmaceuticals, wholesale, retail drugs» and other legislative acts regulating pharmaceutical activities and economic activity).

The opening of the pharmacy business entity assumes observance of the license conditions of the business of retail drugs, and a license. To obtain a license to the State Agency of Medicines, the following documents: application; passport pharmaceutical establishment; documentsp confirming qualification pharmacist; information on the availability of material and technical base etc.

Pharmacy premises should be in the extracted separate from the residential home, or in a built (the additionally) an isolated room, which is located on the first floor and has its own independent access to the outside of the shop floor.

Premises pharmacy: staff quarters, a room or cupboard for storing cleaning equipment, WC with wash basin (in the case of the location of pharmacies in rural areas and the lack of water supply and sanitation, toilet arrangement allowed outside pharmacies).

Floor space for storage of medicines cannot be less than 10 sq.m. Floor space for the staff cannot be less than 8 meters

The total area of the pharmacy should be:

- in the cities - not less than 50 sq.m. (Sales area - not less than 18 square meters);

- for settlements - not less than 40 sq.m. (Sales area - not less than 18 square meters);

- for villages - not less than 30 sq.m. (Sales area - not less than 10 square meters, storage area for drugs - 6 meters, staff room - 4 sq.m.).

Pharmaceutical warehouse should have production facilities, domestic premises support facilities, office space and additional (shields, lobbies, corridors, etc.).

Production facilities - a room, area or zone for receiving, storing and dispensing of medicines, auxiliary materials and packaging with a total area of at least 250 sq.m.

Domestic premises - premises staff (0.75 square meters per worker one shift, but not less than 8 m), dressing room, with water supply and sanitation (by calculation, but not less than 2 m), dressing room, shower , dining, etc.

Auxiliary rooms - a room or cabinets for storing harvested area of not less than 4 meters (minimum set), as well as room for the preparation of disinfectant solutions, archive server, guardroom, classrooms, storage space for working tools for loading - premises - premises preparation and processing of documentation, office head and his deputy, as well as room personnel involved in the process.

Warehouses should be located so as to avoid the need for workers to pass through the production facilities for changing clothes in spets.

Staff pharmacy institutions must have the appropriate special education and meet the qualification requirements.

The same rules consist in Lebanese legislative of opening a pharmacy and license of a pharmacist and documents including the test which all student those who studied in another countries like us, they should pass exam which identification the knowledge of foreign diplomas.

About the pharmacy the same rules with a little change about the place and how much log the area’s most are between pharmacies, like 300 m. diameter area. Lebanese has a good policy which support beginner to open there own pharmacy such give it from banks money to have the own pharmaceutical business and credit of medicine which are arranged for sales and marketing.

# FUNDAMENTALS OF BUSINESS PLAN FOR COSMETIC ESTABLISHMENT AND ITS DEVELOPMENT

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Organization and business planning of professional cosmetics and perfume sale is an actual issue for own business establishing. Probably,an idea to sale perfume and professional cosmetics is not a new in itself, but even under the competition of a high level at the market the new entrants have all chances to be succeed on the assumption that they will manage to find their niche. Every person is eager to authenticity. People are becoming more educated; more often they pay attention to the products they choose. And this tendency is being persisted and increased.

Business planning at a cosmetic establishment – is an independent type of planned activity which is directly connected to the establishment. This is the ordered set of stages and actions, related to situational analysis of the environment, business planning goals' setting, development of business plan, its promoting to the intellectual property market, business plan implementation, monitoring of the plan's performance.

The aim of the work is knowledge improvement in business planning of cosmetic establishment and its development; design of business plan for establishment's development program for the near future.

Within investigation the methods of systematic analysis, monitoring, logical generalization etc. were applied. As a theoretical foundation for the work, the research papers of domestic and international authors in business planning of activities of enterprises and cosmetic establishments were used.

The research conducted has found that such type of business as an establishing of perfumery and cosmetics shop is a super lucrative, subprime and prospective. One of the main conditions of its operation is an existence of economically advantages choice location that is associated with objective economical and financial events and state of the market.

Thus, business planning describes process of enterprise operation, displays how its authorities are planning to reach the goals and tasks, primarily, in profitability. The well developed business plan assists to achieve new positions at the market, to create prospective plans of its development, concepts of new goods and service manufacturing, and to choose rational ways of disposal.

# STRUCTURE ANALYSIS ASSORTMENT OF MEDICINES OF DOMESTIC PRODUCTION

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Escalation of competition between foreign and domestic manufacturers of medicines, saturation certain segments of the market a large number of medications put the question of the formation expedient structures assortment by the domestic pharmaceutical companies. Analysis and evaluation of product assortment is an important step in the development of pharmaceutical company strategy and is the key to making effective decisions on improving assortment policy and improving the competitiveness.

Based on the foregoing, the purpose of our study is the structure analysis assortment of medicines Ukrainian production on the example on product portfolio of PJSC "Farmak", as the leader of the manufacturing sector of the domestic pharmaceutical industry.

During research drugs were grouped according to pharmacotherapeutic groups by ATC-classification and allocated a separate group dietary supplements. Structure of assortment of medicines PJSC "Farmak" according to 2013 is presented in Table. 1.

Table 1

**The structure of the product range and sales of drugs PJSC "Farmak"**

| Group ATC Classification | Number of assortment position | Share of assortment position, % | Sales, thous. pack. | Share of sales, % | Income from sale, thous. UAH. | Share of income from sale, % |
|---|---|---|---|---|---|---|
| A – Alimentary tract and metabolism | 53 | 16,26 | 11 030 | 11 | 442 623 | 25,42 |
| B – Blood and blood forming organs | 12 | 3,68 | 607 | 0,6 | 91 492 | 5,26 |
| C – Cardiovascular system | 36 | 11,04 | 10 585 | 10,55 | 134 368 | 7,72 |
| D – Dermatologicals | 15 | 4,6 | 2 924 | 2,91 | 49 787 | 2,86 |
| G – Genito urinary system and sex hormones | 16 | 4,91 | 651 | 0,65 | 21 127 | 1,21 |
| H – Systemic hormonal preparations, excl. sex hormones and insulins | 14 | 4,3 | 1 124 | 1,12 | 32 262 | 1,85 |
| J – Antiinfectives for systemic use | 16 | 4,91 | 4 207 | 4,19 | 141 290 | 8,12 |
| L – Antineoplastic and immunomodulating agents | 5 | 1,53 | 1 089 | 1,09 | 57 206 | 3,29 |
| M – Musculo-skeletal system | 19 | 5,83 | 2 349 | 2,34 | 4 121 | 0,24 |
| N – Nervous system | 37 | 11,35 | 23 427 | 23,34 | 215 148 | 12,36 |
| P – Antiparasitic products, insecticides and repellents | 2 | 0,61 | 162 | 0,16 | 1 770 | 0,1 |
| R – Respiratory system | 55 | 16,87 | 35 252 | 35,12 | 417 200 | 23,96 |

| | | | | | | |
|---|---|---|---|---|---|---|
| S – Sensory organs | 29 | 8,9 | 6 353 | 6,33 | 76 086 | 4,37 |
| V – Various | 12 | 3,68 | 185 | 0,18 | 38 858 | 2,23 |
| Dietary supplements | 5 | 1,53 | 419 | 0,42 | 17 623 | 1,01 |
| TOTAL | 326 | 100 | 100 364 | 100 | 1 740 961 | 100 |

It is established that in 2013 the company assortment was represented by 321 medications of all therapeutic groups, and 5 dietary supplements. The maximum depth range is characterized by medicines that acting on respiratory system and acting on alimentary tract and metabolism (55 and 53 positions, respectively). Significant share in assortment are taken drugs, that acting on the cardiovascular, nervous systems and sensory organs. Least of all product portfolio is presented antiparasitic drugs, insecticides and repellents (2), dietary supplements (5), antineoplastic and immunomodulating medicines (5).

Conclusions about the prospects of each therapeutic group in terms of generating income can be done from the results of comparative analysis of attitude the share of sales volumes each group of medicines in physical and monetary terms (Table 2).

*Table 2.*

**The distribution of pharmaceutical groups in the prospects for generating income**

| Most promising drugs ("income">"volume") | Promising drugs ("income"~"volume") | Unpromising drugs ("income"<"volume") |
|---|---|---|
| • B – Blood and blood forming organs;<br>• V – Various;<br>• L – Antineoplastic and immunomodulating agents;<br>• Dietary supplements;<br>• A – Alimentary tract and metabolism;<br>• J – Antiinfectives for systemic use;<br>• G – Genito urinary system and sex hormones;<br>• H – Systemic hormonal preparations | • D – Dermato-logicals;<br>• C – Cardio-vascular system; | • M – Musculo-skele-tal system;<br>• N – Nervous system;<br>• P – Antiparasitic products, insecticides and repellents;<br>• R – Respiratory system;<br>• S – Sensory organs |

As established by the analysis, the most profitable groups of medicines is drugs, that affect the blood and blood forming, antineoplastic and immunomodulatory drugs, dietary supplements and medicines, that influence on alimentary tract and metabolism. Should be noted, that these pharmacological groups are promising for implementation in production, because the share of income exceeds the share of sales volume and it will expand the product portfolio of the company, considering minimum depth range of these groups.

Thus, as a result of the analysis, it can be concluded that more than 30% of the assortment PJSC "Farmak" is taken medicines affecting the respiratory, digestive systems and metabolism. However, antineoplastic, immunomodulatory drugs, medications, that influence the blood and blood forming and dietary supplements are the most promising in terms of generating income and expanding product portfolio.

# RESEARCH THE COMPETITIVE POTENTIAL OF MEDICINES FOR PEPTIC ULCER

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In the conditions of the high competition in the pharmaceutical market (PM) when efforts of producers are more and more directed on creation of new competitive advantages and strengthening of the existing market positions, carrying out the systematic analysis of the competitive environment of the enterprise is actual. This will determine the direction of orientation the marketing activities of producers and effective use the competitive potential of medicines trademarks. One of the ways to increase market share and capturing profitable place among competitors in today's pharmaceutical market is the allocation of consumer medicines characteristics and securing the appropriate position in the consumer's mind.

The aim of our work was the research of competitive potential medicines for peptic ulcer at a group of omeprazole which are presented in the Ukrainian PM. In the analysis methods of the marketing analysis, comparative, graphic methods, and also data of analytical system of research of the PM are used.

The analysis of existing techniques for assessing the competitive advantages has shown that the following belongs to the main criteria of competitiveness medicines: indicators of consumer value, economic indicators, indicators of a level of demand on medicines in comparison with competitors. By results of consumer preferences and the PM analysis omeprazole, we have grouped competitiveness indicators according to the main components of the marketing mix. Thus, medicine assessment as "product" was carried out on indicators of a consumption level, trust to the producer and trading to brand. From the point of view of the marketing price tool definition of economic indicators assumed calculation of unit cost of a medical dose and average plan of treatment cost. The following became criteria of an assessment of the medicines competitive environment: a share in market a segment, an indicator of competitiveness and medicines existence in pharmacies. In determining the effectiveness of promoting omeprazole, awareness about a trademark of drugs among consumers was estimated.

Considering the calculated integral indices of consumer properties, price characteristics, conditions of the market environment and support level, we have constructed the map of omeprazole positioning in the market. It is established that positioning of trademarks by the Ukrainian producers ("Farmak", "Darnitsa", "Arterium") is carried out, mainly, being based on policy of promotion. Foreign producers ("Dr.Reddis", "Sandoz") give preference to consumer characteristics of medicines at creation of competitive positions in a market segment.

Thus, when examining the competitive potential of medicines at omeprazole group the indicators affecting the position brands on the market are defined the main and set priorities for positioning among manufacturers in this segment. The results of the estimates of the parameters positioning are the basis for the development of marketing plans and recommendations to enhance the potential of the different pharmacological groups.

# THE IMPROVEMENT OF THE HOMEOPATHIC MEDICINES PRODUCTION IN THE HOMEOPATHIC PHARMACY (DEPARTMENT)

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Alternative treatments are becoming more popular in conditions of the steady annual increase in cases of medical disease manifestations, the environmental degradation and so on. In recent years the attention of physicians, pharmacists and patients has greatly increased in a number of such medicine areas as the homeopathy. An important feature of homeopathic therapy is an individual approach to patients, the implementation of which is possible, first of all, because of the extemporaneous manufacturing of homeopathic medicines (HoMed) on the homeopaths prescription.

However, the development of homeopathy in Ukraine was rather complicated, leading to an imperfect legal framework, regulating production processes in the manufacture of HM, the standardization and quality control and the lack of qualified specialists in this field. In this regard, the development of specialized homeopathic pharmacies, the domestic industrial production of the HoMed in Ukraine goes in a quite slow pace, and the wide range placing of foreign HoMed products on the Ukrainian market proves this fact.

That's why the idea to expand the production of homeopathic drugstores (departments), to improve and develop homeopathic pharmacy is relevant. This is possible in two ways: to increase the number of homeopathic pharmacies or to open homeopathic sections, which are based on existing general profile pharmacies with the license for production activities.

We have conducted some sociological researches among experts of the pharmacy on issues that may arise during organization of the extemporal production of the HoMed.

According to the specially created application form among 400 pharmacists from 11 regions of Ukraine (Kiev, Donetsk, Poltava, Chernihiv, Luhansk, Sumy, Odessa, Kherson, Khmelnytsky, Kharkiv region) were processed near 4400 questions. The data were processed using a specially created computer program for statistical processing of the personal data «PSPPD (program for statistical processing of the personal data») providing the population of HoMed, which makes it possible to obtain more reliable results that can be used in further researches.

We found that according to respondents' opinion there are some issues that should be considered in the organization of the HoMed extemporal production.

The most actual are:

1. The lack of logistical support:

- The lack of methodical recommendations for the workplaces organization in manufacturing HoMed in pharmacies - 35.70%;

- The lack of specialized equipment for the homeopathic pharmacies production - 52.10%.

2. The unregulated personnel provision:

- The lack of industrial standards of labor organization and regulation for specialists in the HoMed production - 23.30%;

- The need for calculating the number of specialists in the HM production with the account specificity and manufacturing loading - 25.70%;

- The lack of qualified specialists in the HoMed extemporal production - 47.70%.

3. The unsettled regulatory support and procedures of import raw materials for the HoMed production - 27.8%.

Today, one of the most important problems of the practical homeopathy is its activity, which is regulated by a number of normative documents for general pharmacies profile - relevant MOZ Ukraine orders controlling production processes. But these acts are not always taken into account the specifics related to the production and quality control of HoMed.

Therefore, in order to improve and develop the homeopathic pharmacy, to organize the qualitative and full population maintenance of the HoMed, and according to the HoMed production specificity in the modern life, we proposed some norms – «Regulation of the homeopathic pharmacy», « Regulation of the homeopathic pharmacy department». The Civil Service of Medicines has accepted these regulations for the further consideration and elaboration.

According to the suggestions above, there are some propositions to improve the organization of the HM extemporal production:

1. The priority direction is to create the homeopathic pharmacy (departments) with the following parameters: the presence of existing pharmacies (departments) of this type, number of doctors who use the homeopathic treatment in their practice, the number of prescriptions for HoMed, the population in the region, and so on.
2. To standardize manufacturing operations depending on the types of medical forms and on spending the working time on them. This will allow in future regulating and systematizing the organization of workplaces, the calculation of staff units of specialists, the general algorithm for creating the specialized homeopathic pharmacy (department), the workplace and also its equipment.
3. To implement provisions of basic departments of the homeopathic pharmacy and, according to it, to create a regional list of basic pharmacies, where it could be possible to study and gain the experience from the organization of the manufacturing function of the HoMed extemporal production.
4. To regulate the legal framework on issues of the homeopathic pharmacy (departments) activity, to procurement procedures and to import the homeopathic stock, to search the staff to the specialized homeopathic pharmacy (departments).
5. To systemize the HoMed nomenclature that is allowed for using in Ukraine.

# MARKET RESEARCH OF DETERMINATION FACTORS OF CONDUCT FOR THE CUSTOMERS RANGE PERFUME AND COSMETICS PHARMACY ORGANIZATIONS

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Last 15 years, changes in Ukrainian pharmaceutical sector had a significant impact on the structure of commodity nomenclature pharmacy organizations. An important role in stock, have not only medicines and other groups means s for the health and beauty, including health and beauty products. This trend is changing assortment structure pharmacy organizations caused economic conditions of their functional activity (high level of competition, the formation of pharmacy chains, format sales - open layout, etc.), And the desire to better meet consumer demand.

The aim of the study research of determination factors of conduct for the customers range perfume and cosmetics pharmacy organizations. During this study we used systematical, marketing, behavioral, situational and process methods.

The experts from the pharmaceutical sector is predicted a growth of pharmaceutical cosmetics market in the coming years due to increasing needs of the population as well as increased marketing moves companies producing perfume and cosmetics products.

To analyze determination factors of conduct for the customers range perfume and cosmetics pharmacy organizations, we use a sociological study of the two categories of users: final consumers, represented visitor of pharmacies in m. Kharkiv and institutional – represented specialists of pharmacy organizations, during January - March 2015. The program included: defining goals and objectives; development tools (questionnaires), surveys, collection of statistical data; processing and analysis of information collected. Reliability of data based on the formation of random sampling size was 50 final and 50 institutional customers of perfumes and cosmetics products.

The bulk of surveyed final customers - is not married women (73.0%), which is consistent with the dominant age group of respondents in the range of 15-25 years (68.0%). Among the buyers is dominated by middle-income (86.5%), who live in Kharkiv have incomplete higher education - 43.5% and complete higher - 33.0%. Considering that women are the main buyers of cosmetic products in the pharmacy, priorities of their choice deserve a special attention. The survey showed that the approach to the selection of cosmetic depend on the age of customers. Especially women of almost all ages appreciate the brand product, only for respondents over the

age of 56 consulting service are paramount. The second most important factor in choosing to age under 15 years, 16 to 25 years and over in 56 is the ease of use of cosmetics, while respondents aged 26 to 40 years have given second place to consultation service.

Among the institutional customer dominated a segment of network pharmacy organizations (76%) with open form of sales (55%) and the number of cash registers 2-3. Age employees, most of which are accounted for specialists with higher pharmaceutical education, is in the range of 25-45 years (75%), with experience from 2 to 5 years in 52% and from 5 to 15 years 31%.

As you know, the main criterion for the formation of perfumes and cosmetics is a brand name, which indicated 98% of respondents. To select product category on commercial equipment in some pharmacy organizations use the categories. However, the results showed that in the most popular pharmacy organizations is separate positioning of medical cosmetics (60%), while the category "cosmetics" and "perfumes" is not used at all.

Selective perfumes and cosmetics products, products of mass-market and middle-market are often as tools for hair care, body and face. Tools for problem skin are separate from other products in 20% of pharmacies. Respondents indicated that in their pharmacy can be applied such category as "For the treatment of acne", "Healthy skin", "Just for men", "For lovely women".

Among the respondents there were no pharmacy organizations where individually positioned children perfumes and cosmetics products. Many pharmacy organizations practicing to layout perfumes and cosmetics products for individual brands.

As well as final customers, employees of pharmacy organizations consider an important factor is promoting the availability of testers for certain types of perfumes and cosmetics. Most pharmacy organizations (54%) who participated in the survey, providing consulting services in choosing perfume and cosmetics products. Thus, 89% of respondents mark to the high demand for consulting assistance choosing the answer "often" and "very often."

Thus, the results of sociological survey testify to the importance of receiving counseling. Currently there is a significant gap between the need for providing consulting assistance in choosing perfume and cosmetics products (77% offinal consumers need to consultation) and the degree of satisfaction (46% of pharmacy organizations do not provide specialized consulting assistance).

# PROVIDING MILITATARIES WITH SETS OF SPECIAL PURPOSE DURING THE ACTIVE FIGHTING

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Regular and timely providing militaries units and health institutions in medicines is important condition for treatment and rehabilitation of wounded and diseased during the active fighting.

The aim of researching is analysis of providing militaries units with sets of special purpose during the active fighting.

We used such methods of analysis as the system – overview, analytical, structural and logical.

During the preparation to fighting, the requirement in resource expressed in sets of special purpose and calculated with records of expected sanitary losses, established type and volume of medical care.

During the active fighting general requirement in sets of special purpose, except the requirement in providing of expected losses, includes the requirement of replenishment combat losses and creation it's proper resources to an end of fighting.

Providing with sets of special purpose has several advantages front a broad assortment of medicines and medical products. It is achieved by efficiency of delivery resource to the center of mass sanitary losses. These sets are easy to transport and fields of storage.

The general requirement in sets of special purpose, which were used in qualifieded medical care and specializeded medical care, such as B-1, B-2, B-4 are 30, 12 and 9 respectively. They are normally calculated near for 1500 wounded and diseased during the active fighting.

Also during the researching was founded that sets, which were used in qualified and specialized medical care have the amount deficiency.

So, B-1 set has deficiency near 14.67%, B-2–45.83%, B-3–37%, B-4–12.22%, BG – 31.43%, ANT – 36.7%, LUCH – 55%, OV – 27.5%.

These results show that the system of provision has some problems in providing. It's may be associated with deficiency financing of militaries units and health institutions in medicines and medical products. As result, sets of special purpose mainly have supplies resources, which can use in a great number during the active fighting. But nowadays the provision of these sets have deficiency financing that's why providing in medicines and medical products cannot be fully achieved.

# FORMATION OF ASSESSMENT ATTRACTIVE AND EFFECTIVE INNOVATIVE PROJECTS IN PHARMACEUTICAL PRODUCTION

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**The purpose of the study.** The purpose of our proposed modified method was the establishment of regulations (standards) assess the attractiveness of investment projects, as an example of innovative projects in the pharmaceutical industry of Kazakhstan compared with those in Ukraine.

**Materials and methods.** In order to select the most significant factors attractiveness of innovative projects in the pharmaceutical industry of their pre-selection was carried out with the help of expert evaluation.

According to the results of the comparative analysis was developed by standard indicators attractiveness of innovative projects, which used the weighted average grades of technical and technological factors, social, institutional and environmental attractiveness of appropriate peer review of domestic and Ukrainian pharmaceutical company.

**Results.** We have studied the existing approaches and methods of evaluation, and selection of innovative projects, resulting in a group of factors have been identified to assess the investment attractiveness of projects. On the basis of these factors has established a system of indicators to measure innovation attractiveness of investment projects. An algorithm for evaluation of investment attractiveness of innovative projects in the pharmaceutical industry. A comparative analysis of national assessments and Ukrainian experts for each indicator of the attractiveness of innovative projects.

**Conclusions.** As a result, a comprehensive assessment of investment attractiveness of innovative projects have been calculated regulations (standards) for each indicator of investment attractiveness of the project by comparing all indicators of investment attractiveness (tab. 1).

Table 1

Performance standards of technical and technological, social, institutional and environmental attractiveness of innovative projects

| Standard indicators of technical and technological innovation projects appeal | | | | |
|---|---|---|---|---|
| Rate of change the material returns | Index of scientific novelty of the project | Coefficient of power increase | Growth rate factor-life of fixed assets | Growth rate the capital-labor |
| 1,45 | 4,1 | 4 | 2,05 | 1,575 |
| Standard indicators of social attractiveness of innovative projects | | | | |
| Index affordable prices of medicines | Growth rate profit allocated for consumption | Growth rate specific weight workplaces that meet the requirements of life safety | Growth rate the index professional development | Pace growth in the share of workers employed mechanized and automated operation |
| 4,175 | 1,225 | 2,25 | 2,85 | 1,325 |
| Standard indicators of institutional attractiveness of innovative projects | | | | |
| Change in the coefficient centralization of management | Changing specific weight employees of the management in the total amount of employees | Change in the coefficient number of workers at the head of 1 | Change in the coefficient number of heads per 1 unit | |
| 1,275 | 3,4 | 2,575 | 1,375 | |
| Standard indicators of environmental attractiveness of innovative projects | | | | |
| Pace decrease in the share of municipal solid waste | Pace decrease in the share of wastewater | Rate of reduction emissions into the atmosphere of dust | Rate of reduction emissions into the atmosphere of carbon monoxide | Pace reduce emissions of nitrogen oxide |
| 1,3 | 3,525 | 3,025 | 2,675 | 2,075 |

## SECTION № 14

# QUALITY CONTROL IN THE PHARMACEUTICAL AND HEALTHCARE INDUSTRY

**PROVIDING SOFTMWARE QUALITY ASSURANSE SERVICES TO VISITORS PHARMACIES FOR EXAMPLE PRIVATE FIRM «GAMMA-55».**

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Today the material success of every enterprise that sells goods to a large extent depends on customer satisfaction. The domestic pharmaceutical market is characterized by rapid development and increasing demand for pharmaceutical products, despite the rise in prices. Is constantly expanding retail pharmacy network, and as a result - increased competition. In such circumstances, due weight must be given to increasing the efficiency of work with consumers, there is an objective need for in-depth study of issues related to quality of customer service as an important factor in building a positive image of pharmacies.

All subjects of the pharmaceutical market, along with compliance with applicable laws and regulations governing pharmaceutical activity should strictly follow ethical rules and regulations of pharmaceutical services to the population and services. Significant impact on the psychology of behavior not only pharmacy staff but also visitors, reveals style service.

Effective operation of any enterprise as a whole and individual members of its staff will only come if there is clear regulation of activities stipulated in the relevant organizational documents of the manager, including job descriptions of staff.

Maximum meet the expectations and requirements of customers in the pharmacy reveals a positive impact on the competitiveness of firms. In this paper, the pharmacy can not do without the principle of quality management «customer orientation». Measures such as pharmaceutical marketing and merchandising is no longer a competitive advantage pharmacies – today it is traditional methods of most pharmacies. Therefore, knowledge of psychological characteristics of sales, the ability to apply this knowledge in practice may be a new competitive advantage pharmacies more effectively meet customer needs, and therefore – to increase the quality of service customers in the pharmacy due to focus on the psychology of the clients.

We conducted an analysis of the pharmacy staff pension fund «Gamma-55» and the factors including psychological, affecting the sales of goods pharmacy. Still a pharmacy pharmacists client not goodbye, and often not even answered his farewell. Also at the meeting with the client pharmacists Pharmacy First greeted not expecting initiatives from the buyer.

Pharmacists did not provide sufficiently comprehensive information available about the product portfolio of product characteristics, so that the visitors could get the impression that most pharmacists have enough professional knowledge. Customer service at the pharmacy was fast, but without identifying them loyalty. Most pharmacy staff used to be limited to the available overall, but without a hat and coat on badge with the name and surname.

We identified deficiencies should be considered employees of the pharmacy and excluded in the future that will improve the quality of customer service and increase sales of pharmaceutical products. This, in turn, finds a positive impact on the competitive position of pharmacy.

We also analyzed modern technology of pharmacy.

The aim of our research were: finding ways to improve the quality of customer service; improve the quality of pharmacy; improve the image of pharmacy; the recommendations for improving the quality of pharmacy and optimization algorithm execution of pharmacy of their functions.

We analyzed the work of pharmacy and found some shortcomings in the work that should be eliminated in the future; developed and proposed a set of recommendations for the implementation of measures to raise awareness (advertising, merchandising) that detects a direct impact on improving the quality of customer service pharmacy «Gamma-55».

We have analyzed regulatory framework for the sale of medicines in Ukraine. Considered and examined current trends reform retail sale of medicines in Ukraine.

We have analyzed the activities of pharmacies according to international standards. We determined the expediency of the process approach promoting clear and timely planning, implementation and control of all business processes and stores of work, their constant improvement, which makes it possible to increase the efficiency of the pharmacy.

On the basis of summarizing review of published data and case studies we set priorities for optimization of pharmacy «Gamma-55» to improve qualityand visitor services pharmacy. We have developed a questionnaire that was offered to fill pharmacies visitors. Given the results of the survey we have developed an algorithm quality service customers in the pharmacy «Gamma-55».

Our results can be used pharmacy and offered to the attention of all entities in the pharmaceutical market of Ukraine, because they can increase the efficiency of pharmacy through the expansion of the committed satisfied customers and increased sales.

# THE NECESSITY TO USE MATHEMATICAL METHODS IN DRUG PRODUCT DEVELOPMENT

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Nowadays, progress in science and technology in the field of pharmacy is intimately connected with intensification of scientific research, which, in its turn, requires mathematical data description. In particular, use of various mathematical methods is an integral part of application pendency during registration of new drug products, introduction of amendments to the instruction on medical use of any drug product, as well as theoretical grounding of experimental studies and assessment of the results obtained during scientific experiments. In addition, mathematical approach not only facilitates precise quantitative description of a certain task via construction of one or another appropriate model, but also provides means for its solution.

As a rule, drug product development contains certain stages, which may vary due to particular tasks of experimental studies, such as: collecting and processing of independent information; experimental selection of factors, which are to be studied in detail; experimental search for an optimal site; obtaining mathematical model of the process in the optimal site; mathematical study of the process model in order to find optimal modes; experimental check of optimal modes.

In order to reflect the key points of experimental studies, it is reasonable to use methods of mathematical experiment design, which are based on analysis of variance and regression analysis. Their use is appropriate when solving such tasks as selection of most significant factors (sampling experiment), conduction of comparisons (comparative experiment), search for optimal conditions (optimization), assessment and clarification of theoretical model invariables, in particular, kinetic ones, investigation of "composition-characteristics" diagrams, etc.

It should be noted that nowadays there are methods that allow use of mathematical models at different stages of drug product development. For example, biological modeling on the basis of various data on physiology, biochemistry, and regulation of processes that occur in a human organism, allow conduction of quantitative estimation of a drug product interaction with the target and the rate of its distribution in the body. This, in its turn, provides the opportunity for better understanding of target potential and selection of those molecules that posses an optimal combination of biotherapeutical characteristics at the early stages of drug product development under conditions of limited clinical information available.

Thus, it is possible to state with assurance that today mathematical modeling is one of the most promising methods to be used in order to improve the efficiency of the process of new drug product development.

## SECTION № 15

## INFORMATION TECHNOLOGIES IN PHARMACY AND MEDICINE

# FEATURES OF USE THE ELMA-SYSTEM FOR COMPLEX ASSESMENT TO THE ACTIVITES OF PHARMACEUTICAL ENTERPRISE

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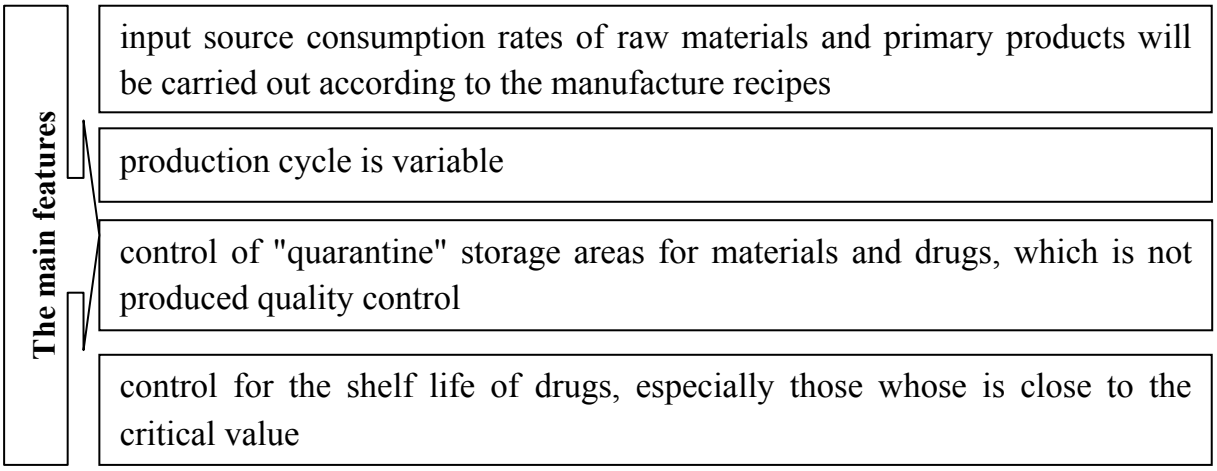
The process of save and quality drugs production is regulated by GMP standard. This standard in Ukraine implemented on all main pharmaceutical plants, because without GMP to complete with foreign manufacturers is it impossible. But GMP standard doesn't contain the requirements for pharmaceutical enterprise electronic management system.

The goal of this work is ground of opportunities of the possibility ELMA-system using in pharmaceutical enterprise.

The work with pharmaceutical enterprise documentation has main features. First of all this is documentation to primary products, raw materials and accessory substances, which have specific of pharmaceutical brunch.

The electronic document management system for pharmaceutical enterprise will be reflect main features (pic.1).




The ELMA-system allows you to create and keep the "electronic-file" with the list of documents for each drug series; reports on the shift production, quality assurance reports, drugs route maps, etc.

Thus, the considered ELMA-system can be used for the electronic documentation management system of pharmaceutical enterprise formation. This will increase the resource using and management decisions efficiency.

# RESEARCH OF SURFACE AND ADHESION ENERGIES OF VAN DER WAALS FORCES BETWEEN SURFACES

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Surface energy or interface energy qualifies the disruption of intermolecular bonds that occurs when a surface is created. In the physics of solids, surface must be intrinsically less energetically favorable than the bulk of a material; otherwise there will be a driving force for surface to be created. Adhesion energy also represents the sum of all energies produced by interactions between the substrate and adhesive itself. Van der Waals forces play a central role in all phenomena involving intermolecular forces.

The aim of this work was to study how surface energies are determined from the intermolecular forces between two surfaces.

The total energy per unit area of two planar surfaces at a distance $D$ apart is given by

$$W = \frac{A}{12\pi D_0^2}\left(1 - \frac{D_0^2}{D^2}\right)$$

where $A$ – is the Hamaker constant, $D_0$ – interfacial contact separation. By increasing the surface area of medium by one unit area its free energy changes by some value γ that called surface energy or surface tension.

At $D = Do$ (two surfaces in contact), $W = 0$, while for $D = \infty$ (two isolated surfaces),

$$W = \frac{A}{12\pi D_0^2} = 2\gamma,$$

where γ - is the surface energies of solids and liquids (for a liquid, γ is usually referred to as its surface tension).

or

$$\gamma = \frac{A}{24\pi D_0^2}$$

In other words, the surface energy γ equals half the energy needed to separate two flat surfaces from contact to infinity, it is half the adhesion energy.

Thus, for calculating surface energies there propose to use an interfacial contact distance $D_o$ that is substantially less than the interatomic or intermolecular centre-to-centre distance.

# USING OF NON-STANDARD ALGORITHMS FOR PHARMACEUTICAL ENTERPRISE DOCUMENTATION WITH ELMA-SYSTEM

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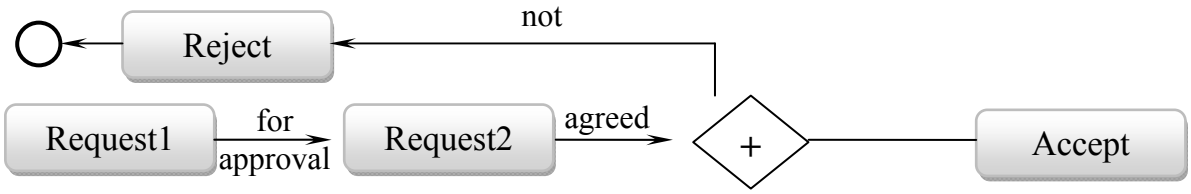
Developments of pharmaceutical brunch based on the advanced technologies, which allow us create new and improve exiting drugs. In a largest pharmaceutical plants management quality system laid on process approach based on the international ISO 9001 standard. For its practical realization are needed software for technological process and maintenance of drugs.

The goal of this work is use of the ELMA-system for non-standard algorithms work with specialized documents of the pharmaceutical enterprise.

In our times modern pharmaceutical production is characterized by lot of documents: normative acts, technological and industrial drugs orders, check quality prepared and it-between product reports. Particularized pharmaceutical documents required use of non-standard algorithms for electronic document versions.

These algorithms could be realized by ELMA system. ELMA have: the transition from paper-based to electronic documentation in the pharmaceutical enterprise; follow out control all pharmaceutical enterprise documentation (for raw materials and all technological process of drugs production stages) requirements.

Each ELMA can be describing by diagrams and notations language with ELMA Wizard module help (pic.1).




With ELMA:

- effectiveness of management decisions in different levels of technological process of drugs production will be increase;
- commercial, analytical and production processes will be automated;
- quality management system non-standard algorithms by ELMA, including all operations and stages of technological process of drugs production, will be realized.

# INVESTIGATION OF DEPENDENCE OF LACTOBACILLI SURFACE CHARGE ON THE CONCENTRATION OF $Ca^{2+}$ IN THE INCUBATION MEDIUM

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Lactic acid bacteria comprise a wide range of genera and include a considerable number of species. Their common traits are: Gram-positive, usually catalasenegative, growth under microaerophilic to strictly anaerobic conditions and lactic acid production. These bacteria are the major component of the starters used in fermentation, especially for dairy products, and some of them are also natural components of the gastrointestinal microflora.

That is why a more detailed study of the influence of the environmental parameters on lactobacilli surface charge is of importance. In this work we investigated the dependence of *Streptococcus thermophilus* surface charge on the concentration of $Ca^{2+}$ in the incubation medium. The surface charge of erythrocytes was evaluated using Alcian blue cationic dye (AB). The amount of bound AB per cell was calculated by the difference in absorbances of the initial AB solution and the supernatant and expressed in nanograms per $10^6$ cells.

| $Ca^{2+}$ concentration, % | 0.00 (blank test) | 0.01 | 0.02 | 0.03 | 0.04 |
|---|---|---|---|---|---|
| Quantity of bound AB by lactobacilli, ng/$10^6$ *S.thermophilus* | 444.1±8.7 | 432±10.8 | 435±9.7 | 443±11 | 428±10.2 |

Results show, that the binding of AB to *S. thermophilus* cells did not change significantly in the investigated range of $Ca^{2+}$ concentrations. Its means that the surface structures of lactobacilli *Streptococcus thermophilus* is not sensitive to changes in the concentration of calcium in the surrounding medium. But for further study the dependence of the charge of the surface structures of lactic acid bacteria on the composition of the environment is necessary to continue research in this direction.

# THE PEARSON CHI-SQUARE TEST IN ELECTRON SPREADSHEETS

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The Pearson *Chi*-square is one of the most common test for significance of the relationship between categorical variables. Usually it realized in special statistical computer programs (e.g. Statistica, IBM SPSS Statistics and others). But all these programs are payware and that is why they often are not public domain software. At the same time there are some simple freeware office applications (spreadsheets), which have intrinsic means for calculation value of the *Chi*-square and clearly recognize relations between categorical variables.

Present work contains sketchy description of calculations value of the *Chi*-square using LibreOffice Calc. After entering data in cells of a spreadsheet, the algorithm calculates number of degrees of freedom and expected frequencies for the two-way table (i.e., frequencies that we would expect if there was no relationship between the variables). Then it evaluates the value of the *Chi*-square. The only assumption underlying the use of the *Chi*-square (other than random selection of the sample) is that the expected frequencies are not very small. The reason is that the *Chi*-square inherently tests the underlying probabilities in each cell; and when the expected cell frequencies fall, for example, below 5, those probabilities cannot be estimated with sufficient precision. The approximation of the *Chi*-square statistic in small 2 x 2 tables can be improved by reducing the absolute value of differences between expected and observed frequencies by 0.5 before squaring (Yates' correction). This correction, which makes the estimation more conservative, is usually applied when the table contains only small observed frequencies, so that some expected frequencies become less than 10. In these cases was used formula for Yates correction. All these actions carry into effect automatically with the help of constructed conditional statement.

On the final stage the value of the calculated *Chi*-square should be compared with the critical estimation which is derived by build-in statistical function of LibreOffice Calc.

The obtained result demonstrated good agreement with conclusion which was obtained by professional statistical programs.

# PROGRAM OF STATISTICAL ESTIMATION OF PROCESSES, DETERMINED PLENTY OF OBJECTIVE FACTORS

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In many fields, including medicine, cosmetics, pharmaceuticals, sports, have to carry out a qualitative comparison of a large number of different, unrelated, randomly distributed features. In some cases, the number of significant factors than a few dozen, which complicates the efficient conduct meaningful analysis. We have to reduce the number of factors, guided by certain hypotheses. At the same time can be lost important information. There are a large number of statistical computer applications, but they all have a common drawback. This is a versatility, which does not allow working quickly with large sets of numerical and logical values.

We have developed an effective method of statistical evaluation of the processes for a large number of qualitative features. Testing of the method carried out in the analysis of indicators of technical and tactical activities football players the basic composition of FC "Metalist" for the period from 2012 to 2014. It is necessary to statistically determine the effect of a set of special exercises on the technical and tactical activities of the main players of FC "Metalist". Game Football Club is part of 39 people. Statistical data processing was carried out using an original computer program recorded in the code FORTRAN'90. Processing includes the formation of statistical databases, calculating activity coefficients players, their average values, confidence intervals and testing statistical hypotheses about the equality of expectations. The activity coefficient player certain tactical and technical action is the number of active steps per unit time. The assumption of normal distribution of the activity coefficients tested separately.

The proposed method has allowed to quickly and accurately perform a statistical analysis of 42 criteria of 45 matches. The results obtained for the whole team of the FC "Metalist" as a whole, for players on the playing roles and individually for each player. Analysis of the results showed no linear correlation between the activity and the time of the experiment. The average value of the exact activity coefficients of the players FC "Metalist" for the period of the experiment was significantly ($p < 0.05$) increased by 32 – 39%. Activity coefficients of FC "Metalist" higher than average command of his rivals not less than 20%. The proposed program is suitable for statistical analysis of normally distributed random variables given large arrays experimental data in the pharmaceutical, cosmetics and medicine.

# STATISTICAL ANALYSIS OF VARIATIONS OF CARDIO- RHYTHM

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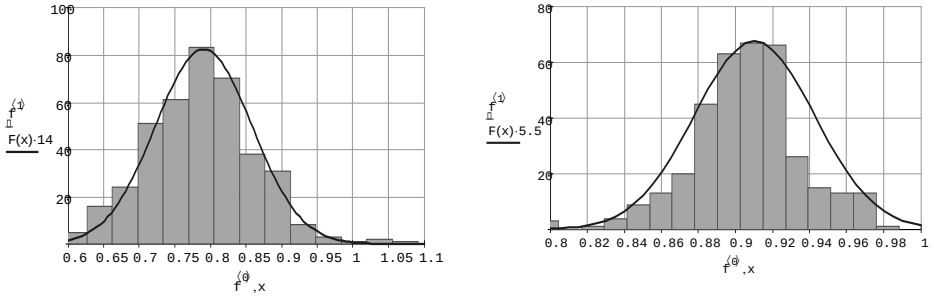
The heart-blood system executes an important role in an organism. It is necessary for his normal functioning. Diagnostics of functioning of this system occupies one of above all places in medicine. Development of computer technique allowed to made this diagnostics with the use of mathematical methods.

One of new methods of study of the state of the heart-blood system by the mathematical analysis is cardio-interval-method. It studies the change of rhythm of heart as reaction of organism on external influence. This method characterizes by simplicity of registration of signals – peaks of cardiograms or other signals, caused by operation of heart.

The sequence of cardio-intervals contains information about processes, flowing not only in a heart but also in the different links of the control system of organism: nervous interlacements, ductless glands, nerve-centers of brain.

There are a few time of measuring of signals of heart - 3 min., 5 min., 10 min., 1 hour and other intervals up to 1 days and a few days. At large time of analysis the changes of cardio-rhythm show up with a period from a few seconds to a few days are «slow waves» bearing important state information organism of the explored object.

The analysis of 5-min rows of information is conducted about the cardio-rhythm of two persons of different age. On the basis of the measured information some generalized parameters were calculated: frequency of pulse reductions, coefficient of variation, index of tension, is built and analyzed histogram of distributing of values of periods of pulse.




Histograms of distributing of periods of cardio-rhythm

# ANALYSIS OF AUTOMATIC CONTROL SYSTEMS IN HIGHER EDUCATION

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At the modern stage there was a discrepancy between operating control system by an educational process in higher educational establishments and the latest requirements for its functioning. In an inheritance from the Soviet system of education, Ukraine received the traditional means of document management at the university. And now, in many schools the documents reflecting the educational process, are formed and stored in the form of paper catalogs with different lists, maps, reports, records, and so on. The market of such systems is gradually formed, where both the commercial versions created by independent producers and systems worked out directly in institutions of higher learning are offered, where these facilities are exploited.

For today practically in every institution of higher learning automated information systems (AIS) operate with next functions: it is a management by the contingent of students; it is planning of educational process; it is an account of current progress and visited; it is a calculation of grant; it is forming of time-table; it is electronic circulation of documents.

Consider some of them.

Program complex "Automated system management institution" (http://mkr.org.ua/) is a set of related programs. It includes modules operating in an environment windows (training module, the dean's office, the applicant, methodical department, human resources, etc.), as well as web portal (mapping class schedules, performance, curricula, charging for a hostel, control Tuition fees and hostel testing of students, recording students to study subjects, etc.

The complex is embedded in many universities, particularly in the National University of Pharmacy, the National Law University et al.

System "Sail schools" (www.parus.ua/ru/263/469/) allows accounting students (form of training, the availability of student contract, budget form, the number of records in the context of faculties, departments, specialties, courses, groups, student enrollment, analysis of quantitative and qualitative data on students). The system also provides the control students (monitoring of attendance and organization of

admission to the territory of the university dormitories, libraries, automatic registration of entry, exit, movement of students, time management gaps).

The Ministry of Education recommends for implementation in universities software "Automated system of" Higher education institution ", developed by the Research Institute for Applied Information Technology (www.ndipit.com.ua/ru/rozrobky/asu-vnz/). The system includes speakers "Admissions Committee" AS "Dean" and AS "Campus". Automated control system of the educational process is designed to automate the activities of personnel training department, deans, chairs and management of higher education. The system consists of a central database, and two automated systems, "Calculation of the load of teachers" and "Scheduling classes." The system is designed taking into account the characteristics of the organization of training in the light of the Bologna process.

Software PE "Politek SOFT" (www.politek-soft.kiev.ua/ru/) is intended for educational institutions of Ukraine from I to IV accreditation levels, covers almost all aspects of their activities, registered in the Register of producers and distributors of software has a newsletter from the Ministry of Education and Science, Youth and Sports of Ukraine on the application in higher educational institutions of Ukraine.

The package is built for a client-server technology that allows you to install it on multiple computers that are connected to a local network and work with a single database. The use of additional Web-scripting allows access to a database of individual programs packages from the World Wide Web Internet. As a server, database management using FireBird.

The package has a convenient report builder that lets you create and edit existing accounting documents using HTML - Hypertext Markup Language. Accounting documents, which generates a packet can be viewed before printing programs in MS Word, MS Excel, Internet browser, and further edit according to user preferences.

All of these ACS characterized the relatively high cost, because they require the upgrading of existing systems for a particular university.

IP personal development, tend to be less stable, more dependent on their personal support developers worse documented. However, the systems developed directly in higher education, it corresponds exactly to the specific conditions and requirements quickly and flexibly responds to changes in legislation and the general economic situation, and they are more convenient for use by persons of certain specific educational institution.

# COMPARATIVE ANALYSIS OF PRODUCTION TECHNOLOGY OF BEER IN UKRAINE

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In earlier times, the brewing process was quite different from the present. Brewery housed in small buildings, mash cooked in cast iron or iron boilers, fermented in wooden vats and kept beer in oak barrels. Malt do so: grain soaked in a river or lake water, then germinated for several days, spreading a thin layer under a canopy, dried in the sun, clean, milled on hand mill. To improve the taste and aroma of beer used pine tar, ash pear, sage, benedict root. To give the young beer taste of old, it put peel oranges. To correct a wrong taste sour beer brewed and used grated dry hop beech and ash.

Modern technology of beer production includes the following main steps: get the malt from barley, cooking of mash, fermentation, maturation of beer, processing and bottling. This is a long complicated process, which lasts for 60-100 days and depends largely on the skills of the Brewer.

In this work the comparison of most popular brands of Ukrainian beer in our country and their production technologies, chemical analysis. With these brands of beer were conducted a few experiments, such as laboratory analysis of beer, the comparison between the various types of beer to taste and smell, comparison of production technology. They held the research staff of the various commercial and economic institutions of higher education of our country and rendered its verdict. The tasting was done by ordinary people, who talked about the technology of each brand of the drink. The tasting also chose the winner. Another experiment was conducted, it was the physical-chemical and biological analysis, which takes into account the organoleptic indicators, the appearance, taste and smell, the safety of the product (alcohol content of different chemical substances),

On the basis of the obtained experimental data built tables, charts and graphs to illustrate data. Comparison of various characteristics was made. As a result of all the work, after comparing all the data found on the quality of different brands of beer, advantages and disadvantages.

# THE MODEL OF THE KINETIC PROCESS AT SMALL ELIMINATION VALUE

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The environment is an important factor that determines the condition of the human body. Besides positive affecting factors, there are few other factors, that can affect in a negative way. One of such factors is an appearing inside human body of substances and other agents that can cause different negative effects and can lead to the human death. The factor that determines the condition of the human health is an injection of different agents into blood circulatory system, which can later leads to the negative consequences. To that kind of agents we can include different poisonous, narcotic, alcoholic and other substances, that can lead to the disruption of the functional activity of different organs of the human body, and eventually can result in a death of the person.

We decided to investigate the model of the biophysical kinetic process, that occurs in a human body in a moment of injection of the fixed volume of a specific dose of a biologically active substance according to the exponential law and achieving equilibrium concentration in a given volume, which contained in an volume that increases with time, until the establishment point of the equilibrium concentration in the whole blood volume.

In this article, we have used two-part model to analyze the dynamics of the dispensation. This model can also be used in a magnetic resonance imaging in the calculation process of the required amount of contrast agent injected into the circulatory system of humans. This model can also be applied in the case of blood loss resulting from injuries, which require restoration of the normal blood volume using injection of the saline solution.

Eventually, we have considered the dynamics of change in the concentrations of substance in the blood at the different ratios of the coefficients for the injection and dispensation for fast speed processes, when value of the coefficient of the elimination can be ignored.

# TRENDS IN THE USE OF SOFTWARE PRODUCTS IN THE LEARNING PROCESS.

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Students of the departments of economics in the process of learning and in the subsequent work are faced with the problems related to the processing of big data volumes and to the complex calculations, thus they must possess the practical skills of mathematical modeling in economics. Therefore study process requires special software that allows automation of the process of modeling. In addition, special software can help to increase students' engagement, improve the quality of their independent work, as well as to enhance the training. Today there is a number of programs that support various statistical calculations .

Currently, the following software solutions are used during the study of econometrics: spreadsheets (Excel); mathematical framework MathCAD; general purpose statistical software, that contains a wide range of statistical methods (Statistica, SPSS); specialized software designed to solve econometric problems (EViews, Stata); projects focused on programming (Project R et al.).

Let’s briefly describe each solution.

Excel is widely used due to its simplicity and relatively low cost. It allows you to research correlations and to build forecasts. Furthermore, this software can import data from various sources speeding up data entry. The main disadvantages of this software are: the difficulties in dealing with very large data sets, as well as difficulties during implementation of complex algorithms. This software doesn’t support simultaneous access to the same file; it also doesn’t have any flexible mechanisms to restrict access to the data, whereas in practice, some data should have a limited access.

MathCAD is mathematically oriented programming language designed for building algorithms that solve mathematical, scientific and technical problems in the most convenient, compact and easy to understand way. The system has a lot of options to perform the most common symbolic calculations and transformations. It has a wide range of instrumental, graphical and analytical tools. It has powerful mathematical capabilities that allow problem solving without having to call external procedures. On of the program features is support and ability to choose between various unit systems: SI, CGS, MKS, English, it also allows you to create your own. The results of calculations, of course, also receive the proper dimension and unit system. Benefit of this feature cannot be overestimated, since it allows to track errors in the calculations.

STATISTICA and SPSS is a spreadsheet with the menu system, designed to work with spatial data and time series, that provides automatic reporting of the

simulation results. SPSS program focuses on applied research in the social sciences, and, as a consequence, the lack of modern methods and models of advanced econometrics distinguish it. A lot of books, that explain how to use the package, are written and published. A basic set of popular statistical methods of analysis is implemented. Developers of software products offer a single-user and multi-user licenses for educational activities. The abundance of options and settings complicates the development packages.

Eviews and Stata are commercial software, developed for economists in 1994 and in 1985 respectively. The program provides the possibility of programming any sequence of commands. Software packages contain complete data sets to demonstrate and study their features. Developers on their own sites offer multiple licenses of their software (from student to professional). Both packages provide numerous opportunities for the analysis of time series and panel data. One of the benefits of these programs is the availability of low-cost student version. The drawbacks are: limited number of books that explain how to work with the package.

Project R: R is a programming language and software environment that is used to perform statistical calculations and construction of graphical objects. R is open source software that is freely distributed under GNU license. GNU license agreement gives you a right to make a free copy, modify, and distribute the code. The main ideas of R CRAN (Comprehensive R Archive Network, http://cran.r-project.org) system are constant expansion, collective testing and prompt distribution of applied data processing tools.

The software contains a large set of statistical functions, and also has built-in help and tips. R language provides the user with almost unlimited possibilities for data visualization. Since R is widely used by professional statisticians, the most recent developments of statistical science are rapidly becoming available to users worldwide R in the form of additional libraries. These libraries (there are already several thousand) can be freely downloaded from the project website, or from the author's websites. Programming language R is the most powerful free software tool with an incredibly wide range of libraries. No commercial system of statistical analysis is developing as fast as today R.

R is widely used by the analysts from the largest IT and finance companies, leading universities and research centers. Thus, it can be sated that the skills of R-programming provide an additional competitive advantage in employment.

Project-oriented programming language R and its only English based syntax are making R difficult to study. However R has many advantages compared with other software. Unlike commercial statistical software license costs, which can be several thousand dollars, R is distributed free of charge.

Can be considered appropriate to use in the classroom some tools software environment R, which is now the de facto standard for statistical computing.

# MATHEMATICAL MODELLING IN PHARMACOKINETICS

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Mathematical modeling is the main methodical approach in pharmacokinetics. It is the processes of absorption, distribution, metabolism and excretion of medicinal substance in the organism. According to data about the concentration of a preparation in biological tests, through certain intervals of time, the curve concentration–time is constructed. The curve mathematically described by one or another way. To summarize, the pharmacokinetics possesses are difficult mathematical apparatus that used for the solving the systems of the differential equations that also may including the nonlinear equations.

Linear chambers are the most widespread models in the clinical explorations. Recoiling to it, the organism is represented the number set of homogeneous cameras (in our report it is three most widespread in clinical trials (Fig.1): tissue – the place of injection, blood and body), that are different in the extent of medicinal substance that is penetrated into them. Moreover, preparation can pass from one camera into another. Though the pharmacokinetics of many pharmaceuticals are corresponds to characteristics of two–chamber open distribution model, sometimes, for interpretation, it is better to use more difficult models. According to characteristics of three – chambered model, the process of decrease in the serum concentration of many opioids, muscle relaxant and anesthetics are better when the preparation comes to the central camera and eliminated from it interpreted.

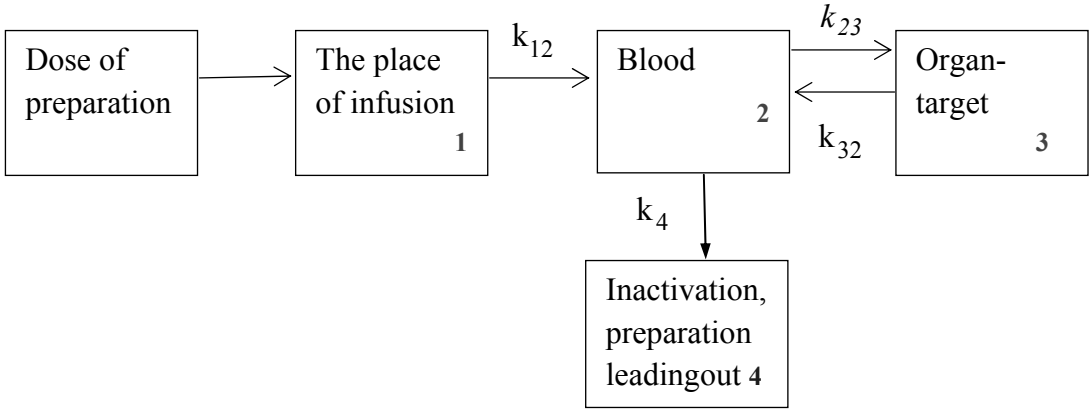


Fig.1. Three – chambered pharmacokinetic model

A double – chambered model was got in many works. The aim of this work is the three – chambered mathematical model.

The system of differential equalizations, describing the indicated process, is below given.

$$\begin{cases} \frac{dC_1}{dt} = -k_{12}C_1 \\ \frac{dC_2}{dt} = k_{12}C_1 + k_{32}C_3 - (k_4 + k_{23}) \cdot C_2 . \\ \frac{dC_3}{dt} = k_{23}C_2 - k_{32}C_3 \end{cases}$$

The decision of the system of differential equalizations looks like:

$$C_1 = C_0 \cdot exp(-k_{12} \cdot t);$$

where $C_1$ – the concentration of preparation in the chamber number 1; $C_0$ – initial concentration of preparation.

$$C_2 = \frac{k_{12}C_1 + k_{32}C_3}{k_{23} + k_4};$$

where $C_2$ – the concentration of preparation in the chamber number 2; $C_3$ – the concentration of preparation in the chamber number 3:

$$C_3 = C_0 \frac{k_{12}k_{23}}{k_{32}k_4 - k_{12}(k_{23} + k_4)} \cdot exp(-k_{12}t) - exp(-\frac{k_{32}k_4}{k_{23} + k_4}t).$$

CONCLUSIONS

The three – chambered model as a system of differential equalizations, describing the pharmacokinetic processes in work has been built. The analytical decision of the system of differential equalizations has been created.

# SYSTEM ASPECTS OF CHANGES PROOXIDANT-ANTIOXIDANT SYSTEM AT THE ACTION OF EXTREME FACTORS ON THE BODY

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It is known that the impact of extreme factors (the action of ionizing radiation) on the body causes changes in the functioning of bioantioxidants (BAO), which is closely associated with changes of lipid peroxidation (LPO). Changes in the nature and functioning of the LPO BAO have distinct features of the system response of the organism. The literature describes the systemic aspects related to changes in the values of total antioxidant activity of the organism (AOA) and its individual components. Patterns of the regulation of these processes at different levels of the organization have not yet fully opened.In this connection for the problem in question are extremely important aspects of the most common systemic determinant of prooxidant-antioxidant homeostasis processes maintain a dynamic equilibrium. Purely practical, it is connected, in particular, with not sufficiently informative to estimation the nature of the processes according to the values of individual parameters measured at the particular time.

Research methods included: building a multi-agent model (heuristic conceptual modeling), carrying out with the help of this model, numerical experiments (phase portraits) and a comparison of their results with the results of statistical processing of real material. This approach seems to be perspective for the development of methods for rapid assessment of the extent of damage under the action of radiation.

Numerical experiments of adaptive mechanisms of biosystems were conducted using the heuristic conceptual modeling allowed to find the relationship between the close connection of the system parameters of lipid peroxidation and antioxidant system, its efficiency and reliability. The relevant working hypothesis was formulated and was tested on experimental data: smaller (compared to tocopherol) stability with radiation exposure on rats compared with the control should be observed of the total antioxidant activity. If radiation exposure is carried out in conjunction with the intake of antioxidants - wheat germ oil, this aspect of the difference between the experiment and the control will be much less pronounced.

# MODELING OF CHEMICAL REACTIONS USING FREE MATHEMATICAL PACKAGE SCILAB

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The study and modeling of chemical reactions is actual problem for modern chemistry. They allow to accelerate and optimize the procedure of creating of new preparations and prevent transformations of medicine compounds that lead to lose of consume or commercial characteristics. The investigation of the processes and application of the obtained results in medicine and agriculture allow to deal with the diseases and prevent the growing old of organism.

For analysis of obtained results one need the mathematical techniques and tools. Here the mathematical packages which are able to solve the systems of differential equations can be brought to the fore.

Modeling of chemical reactions is considered in this work. The problem of modeling is reduced to the system of differential equations relatively concentration of the reagents and reaction products. Different types of reactions are considered here: simple isothermal reversible reaction, complex parallel and consecutive isothermal reactions, isothermal reversible reactions of the second kind and non-isothermal reaction.

To solve the differential equations we use freeware mathematical package Scilab. The dependences of the substance concentration and its temperature (in the case of non-isothermal reaction) vs. time for every reaction are plotted.

Modeling of chemical reactions is conducted, solution of systems of differential equations to which these reactions are reduced is performed, the numerical results are presented and their comparison with results obtained in the commercial package Mathcad is made in this report. We can make a conclusion that the freeware package Scilab abilities to solve of systems of differential equations are not inferior to commercial package therefore it can be successfully used for modeling of chemical processes. The package also includes a great number of tools for editing of the displayed plots and it has considerable advantage, namely, it is freeware.

# MATHEMATICAL ANALYSIS OF SFYGMOGRAMMY

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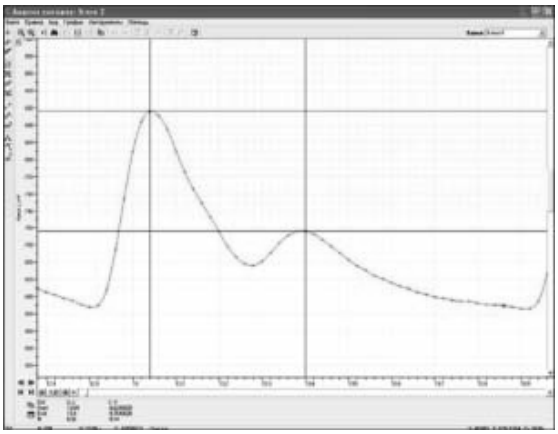
**Sfygmografy** is the method of graphic registration of pulses oscillations, which is allowing to judge about their resiliently-viscid properties. Sfygmogramm registers by the sensors, which set on the areas of body with the distinctly expressed pulsation of arteries. The data allow to judge about atherosclerosis of certain areas of vessels, hypertensive illness and row other pathological processes which elasticity of vessels is violated.

The basic systole wave of sfygmogramm (see a picture) is begun with the steep getting up - anakroty, blood conditioned by the rapid receipt from a left ventricle in an aorta in the period of banishment. The top of systole wave corresponds to the moment of achievement of maximal pressure in an aorta. After it there is the smooth decline of basic systole wave (katakrota), which at the end of phase of banishment passes in inzisury (minimum on the graph). The lowest point of inzisury corresponds to the moment of closing of valve of aorta.

The analysis includes the temporal analysis of separate elements of sfygmogramm and description of form of curve which is very characteristic at some diseases.



Parameters of sfygmogramm are:

1. Index of augmenters.
2. Index of reflection.
3. Sharpness of pulse wave.
4. Indexes of peripheral resistance.
5. Relative size of dykroty wave.

There were made the temporal analysis of a few sfygmogramm.

# THE VIRTUAL LABWORK ON PHARMACOKINETIC

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UNESCO has declared the two basic principles of the modern education: "Education is for everyone" and "Education is lasting during life." However, the traditional forms of education are not able to provide a high quality of these principles. This is dictated by the emergence of new forms, such as a distance learning form. For distance learning there is an issue of acquisition of practical skills of learners. Their receipts during preparation for any laboratory work. Are an integral part of the traditional educational process. Is there an alternative? It's no a secret that technological progress has changed dramatically the skills needed for scientific researcher . In the first place there are the skills of planning an experiment based on the technical equipment. In addition, many objects of experiments may be a considerable distance from the researcher. The Means of communication are, more than ever, significant in the modern science and industry. All this factors lead to the possibility and necessity of the use of the virtual labs in the learning process for all forms of learning.

Based on the pharmacokinetic model with subchambers we have developed a virtual laboratory work on pharmacokinetics. Many different factors, such as sex, weight, age, and the water balance of the patient and the random factors have been taken into account. The program is equipped with a user-friendly interface. The object of the research is the process of absorption and excretion of substances from the human body. Modeled by a one-time intramuscular injection. The concentration of the studied substance is monitored in plasma and urine. Researchers need to find the coefficients of absorption and elimination, the maximum concentration of a substance in the blood, the appropriate time and half-life for each patient. According to the results of tests of several patients need to find confidence intervals and make a final conclusion. The accuracy of control of finding numerical values is automated. According to the results of the virtual lab, the program generates a result file that is sent to the teacher. The algorithm of the virtual laboratory work is implemented in C++ code.

# THE FEATURES OF LASER HAIR REMOVAL

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The goal of the report is to present the main statements of the implementation laser technologies for solving cosmetic problems.

The knowledge of the structure and features of physiology of the skin, its biophysical characteristics, mechanisms of interaction laser radiation with biological tissues requires for establishment and improvement the laser technology for solving cosmetic problems. Also for such problems as rationale choice of parameters the laser beam and the methodology of the procedure. The removal of unwanted hair is a problem that worries both women and men. In cosmetology it is used two approaches, which are defined as:

- the depilation - removal of the hair shaft, located above the surface of the skin (shaving, chemical depilation, creams, ointments, waxes et al.);
- the epilation - removing hair from the root part, at which the damage of the follicular unit, which creates the final odds for hair growth ceases.

Laser hair removal is a method of removing unwanted hair using laser radiation. Compared with other methods of laser hair removal it is more effective, less painful, and one of the most popular technologies. The effect of laser hair removal is prolonged, that is, hair growth continues to be violated, and their number decreases after completion of epilation.

The mechanism is poorly understood, but it had discussed several options for the development process, such as:

- Thermal effect causes the coagulation of the blood vessels that feed the hair follicle. It leads to gradual atrophy of the follicle and stop hair growth;
- Thermal effect starts the process of programmed death in the cells of the follicular epithelium, which leads to atrophy of the follicle;
- There is a violation of the regulation of the phase of hair growth due to the violation of interactions between growth follicle cells.

Side effects of laser hair removal are possible persistent disorders of pigmentation, peeling, itching, erythema, swelling, blisters, pain factor, and in rare

cases - the scars as a result of severe burns.

To achieve the desired results and reduce the side effects requires an understanding of biophysical processes and informed choice of the radiation parameters, taking into account the individual characteristics of the skin.

More reasonable theoretical basis of the method of laser hair removal is considered to be the effect of selective photothermolysis.

The selective photothermolysis (selective laser coagulation) method of heating the tissue when exposed fotodekstruktsii piece of cloth containing a specific chromophore without thermal damage to the rest of the biological tissue in which the chromophore is absent or present in smaller quantities. The principle of selective photothermolysis has been proposed in 1983 by Anderson and Parrish and consisted of using a special thermal effect of the light energy with the wavelength which has the maximum difference in the absorption of the target and the surrounding tissue.

In the method of laser hair removal is considered to be selective chromophore melanin, and the choice of parameters of the radiation is determined by:

- The depth of hair follicles on the surface of the body;
- The coefficients of absorption and scattering of the laser beam, which determine the depth of its penetration;
- Thermal relaxation time of the epidermis and follicular structures, as necessary rate matching the ebb and flow of heat in the hair and the surrounding soft tissues;
- The rating zones biostimulation and destruction;
- The dependence of the effect of laser radiation on the hair follicle from the stage of the physiological condition of the hair.

With all the features of the structure and biophysical characteristics of fabrics when choosing the parameters of the laser radiation it is necessary to consider the following options:

- the wavelength;
- energy characteristics;
- pulse duration.

The report discusses the conditions for achieving the maximum positive result given laser hair removal skin type (according to table Fitzpatrick skin type definition) and the hair growth cycle.

# TO THE IMPLEMENTATION OF DISTANCE LEARNING

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Modern postgraduate education for pharmacy specialists should be carried out throughout the work, it is necessary for the continuous expansion and deepening knowledge and improvement of professional skills. So we can confidently say that stages of postgraduate education of modern specialists of practical pharmacy should be replaced by a permanent training activities aimed at improving and learning specialist, that providing reorientation from supplying knowledge on the formation of competencies.

Distance learning is a new technology in education, based on the principle of self-study and expressed in a meaningful process of interactive communication of educators and trainees through informational and communication technologies that direct and provide trainees with necessary amount of educational material. This form of training enables continuous training on the job, it is democratic and accessible to all social groups and it is also economically feasible.

Based on the foregoing, we decided to install modern real possibilities of training courses (TC) of pharmacy specialists on the application of distance learning.

To achieve this goal we used the following methods: observation, interview, a questionnaire to analyze and summarize the experimental results, and to state the research. Trainees of TC have different social, physical, intellectual, geographical, technical capabilities, and they were offered to conduct questionnaire to study them which is necessary for the future TC courses in distance learning.

The research was conducted during 2014 among trainees of TC of specialists on-site pharmacy department cycles in four cities of Ukraine.

To explore the possibilities of distance learning trainees were offered a presentation of the distance course "General pharmaceutical aspects of modern pharmaceutical science and practice" with further answers to questions and conducting questionnaire.

The questionnaire was developed by the staff of the department and contained general information about respondent (age, seniority, position) and eleven targeted questions. The questionnaire was attended by 220 trainees of TC.

According to the questionnaire it was revealed that 34 % of the respondents do not have access to computer use for their own purposes, 20 % are unable to use Internet resources.

According to the preliminary calculations the term of studying at the computer courses increases about twice, but it makes it possible to improve the content of education, improve self-study, activity and creative potential of trainees and that is also important in modern conditions – it is an opportunity to take TC on the job.

However, analysis of the results of the questionnaire showed that it is necessary to give trainees a choice of using traditional or modern distance learning because 34 % of pharmacy specialists today do not have technical capabilities.

# SECTION № 16

# COMMODITY SCIENCE

# COMMODITY CHARACTERISTICS OF PREFILLED SYRINGES

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Experts in the field of medicine and public health in the whole world realize valuable advantages of prefilled syringes which occupy 25 % of total market of systems for injection administration of medicinal products and thus shows the highest rates of their growth. Prefilled syringes (PFS) are used more and more often as initial containers for most of high-quality injection medicinal products due to their advantages comparatively with traditional package types. Anticoagulants, antiviral, antianaphylactic agents, preparations used to treat disorders of hemopoiesis, monoclonal antibodies and also vaccines are attributed to therapeutic groups used most often in prefilled syringes.

Depending on material of which prefilled syringes are made they can be glass or plastic. In scales of the global market part of glass ones takes 95 % expressed in money units and a little bit greater – in natural expression.

Glass always was preferable material for manufacturing of all kinds of syringes. However, in these syringes a drug contacts with various kinds of materials: glass, needle, needle glue, protective needle cap, piston. To solve this problem many manufacturers have developed high-grade glass syringes syriQ InJentle in which a preparation contacts only with glass and rubber as well as during storage in vials.

Plastic prefilled syringes are on stage of elaboration. Constant development of manufacturing technologies of polymers has resulted in creation of plastics with better parameters of lixiviation and extractability in comparison with glass products.

Only three components of polymeric prefilled syringe SECUREJECT are in direct contact with a product (a drug / vaccine / liquid): body and head of a syringe (made of medicinal inert polymer), piston (preliminary sterilized, made of compatible material) and preliminary sterilized needle of stainless steel AISI 316L. Both parts of a syringe (needle from below and rod) are tightly closed with plastic capsules during molding process. This protects a syringe from contamination and casual pressing.

Prefilled syringes SECUREJECT are very convenient in use for daily injections of drugs carried out by nurses and doctors, and also for providing injections of solutions of lyophilized powders, because after dissolution of a preparation it can be soaked back into a syringe and it’s possible to make an injection with the same needle (without additional syringe). Being ready to use and requiring only removing of a cap, they can become very convenient during large-scale safe vaccination.

# APPROACHES TO STANDARDIZATION OF LABELING FOR PRESCRIPTION DRUGS ABROAD

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Today necessity for standardization of prescription drug labeling is still an actual problem in the whole world and, in particular, in the USA. According to reports of Food and Drug Administration (FDA) there are two main reasons for such a problem: the first one is inadequate patient understanding of prescription dosing instructions and warnings, the second one is lack of universal standards and regulations for medication labeling which leads to variability in labels on packages with prescription drugs.

The aim of our study was to highlight trends and approaches in standardization of labeling of prescription drugs abroad.

Now for such medications the FDA requires that certain information appear on the drug container label: drug name, pharmacy name and address, serial/lot number of the prescription, prescribing physician name, patient name, and instructions for use. Beyond the FDA requirements, state boards of pharmacy are responsible for establishing further standards. In response to such regulations, national pharmacy chains in the USA have developed 31 different label styles, resulting in variability in the clarity and complexity of medication use instructions.

The existing evidence base for label standards supports the following practices: use explicit text to describe dosage and interval in instructions; use a recognizable visual aid to convey dosage and use instructions; simplify language, avoiding unfamiliar words and medical jargon; when possible, include indication for use; include distinguishable front and back sides to the label; organize the label in a patient-centered manner; improve typography – use larger, sans serif font; when applicable, use numeric instead of alphabetic characters; use typographic cues (bolding and highlighting) for patient content only; use horizontal text only; use a standard icon system for signaling and organizing.

Beyond the content and format, one of the most important things on the prescription drug label is the “signal line” or dosage instruction. This information also causes the most difficulties. It is the information that patients are looking for, yet there are high levels of variability in how such information is presented.

Thus, elaboration of uniform, standard and substantiated design of labeling easily perceived by patient and pharmacist still remains the live issue in the world.

# INSPECTION ANALYSIS OF PHARMACEUTICAL GOODS OF A SMALL RANGE

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Today, range of goods, which are realized in pharmacies, is quite diverse. By order of the Ministry of Health of Ukraine № 498 "On approval of accounting of goods that are entitled to buy and sell by pharmacies and their subdivisions" from 06.07.2012 year, a new list of products that are entitled to buy and sell by pharmacies and their subdivisions was approved.

The new list of goods according to the order number 498, compared to its predecessor (the order of the Ministry of Health of Ukraine of 26.11.2004 № 577) is more detailed and contains the following items:

- medical devices (including optics), medical equipment;
- items and personal care products (products for oral care, skin, hair, shaving and after shaving, toilet soap, shampoo, sanitary napkins);
- natural and artificial mineral water, drinking water canteen;
- cosmetic products (creams, salts, lotions, scrubs and other means of operating hygienic, prophylactic and aesthetic functions) except perfume and make-up;
- functional foods, foods for special dietary consumption (including baby food, nutrition for athletes and the elderly), dietary supplements, drinks, not related to dietary / food for babies;
- repellents (including electrical devices for use with removable cartridges repellents);
- disinfectants;
- devices for the control and regulation of climate protection (ionizers and humidifiers, thermometers);
- devices for purification of drinking water and replacement filter cartridges to them;
- objects for babies care, which are not registered as medical products;
- books on medicine, pharmacy and a healthy lifestyle;
- special clothing for workers of Medicine and Pharmacy;
- supplies for persons with disabilities.

For today in drug stores a wide range of parapharmaceutical goods is presented, in particular cosmetics of therapeutic and prophylactic action, of various production (France, Germany, Italy and others), of different price category, for various cosmetic problems. In recent years all over the world topic of a healthy lifestyle is urgent, so in many European countries medical-prophylactic cosmetics is on equal basis with drugs, namely dermatological profile.

We are particularly interested in paragraph in the list about cosmetics, namely, creams, lotions and other means of performing hygiene, preventive and aesthetic functions. At this point, according to the current order number 498 is present amendment that the pharmacy can only carry out the implementation of preventive and curative cosmetics except perfumes and cosmetics.

After analyzing the range of cosmetics in pharmacies in Kharkov, it was found that pharmacies are being implemented cosmetics of different forms such as creams («Face Cream VICHY lift-aktiv fleksi-lift wrinkle», tonal tone number 25, 30 ml; «Face Cream FILORGA BB perfect», tonal tone number 02, 30 ml; Face Cream «VICHY AeraTonPyur tone fluid for normal and combined skin», tonal tone number 35, 30 ml; «Face Cream LaRoche», tonal tone number 13, beige and sand, 30 ml); gel-creams («Gel-Cream LIERAC Hydra Chrono Plus», tonal tone sand, 30 ml); powder («Powder Face LaRoche» Toleran mineral tone 11, 9.5 g; "Powder compact VICHY tone ideal" tone light, 10 ml); mousses («Mousse LaRoche Toleran face», delustering tone number 02, 30 ml; LaRoche toleran tone delustering tonal mousse 02 SPF 20, 30 ml); emulsion («Emulsion face LIERAC» tonal sand 30 ml).

Based on data from the list of ingredients of cosmetics, it has been found that among them, there is a coloring pigment which is used only in decorative cosmetics. Based on this we can conclude that cosmetic products listed above do not belong to a group of health-care facilities, and are directly related to decorative cosmetics, which contradicts the list of goods according to the order № 498.

Also among the items presented in the pharmacies it were colognes of different manufacturers, that is also contrary to the established list according to the order number 498.

Based on the inspection analysis of pharmaceutical products of a small range, we made recommendations for the pharmacies about goods which are realized there and belong to the list according to the current order number 498.

# RESEARCH OF SENSITIVITY INDEX IN PREGNANCY TESTS

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To diagnose pregnancy means to establish the fact of pregnancy and its term.Timely and accurate diagnosis of pregnancy and definition of its term are needed to prevent complications, premature birth and prolongation. In addition, early diagnosis of pregnancy allows eliminating of harmful conditions in the first weeks of pregnancy, performing specific recommendations for its preservation, eliminating harmful factors influence, appropriate correction of life plans, diet, work, sexual activity and other aspects.

The aim of our work was to study pregnancy tests on the pharmaceutical market of Ukraine in terms of sensitivity and detection of tests with the highest performance.

Pregnancy Test is a quick qualitative immunochromatographic test for human chorionic gonadotropin (hCG) in urine specimens for early detection of pregnancy.Human chorionic gonadotropin is a glycoprotein hormone produced in the early stages of pregnancy. Analysis of literature has shown that in normal pregnancy hCG is detected in urine and serum soon after conception and reaches the level of 5-50 mIU / ml during the first week of pregnancy. The test is designed for use in hospitals or at home.

During the work we have analyzed the market of pregnancy tests by the sensitivity index, which is one of the factors in the selection.

When analyzing the range, it was found that there are tests with different sensitivity: 30, 25, 20 and 10 mIU / ml.The least sensitive are simple strips, and the most susceptible are Jet tests. The dependence between test sensitivity and gestation term at which it can be used has also been determined . Thus, tests with a sensitivity of 10 mIU / ml allow pregnancy indication on the 7th day after fertilization, the ones with sensitivity of 20 mIU / ml - on the 7-10th day after fertilization.And only the tests that have sensitivity index of 25 mIU / ml can be used from the 1st day of delay.

After analyzing the pharmaceutical market of Ukraine, we have found that the highest sensitivity possess "Clearblue" and "Lady's test" tests , which can be used from the 1st day of delay.

Consequently, the sensitivity index is one of the factors when choosing a pregnancy test.Study of sensitivity index has allowed us to identify tests that possess the highest values, which allows to diagnose pregnancy from the first day of delay.

# COMMODITY ANALYSIS OF SINUFORTE AND DETERMINATION OF PROSPECTIVENESS OF ITS USE IN MODERN ANTRITIS PHARMACOTHERAPY

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During the massive increase in acute respiratory infections, influenza epidemics, the number of patients with antritis increases many times. Choice of treatment method is often of great difficulty for an otolaryngologist. Not so long ago on the Ukrainian pharmaceutical market Sinuforte preparationhas appeared, which comprises natural ingredients including juice of cyclamen tubers , which has a long history of use.

Therefore, the purpose of our study was to investigate consumer properties of Sinuforte drug, to hold commodity analysis of this drug and establishing the feasibility and prospectiveness of using it to treat antritis and prolonged rhinitis .

Sinuforte is a lyophilized powder in the ratio 1: 1 of water / ethanol extract of Cyclamen europaeum tubers .This structure enables the production of solutions of various concentrations and is the major advantage in the use of cyclamen drugs in the treatment of rhinosinusitis , allowing to use individual approach in dosage.Acting intranasally, the drug activates normal physiological processes for cleaning nasal mucosa and has a constructive effect on the mucous membrane and festers that accumulate in the nasal cavity and paranasal sinuses.

Dosage form of spray is the most optimal form of release for the treatment of the upper respiratory paths diseases. Nozzle dispenser sprays fixed amount of drug which prevents the possibility of overdose and side effects development.The drug Sinuforte is produced according to the GMP standards, under sterile conditions, which enables bacteriological loading avoidance .Thanks to freeze-drying of the juice is excluded need of using preservatives and stabilizers in the manufacture of the drug.The drug composition enables production of solutions of various concentrations, allowing to use individual approach in dosage. The mechanism of action of the drug is associated with activation of natural physiological processes of nasal mucosa cleaning. High clinical efficacy and safety have been proven by numerous clinical studies in advanced ENT clinics in more than 15 countries of the world.

Thus, as the result of the consumer properties of Sinuforte study, commodity analysis of the drug, the prospectiveness of its use in modern pharmacotherapy of antritis has been determined.

# GOOD STORAGE PRACTICES AS A MAIN FACTOR OF RETENTION OF DRUGS QUALITY

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Guarantee of drugs quality in terms of social significance is one of the most important tasks of the state in health sector. Currently, the most acute is the problem of falsification of medicines that affect the quality of drug maintenance of the population. But, even genuine and qualitative drugs under the influence of external conditions can come into disrepair, lose efficiency and become dangerous. In this regard, problem of drugs storage is actual.

Most drugs need special storage conditions associated with their physical and chemical properties, toxicological groups.

By international and particularly European requirements principles GSP, together with the principles of GMP and GDP, and must observe the manufacturers and distributors of medicines and pharmacy.

Since 2011, Ukraine has been is a member of PIC / S - Pharmaceutical Inspection Cooperation System of the European Union and other developed countries. In this regard in Ukraine these standards are enacted as a mandatory requirement of licensing conditions for all operators of the pharmaceutical market.

Improper storage of drugs can trigger processes that lead to changes in their chemical composition and physical properties (sediment, discoloration, physical state). Thus drugs are inactivated, decompose and become unfit for use before the end of their shelf life. A wide range of medicines of modern pharmaceutical market (more than 14 thousand names) and a large number of normative documents, that regulate organization of drug storage, require systematization and comprehensive assessment.

Storage of medicines and materials must meet specified on the labeling information based on the results of stability tests and allow storage temperature and relative humidity.

Accordingly, it is necessary to describe methods of storage and movement of materials and medicines, and, if necessary, to provide information on the organization of actions relating to product recall .

So, introduction of requirements of “Good Storage Practices” into working of blighty manufacturers and distributors will ensure the quality of medicines throughout their "life cycle", it means to manage the storage of drugs in their manufacture, wholesale realisation (distribution) and retail sales.

# MODERN STATE IN MARKET OF CATHETERS IN UKRAINE

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Catheters were used by mankind since ancient times. Ancient Greek physicians used hollow metal tubes which were introduced through urethra into a bladder for its discharging. There is an opinion, that elaboration of the first catheter is attributed to Erasistratus (3rd century B.C.).

Catheter (Greece "katheteruri" – to lower down) is medical instrument in a form of tube, intended for discharging or introducing of liquids (e.g. medicinal products) and radiopaque substances into natural canals and cavities of a body, blood and lymphatic vessels, and also for withdrawing of contents with the diagnostic or medical purpose.

The objective of the given work is to study classification of catheters which are used in medicine now and also countries-manufacturers and firms which deliver these commodities to the domestic market of Ukraine.

One can distinguish the following kinds of catheters: soft (which are made of rubber or plasticized polyvinylchloride) and rigid ones (for example, made of metal).

It's possible to allocate two main groups of catheters: vascular and cavitary ones. To the latter one can attribute widely used urinary catheters intended for inserting into urethral canal with the purpose of bladder discharge when it's impossible in natural way. Vascular catheters include central and peripheral venous and arterial cannulas. They are intended for introducing of medicinal solutions into blood flow (or for withdrawing of blood for one or another purpose - for example, for detoxication) and inserted through skin.

There are about 504 trade names of products of this kind. The firms-manufacturers of catheters which are most claimed by consumers includes: Jiangsu SUYUN Medical Materials, Unomedical, Galmed, B. Braun, BD, Apexmed International, SURU International, ANIOS, Perouse Medical, Rusch, the Alphabet, 3M, Flexicare, Simurg, Unox, Minimed, Teleflex, Bard, Technocomplex, Kammed. By consumer demand and amount of production bought in Ukraine the sequence of countries-manufacturers is the following: Ukraine, China, Germany, Poland, Byelorussia, France, Russia, Great Britain, India, Italy, Netherlands, Slovakia, Egypt.

As it can be seen from the submitted list of countries, Ukraine takes important value for our consumers. Therefore potential for promotion of science and manufacturing technologies of catheters in our country constantly grows.

# TUBA – IS RATIONAL KIND OF PACKAGING FOR COSMETIC GOODS

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In today's world of cosmetics use various types of packaging, from exclusive and expensive bottles to convenient and practical tubes. Consumer in choosing of cosmetic product, in addition to cosmetic effect is also guided and convenience package. Analyzing the range of cosmetic goods on the market of Ukraine, we came to the conclusion that the leading place among the presented range of cosmetic packaging takes tuba. It is not surprising, because the tube reliably protects the product from the environment, it allows you to dispense the contents without any additional devices, tightly capped immediately after use, do not expose this product to microbial contamination, provides long-term storage.

There are three main types of aluminum tubes (metal); polymer; laminate (composite material - a combination of plastic and aluminum).

*Aluminum tube* - is not weld membrane in her neck is a physical part of the tube, and with repeated flexion (rolling) "tail" of the tube is obtained almost hermetically packaged product. Aluminum tubes have the highest barrier properties compared to other types of tubes. When deformation aluminum tubes will not be returned to its original state as a result of the air does not get inside the tube and the product is not subject to oxidation. Aluminium tubes are also widely used in the pharmaceutical industry. But also this type of tube has its drawbacks, namely low resistance to mechanical stress. When squeezing the contents of the tube, or at random mechanical deformation on the surface of the tube formed dents, spoiling the appearance of the tube. In the field of education dents decorative coating is destroyed and lost the appeal of the finished product.

*The polymer tube* - seamless, comfortable, practical, attractive packaging from soft polyethylene. Polymer tubes can be transparent and opaque, with lacquered glossy or matte finish. This depends on the specific content of the pigment in the material composition of the tube and the outer cover. Polymer tubes, due to the elasticity of the material is not deformed during use. After extrusion plastic tube sucks air and takes the original form. This "flexibility" is achieved due to the lack of permanent deformation of the material tube and is not always beneficial on the content of products. Indeed, with the air in the tube can penetrate bacterium. One drawback of this type of tubes - a low barrier properties, as well as the fact that it

easily penetrates through the plastic oxygen and water vapor. Therefore, the polymer tubes do not pack the products that require high barrier properties of the package.

*Laminate tube* - it is ergonomic, comfortable, universl and attractive outer packaging. On laminate tubes is necessarily present seam. Modern technologies allow to make the seam is very neat and almost invisible.

Today on the market there are two types of laminate tubes: - PBL (Plastic Barrier Layer - a plastic barrier layer), - ABL (Aluminium Barrier Layer - aluminum barrier layer).

Laminate tube with barrier layer PBL is a complex chemical compound based plastics. The protective properties of PBL - laminate significantly inferior to those of ABL, they cannot provide complete protection from the contents of the tube microbial contamination, the influence of sunlight, air and water penetration. Laminate tubes type of PBL used for packaging cosmetic products with a low content of active and special additives.

Laminate tube with barrier layer ABL is a thin (12 - 40 micro mm) aluminum foil. Between the outer and inner layers is a barrier layer of aluminum tubes. It effectively separates the product and the external environment of the product is not necessary to evaporate the substance in the tube with the product will not get harmful substances from the external environment. Thus, ABL tube becomes impossible oxidation, fermentation, chemical and physical changes of production. The outer layer of the composition of materials in the ABL - polyethylene. Because of this layer tube is pleasant to touch. Polyethylene can be painted in any color or made transparent. The outlet tube type of ABL sealed protective membrane. Then, the resulting tube screw cap (buschon).

Laminated tubes well keep their shape during transport and use. Therefore, laminated tubes are far ahead of aluminum tubes for visual appeal and plastic tubes for protective properties, and it is a strong advantage in the fight for the attention of buyers. Laminated Tubes have all the advantages of aluminum tubes, but at the same time provide ample opportunities for decorating the appearance and ease of use.

According to the results of research, it was found that the leader among Tubna packages is laminate tube with a layer of ABL. Summarizing the analysis of tube packaging the following conclusion: the highest level of protection provided with a layer of laminate tubes ABL. Laminated tubes with a layer of ABL recommended MoH Ukraine as packaging for products with high demands on storage conditions:

- for packing of medical and preventive goods;
- baby creams;
- effective cosmetic goods with a high content of active and special additives.

# MERCHANDISING ASPECTS OF DEVICES FOR MONITORING LEVELS OF BLOOD GLUCOSE

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It is known that diabetes is a serious chronic disease that affects all the organs and systems of the human body. This disease occurs in violation of the endocrine part of the pancreas, resulting in the amount of glucose in blood or lack or in excess. To monitor blood sugar levels for the prevention of diabetes and to control the disease a special handheld device - glucometer,is used. It helps at any time to determine the level of glucose in your own body. Blood glucose meter is a device whose primary function is independent measurement of human blood sugar.

The main criteria for instruments to monitor blood glucose levels are: ease of operation; price; characteristics (speed of analysis, the type of test strips); measurement accuracy; ease of use. According to the principle of existing blood glucose meters divided into electrochemical and photometric.

Photometric glucometers register the change of color of special test zone. These devices work on capillary blood. Electrochemical blood glucose meteris built on the principles of complex chemical interaction of blood glucose with special chemical elements.

During this interaction is allocated current, that registers the device. These are the most common blood glucose meters, are accurate and require a minimum of blood to measure. But photometric and electrochemical blood glucose meters, which are widely used in many countries, are invasive, require that puncture the skin Fence blood samples and use disposable test strips. The main disadvantages of many models of blood glucose meters are: the need to the application of low blood volume is an error in the survey, the optical zone of the device need to be cleaned, the need to rub a drop of blood on a test strip pitch 1 minute after application, the effect of hematocrit, cholesterol, triglycerides, some drugs on the measurement results, the lack of protection from improper measurement procedure.

Also, the complexity of determining the concentration of glucose in the blood «in vivo» due to the fact that the concentration of glucose in tissues is ten times less than its concentration in the blood and thus ruled out the use of chemical reactions. Glucometers latest generation spectrometric called for their application does not need the integrity of the blood (noninvasive method). Glucometer translucent palm weak laser and then generates indices on the spectrum, which are developed in the United States.

These devices do not use test stripes, they are the most accurate, but the most expensive. Scanning earlobe patient infrared rays - a method opened in Ukraine.

For blind diabetics and diabetics with low vision produced glucometers, that say, but they are the most expensive.

Consequently, current and future, today is the creation of non-invasive blood glucose meters that will relieve diabetic patients from injury and will allow for more frequent monitoring the concentration of glucose.

# ASPECTS OF COMMODITY RESEARCH OF MEDICINAL THERMOMETERS

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Galileo Galilee is considered to be the inventor of thermometer. He has created the device consisting of an air containing ball and thin tube with water. When air in a ball was heated up or cooled, water column changed its height accordingly. However, was not applied in medicine. The first medical thermometer appeared in the XVIIIth century which was one foot in length and was very inconvenient in use. After long period of time thermometers became more advanced, and now in the world there is very large variety of these goods.

The purpose of the given work is commodity analysis of assortment, application and consumer properties of medicinal thermometers in the domestic market.

Thermometer (in Greece θέρμη - heat; μετρέω - to measure) - the device for measuring temperature of a body, air, ground, water and so on.

As a rule, most of diseases or pathological processes in a human organism are accompanied with changes of temperature parameters in a body. Increased temperature is the first sign which specifies to the beginning of disease. Besides, changes in temperature parameters at early stages of disease help to fix the exact diagnosis more precisely. Therefore daily measuring of temperature parameters and their daily account are obligatory procedures which allow to control state of a sick person. The thermometry is carried out two times a day - in the morning on empty stomach and in the evening (before last meal).

In order to measure temperature various kinds of medical thermometers are applied: mercurial (which working principle is based on ability of mercury to expand under temperature increase); electronic (high-technological, universal devices in which one side has a thermosound, another one has a display to output data obtained by temperature measuring which can be made in different ways - orally, rectally or under one's arm); contactless infra-red (with presence of supersensitive detectors reacting on infra-red rays coming from a human body; they allow to obtain exact temperature parameters by directing thermometer onto an object measured without touching its surface. In their turn these thermometers are subdivided on aural, frontal ones and thermometers-papillas); single-use ones presented by several thin plates on which dot sectoring is rendered and parameters of temperature are determined by

color of points.

The most wide-spread thermometers on the Ukrainian market are:

- mercurial: "IGAR" (W.H.G Medical Equipment Co., LTD under the order of the firm "Igar", Ukraine); "Steklopribor" (Ukraine); "Impex-Med" (Russia); Gamma T 50, Gamma (Taiwan); Medicare MC-RT (Great Britain);

- contactless infra-red: Hebei Create (China); HM Digital Inc. (USA); Baby Ono 116 (Poland); Maniquick MQ150 (Switzerland); CITIZEN CT-461C; OMRON Eco Temp Basic; OMRON Flex Temp Smart (Japan); ARZUM BEBBE THERMOMETER (Turkey); aural One Second from HoMedics (development of the USA, manufacturing of China); Medisana CL 76120 (Germany); children's thermometers Topcom TH 4655, measuring temperature of ear, throat, forehead (Holland); multifunctional – Topcom TH-4655 (Belgium);

- electronic VEGA MT J18-BC (Great Britain); Vega MT418-BC (Germany); Terraillon 06548 (France); Meditech AMDT-12 (Japan); Little Doctor LD-300 (Singapore); Bremed BD1130 (Italy); LONGEVITA MT-4218 (Great Britain); AEG FT 4904 (Germany); Microlife MT-3001 (Switzerland); MEDICARE MPTI 025; DT-806 C, Heaco (Great Britain); Medisana FTF (Germany); Beurer FT 09 (Germany).

Thermometers are manufactured according to requirements of the standards for a certain type and also graduated in Celsius degrees (°C) by the International practical temperature scale.

Glass mercurial medical thermometers are packed into initial package by the piece, and then in a cardboard box on 12 piece (according to the normative document on a concrete kind) or a pack (secondary or group packing). The complete set of delivery should include the thermometer and the operational documentation. Under the order of the consumer the thermometer can be delivered without a case.

Thermometers in initial packages should be packed into the shipping package providing their safety during transportation and storage. It’s allowed to transport by any kind of closed vehicles.

Storage: in place protected from atmospheric precipitations, under temperature from – 35°C to +42°C avoiding mechanical, chemical and physical influences.

As a result of research of medicinal thermometers assortment provided by us it was found, that by its functionality the widest and various assortment of thermometers in Ukraine is submitted by manufacturers from foreign countries. Therefore, for our country it’s necessary to improve researches in the field of new kinds of given production, and also to adopt the experience of foreign manufacturers concerning variety of thermometers assortment and methods of their manufacturing.

# COMMODITY ASPECTS IN RESEARCHES OF SPORTSMEN NUTRITION AS PHARMACY GOODS OF SMALL ASSORTMENT

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In recent years the domestic Ukrainian market is very rich in products for sportsmen, namely imported special nutrition and produced domestically. Ukrainian consumers pay attention to the quality and effectiveness of these products, because we want to be beautiful, healthy and slim.

The objective: from commodity standpoint to analyze purpose, range and consumer properties of sport nutrition products in the domestic market as pharmacy goods of small assortment.

Sport nutrition is special group of foods produced mainly for people of active lifestyle and exercise. Today it is widely used by professional sportsmen and ordinary sport fans. In Ukraine this kind of production is related to foodstuff or nutraceuticals.

Sport nutrition is usually classified as following: high-protein foods, carbohydrate-protein mixtures, aminoacids, nitric oxide donators (NO-formulas), fat burners (for example, L-carnitine), special means, creatine, anti-catabolics (BCAA (Branched-chain amino acids), phosphatidylserine), substances increasing testosterone levels, strengthen joints and ligaments, vitamins, minerals, vitamin-mineral complexes, energetics and isotonics.

In today market of sport nutrition there are many companies producing this type of products. We have analyzed and specified the most popular and claimed manufacturers of foodstuff for sportsmen in the Ukrainian market. Rate of manufacturers of sport nutrition is the following: Multipower (Germany) - 21%, Twinlab (USA) - 13%, Prolab (USA) - 10%, Optimum Nutrition (USA) - 10%, Weider (USA) - 6%, Ironman (Russia) - 4%, other manufacturers - 36%. Domestic company Delmas existing for 21 years in Ukraine produces now more than 50 kinds of sport nutrition products under the brand name "Vansiton".

Our studies have shown that the presence of domestic manufacturers of sport nutrition is very poor and most of products are from the United States and Europe. The results indicate the potential for further expansion in the production of these products.

High-quality food additives are good means to maintain sportive form, health and to achieve sportive goals.

# RESEARCH LABELING CHILDREN'S DISPOSABLE DIAPERS

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It is difficult to overestimate the role of diapers in the life of the modern family. Caring for a newborn child and the first years of life. Without proper supervision of a child who cannot yet fully meet all your needs, it is almost exposed to any diseases. The use of disposable diapers helps maintain hygiene baby without spending a lot of effort and save time. Because of the wide popularity, and due to the fact that these products are in direct contact with the skin of the child, the state must ensure the highest quality and safety of medical devices, thereby investing in maintaining the health of the nation.

Disposable diapers for children - product with absorbent layer of wood fiber materials and layer of crystals super sorbents single use to absorb and retain urine child. Care designed for newborn children and toddlers and children of preschool age.

The aim was to study the labeling of children's disposable diapers on the pharmaceutical market of Ukraine.

Accordingly, data from the State Register of medical equipment and medical supplies, we analyzed of labeling children's disposable diapers registered in Ukrainian pharmaceutical market.

The packaging states symbol of the diaper, baby weight range, brand, number of items in the package, country of manufacture, name of manufacturer, trade mark and address different features of diapers under their technical requirements, the date (month) production, warranty period date, barcode, indications utilization "Do not throw down the drain", terms of use. Widely distributed the graphic symbols and pictures to explain consumer characteristics, application products, etc. Unfortunately, most manufacturers do not fully illuminate the composition of their products, and some brands generally limited only indicating composition balm. General labeling does not fully meet the needs of consumers, because information printed to small font, continuous text without breaking into paragraphs. It all making it difficult to read.

Selected product samples generally showed good results when conducted analysis of consumer characteristics and meet all the standards that were used in this study. The main defect of the product is not quality labeling that does not give complete information about medical product, including its composition, that does not meet the standard documentation.

# SECTION № 17

# SOCIAL STUDIES

# CHILDFREE AS A PHENOMENON OF MODERN SOCIETY

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Modern society is bright and unusual. It is manifested in such social phenomenon as childfree. Childfree is an ideology and practice which appeared in the early of XXI century in the USA and promotes childfree life. This phenomenon is widespread in European countries. Index of 40 % of single Europeans impresses, in particular in Germany index reaches 50 %. Ideology of childfree became the Ukrainian society's phenomenon too. Distribution of childfree is connected with status of woman which changed with extension of human rights. Modern woman has all the possibilities to deny a standard model of patriarchal family in which a woman played a main role in birth and upbringing of children and job around a home. The main motivations of childfree are: 1) a wish to have more free time for leisure, hobbies, friends, off-hour work; 2) fear of fatherhood as an irreversible step; 3) fear to lose emotional and physical intimacy with a partner because of baby; 4) fear of birth of child as a harmful factor to career growth; 5) lack of biological desire to parenthood.

Ukrainian psychologist S. Hutsol is sure that unwillingness to have a baby caused by material problems has already solved now because even in the high developed countries a level of birth decrease, although the level of material well-being of families is significantly higher. We should note the fact of increasing of the number of babies who have birth physical and mental disorders. For example, in Ukraine annually born 13 % children with moderate deviations (so-called debility), 16,5 % – inferior, and 3,5 % – a crippled children (with no arms, no legs). Psychologist and expert of childfree L. Nedostup notes that childfree regarded in Ukrainian society as a selfish people who have nothing "inside". In fact, people who don't have children can reach their parental instinct due to the children living in orphanages.

Researching of childfree couples shows that they are well educated and more popular as professionals and less prone to respect traditional gender roles and customs, tend to live in cities.

The gender aspect of this phenomenon shows that women want to be childfree for freedom to work on men for the sake of freedom from work. From 1/5 to 1/3 of respondents childfree in Ukraine are men. Many researchers have noted that childfree is less "socially comfortable", they are more inherent selfishness and individualism.

However, researchers are unanimous rest of this phenomenon that childfree will exist in the future it will become stable trend. There is a number of reasons: 1) unwillingness to sacrifice personal space for the child; 2) the absence of compelling reasons to have children; 3) unwillingness to waste time on parenting; 4) active aversion to children; 5) pets; 6) satisfaction by playing with the children of relatives or friends.

So the ideology and practice of childfree is a way to nowhere. This is the path that leads to a dead end. It violates the main principle of life – a natural reproduction of human life. To minimize a childfree a set of measures promoting full family as the highest value of society is needed.

# THE HISTORICAL SIGNIFICANCE OF THE SOPHISTS'ACTIVITY

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The modern world is characterized by intense globalization processes. The content and orientation of these processes involves formation of common informational space as well as maintaining the human individuality of its participators. Therefore, one of the most important tasks of civilized society is to develop its communicative culture.

Informational Age society can be characterized as an individualized community (U. Beck) which consists of autonomous actors. That's why, it is number of individual skills in sphere of communication, rhetoric, logic, methods of formation, processing and broadcasting of information which is especially in demand today. In this situation an urgent social need for people who know how to think independently, express and defend their own position, persuade and motivate people to action, taking advantage of the only logical tools is evident.

The implementation of aforementioned tasks requires not so much technical methods as special means of "art", including elements of philosophy, logic, psychology and rhetoric. In the history of culture such kind of ambitious educational and cultural project has been already realized. It was aimed at intellective and verbal human capabilities, their cultural meaning and necessity to rethink different aspects of social life. Ancient Greek Sophists were the initiators of this great project.

The significance of sophistic activities was often neglected and contrasted the philosophical achievements of their legendary critics and opponents, such as Socrates, Plato and Aristotle. The aim of this article is to do objective analysis of the Sophists' contribution to the formation of Western science, philosophy and value system.

The Sophists are well known intellectuals, who took an active part in social and cultural life of Ancient Greece in the middle of the fifth - the beginning of the fourth century BC. The most famous Sophists are Protagoras, Hippias, Gorgias, Prodicus, Antiphon, Thrasymachus.

The Sophist is a positive term meaning wise, experienced or just an expert. However, unusual for ancient Greek lifestyle, voluntary attitude to tradition and established values, innovative approach to education and training, depreciation for classical canons of scientific rationality has formed a negative image of the Sophists in the history of European culture.

It should be considered both negative and positive aspects of sophistic innovations to determine the contribution of the Sophists in the evolution of Western culture and science.

The most criticized disadvantages of sophistical practices are the following: conscious violation of logical laws and invention of different logical and rhetorical tricks, denial of objective truth as the goal of cognition and focusing on issues of knowledge utility, moral relativism, criticism of religion, cosmopolitanism and vagrancy and charging tuition fees as well.

Each of these negative features can be contrasted with the thesis that points to the positive aspects of sophistical practices. In the words of the culture historian Sergei Averintsev, the Sophists enriched Greek culture and contributed to “victory over inertia of pre-reflective cultural mode”.

1. Sophism demonstrated the advantages of words in comparison with arms. Logical tricks were a kind of provocation and motivation to learn language and its instrumental possibilities.

2. The Sophists neglected searching for truth that’s why we can’t consider them to be philosophers. However, the pragmatic setting of their tuition improved the links between theoretical and practical knowledge.

3. Renouncement of traditional values expanded freedom, developed the idea of equality for all of the people and maintained their individual moral choice. Protagoras’ anthropological image of "man as a measure" involved not only the conflict with established morality, but also a formation of responsible person.

4. The cosmopolitanism of the Sophists anticipated the modern era globalization, marked by crossing the boundaries, free exchange of information, and creation of common space for traditionally isolated “atomic” cultural worlds.

Professional teaching, civilizing activities, raising the educational level of contemporaries and researches in the fields of logic, rhetoric, linguistics emphasizing the practical aspects of knowledge show us the significance of the Sophists’ contribution to European culture.

# THE ISSUE OF *THE ALIEN* IN PHENOMENOLOGY OF B. WALDENFELS

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In the situation of dynamic, information-packed world people are permanently expanding their communication horizons. Thereby, existential horizons defining the boundaries of "intimate person" (N. Berdyaev), are often being deformed, "retreating to the center" under the active pressure of the Other. Having experienced the impact of new social and cultural circumstances, modern European philosophy has undergone a division into “normal” philosophy and “extreme” philosophy. Globalization and advances in science as well make us constantly deal with the fact that phenomenologists called *the Alien*. Alien in general is a type of phenomenon that can’t be ontologically explored. Thus, comprehension of *the Alien* phenomenon becomes actual for conscious awareness of contemporary world and human.

*The Alien* problem is being investigated in conception of modern German philosopher, representative of phenomenology, Bernhard Waldenfels. Phenomenology as philosophical trend, interested in the mechanisms, content, levels modes and states of consciousness, pays special attention to the motive of human "life-world". “Life-world” is a space of interaction that determines the circumstances and ways of man's awareness of his being-among-others. Every interaction is going beyond, transcending. In the act of transcendence, we find the presence of the Other. Various manifestations of alien, strangeness and otherness are the subject matter of xenology, the trend in modern phenomenology, which appeared due to the works of J.-P. Sartre, M. Merleau-Ponty, E. Levinas.

The concept of *the Alien* is a result of phenomenological transformation of existentialist concept of *the Other*, which goes back to the classical notion of *non-Self*. In contemporary philosophy t*he Alien* motive is analyzed by means of B. Waldenfels’ responsive phenomenology, which characterizes the *Alien* as something "extraordinary". Waldenfels, having examined the history of this issue, determined *the Alien*’s locality. *The Alien* as a hyper-phenomenon, a special kind of phenomenon, is always out of reach, and, as a consequence, out of “domestication” and appropriation. Intentional rationality, a traditional instrument of classical phenomenology, weakens the radicality of *the Alien*, putting it in line with what is already known and depriving its attribute of otherness.

The conception of Waldenfels allows *the Alien* remain original. Responsive phenomenology operates with such an asymmetric categories as "claims" and "response" in accordance with the lack of symmetry between “our own” and “alien” phenomena. Reconciliation with *the Alien* does not mean its appropriation. Being in the mode of response presupposes that "question" and "claim" are always secondary: in the foundation of our own existence "the answer to *the Alien*" has been already laid in recognition of its absolute incomprehensibility and ontological autonomy.

# THE MAN FACE TO FACE WITH DEATH IN PHILOSOPHICAL AND LITERALY TRADITION OF PLATONISM AND EXISTENTIALISM

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The urgency of the problems caused by the aggravation of metaphysical human needs related to adaptation in the world that has become more complicated. The circumstances of our time (such as virtualization and desacralization of culture and values, the rapid dynamics of social changes and the ultimate stress situation of contemporary historical choice) are the social and cultural background for questioning about death. Universality and inevitability of death is not a reason to ignore it. In contrast, only unraveling the knot, one can gain some confidence in the future and go to their final consciously and courageously.

The motive of death is not a new one for philosophy. Death was always referred as the main life event that helps to comprehend the sense of existence and to identify its content and direction. Philosophy has extensive experience in solving key problems of human, and if one could combine ancient wisdom with modern observations, it would be possible to synthesize a new approach to these eternal questions.

The aim of our work is to analyze the existential situation of "face-to-face with death" in terms of two literary and philosophical traditions - Platonism and existentialism of Albert Camus. In the first case the attitude to death is represented by Socrates as a character of Plato's dialogues "Apology of Socrates" and "Phaedon", in the second – by Meursault, Camus' character of "The Stranger".

Our selection of philosophical examples was determined by similarity of plot circumstances: in both cases the reason for meditation on death are trial and death sentence, in both cases the death of a character became the result of his own choice and life strategy; both Plato's and Camus' personas treated with a daring philosophical message to all of mankind, explaining their position and forcing everyone to thought.

In the concepts, that we have chosen, there were represented two approaches to the problem of death as an existential problem: the *heroic* and *absurd*. Fictional Socrates chose an approach that was mentioned as "heroic". In this case heroism refers to the ancient idea of freedom as human's confrontation to fate. Socrates in Plato's writings accepts his destiny and, at the same time, overcomes it. The thinker sees the positive meaning of death in liberation of soul. Death for him is not a fact but an act, that lets a wise man be free. Meursault, Camus' character, on the other hand, denies the sense of life and considers death to be both the apotheosis and the end of total absurdity. Border situation for him is a reason to make a reader accept his own finale and to leave him provocatively face to face with unanswered question.

Man of the XXI century lives in alternating states of sleeping routine and borderline situations. The only possibility to overcome the fear of death for him is to make his existence the subject matter of philosophical reflection and try to make sense of the fact of his mortality.

# CRIMES OF NAZI GERMANY ON THE TERRITORY OF KHARKIV DURING WORLD WAR II

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The aim of the research is the study of crimes of the fascist invaders during the occupation of the city of Kharkiv in the period from October 1941 till August 1943.

In the process of research the author investigates the criminal system of elimination of Kharkiv, created by Nazis and their servants: terror, hunger, gaswagens («murderers») and other. Among the terrorist methods applied by Nazis, it is especially necessary to distinguish the genocide of Jewries, Gipsies and mentally ill townspeople. On the territory of city there were found more than ten places of executing and mass burial places of habitants of city: Drobitskyi Yar, Forest-park, camps of war prisoners, Saltov settlement, places of the public hanging in Sumskaya street and Blagoveshchenskiy market and other places.

History teaches that punishment follows after the crime. And the trial over Nazi criminals and their helpers, that was held in Kharkiv in December 1943 became its proof. This was the first trial of war criminals.

It is needed to be underlined that before the Great Patriotic war more than 902 thousand townspeople lived in Kharkiv, in August 1943 the quantity of habitants of the city grew short to 200 thousand people.

It is well-known that without the past the future is impossible, and the generation that does not know the history can not deserve the proper «tomorrow». Everybody must know the history of their family, home town, where their grandmother and grandfather, mother and father lived in. And the most important – is to remember the errors resulting in death of millions of people.

# BAROQUE IN UKRAINIAN LITERATURE

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Symbol of the way is one of the most common in baroque literature. The aim of the study is to analyze the image of the road in H. Skovoroda as a bright author of Ukrainian Baroque art.

The positive perception of the archetype of the way of the new Ukrainian literature largely attributed H. Skovoroda who showed this image as endless possibilities for human and free implementation of it. A long life way is treated as a chance to cleanse at the way to God through repentance. The man appears as a traveler, and his life is an existential journey.

The perfect way for philosopher is a journey of alone man to a heaven of mind to God. As the sky is metaphorical so the traced path can be considered as nominal. However it was not enough for Skovoroda to go imaginary road. The purpose of the trip was to get closer to the truth, to cut down, to know itself, to calm passions. To become a traveler means to force itself to feel that life is the road and everything leaves a trace; man is just a traveler, and if it is too much in your luggage (troubles, preferences, emotions) it will be harder to overcome your way.

Philosopher analyzes the life way of a man and points the following issues: the person can be reckless traveler and don't often aware of the purpose of journey; to start a path alone is much easier than sending close person.

Thus, H. Skovoroda includes to his works the symbol of path in the traditional contexts which promotes an exhaustive disclosure of this archetype. However, studying the works of the philosopher can make a deeper analysis of the image of the path including the image of his own life's journey how it was seen by the author. H. Skovoroda passed his way in solitude, but not away from people.

H. Skovoroda introduced a philosophical interpretation of the image of a path-journey in Ukrainian baroque literature, extended a poetic understanding of the human journey. An image given in the works of philosopher appears as a universal process of becoming a man or a search for God, the sense of his own existence, of truth as for freedom from their homes and their responsibilities. The journey even interpreted as doomed not to know peace when a person can not reach the truth, to find themselves. Each reader understands the symbol of the path in the work H. Skovoroda through its own experience and emotional mood.

# ARCHETYPES OF CARL JUNG AND RELIGIOUS IMAGES

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Carl Gustav Jung is a famous psychologist of XX century has studied types and functions of dreams and faced with so called “archaic remains” (Sigmund Freud). He introduced a definition “archetype” to a science. What is the meaning of this definition?

Usually man is able to find out the meaning of his dream with a help of individual associations. But are such dreams which can not be associated with real life because of strange symbols in them, its frequent repeating and strong emotional colour. C. Jung called such dreams as archetypical. According to his point of view archetype is a set of motives which can differ in details, but has the same sense. Psychologists insisted that it can’t be classified as inherited view we got by consciousness, because we won’t be surprised of its appearance.

C. Jung gives several examples of his practice when his patients had dreams with religious symbols which sense wasn’t clear. For example, dreams motives of a girl of eight:

- evil animal, snake-like, many-horns monster killing and eating other animals; but God appears from the four corners in image of four gods and resurrect the dead animals;
- Ascension to the heaven where pagan dancing takes place and descent into the hell where angels make good deeds.

Her dreams had special character and contained a philosophical subtext. We can suggest that the child got this idea in the process of religious upbringing, but she hadn’t any considerable religious experience and she didn’t have any idea about apocatastasis (resurrection of the dead).

Why the archetypes are needed? What is their sense? We are driven by the forces which are not following to our consciousness but in spite of the considerable level of individual freedom a modern man is susceptible to their influence.

# MYHTOLOGICAL IMAGES AND PLOTES IN ART OF MODERN OF THE FIRST HALF OF XX CENTURY

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The border of epochs is accompanying crisis which held a change of the way of thinking, remove to other philosophical model of outlook. Art tends to reach the time and to represent a new life in its works and convey a mood of epoch. Early of XX century was marked by different events, such as: industrialization, the World War I, epidemics, collapse of empires, devastation and famine which destroyed a world balance. Artists tried to get a lost harmony. A new problem was established at the end of XIX – early of XX centuries. Symbolism had a considerable influence on the choice of plots and its interpretation in Modern. Art of Modern is characterized by interest to mythological characters and allegoric motives.

Myth became a way of rethinking of reality and has demanded from artist three elements: myth itself, historical epoch and picturesque language. Revival of myth in the art of XX century was based on the new attitude to myth as a saver of basics of the future culture. Myth changed the universal imagination about world order in sensory-specific form, and this property is inherited from his art.

German, French, Belgian symbolists often presented sphinx as an ideal hero for artist of Modern, which combined a woman, a bird and a lion. Centaurs were popular image that demonstrated a man power. It was important for Modern a mythological hero who demonstrated the natural essence of man.

Orientation at the organic natural forms was one of the features of Modern.

The representatives of Modern weren't interested in nature at all but in its separated parts. Objects and nature phenomena were understood by Modern in symbolic and mythological sense. For example orchids and lilies symbolized a tragedy and a death. Bells showed a wish, sunflowers meant sunlight, rose and narcissus meant tenderness and beauty, tree symbolized a life tree, cognition. Mythological image of swan attention of its beauty, allegory of doom in Ancient Egypt considered as a symbol of the city of Sun and often was in Christian iconography near paradise tree.

Vrubel's painting "The Swan Princess" a woman-bird who presented a woman beauty acquired attracting softness swan appears in the frames of theatre performance.

Popular theme and plot of Modern was an idea of growth, manifestation of vitality, immediate breakthrough, unconsciousness feeling, direct expression of the soul, awakening, formation, development, youth, spring.

Professional art renewed a connection with a folk culture. It concerned content and form of presentation. Pagan mythology "World Tree" was demanded by artists of Modern as a stable life-affirming world model. It served as a content and structural basis of paintings by M. Roerich and M. Boychuk.

The fine arts overcome the limits of specific historical time, carried the multidimensionality of space. Appeal to the national mythology expanded temporal and spatial boundaries of art and has identified a high degree of generalization visual language of modernism.

# POLITICAL PREDICTION

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Theses:

- the main reason, that motivate man to do predictions is facts, which future he doesn't know, but they are very important for decisions which are making today;
- there are two kinds of predictions in politics: internal and external;
- political predictions developed to improve efficiency and effectiveness of decisions, to avoid unwanted way of developments in different directions of political life and when politics influence on economy, social and spiritual life;
- • the concept of "political forecasting" means a multi-faceted and activity of special research and development forecasts of numerous components of the policy, in their diverse relationships and interactions, as well as in relationships with other spheres of social life: economic, social, and spiritual;
- the main points of political prediction are detection of perspective political problems and finding the best ways of solving it, to optimize control of political processes, and also to foresight wanted or unwanted political developments;
- policies favor the most effective and at the same time the least predictable tool for social change;
- Components of the modern picture of the world - the complexity, uncertainty, stochastic, non-applicability of deterministic descriptions at bifurcation points - all of this is consistent with the empirical experience deadlocks, the elimination of which has devoted its efforts Kant;
- the same reason can generate different results;
- political prediction has a great influence on politics in general;
- political prediction is important, required and powerful aspect in politics.

# SOCIAL UTOPIAS OF THOMAS MORE AND TOMMASO CAMPANELLA

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Thomas More is an English jurist, philosopher, and politician. His main work is «Of a Republic's Best State and of the New Island Utopia».

At the beginning of the book Thomas More pays attention to unequal social status of the estates in England. Then he describes beautiful and happy life of Utopia island where is no private property and everything belongs to everybody. Everybody work and the working day lasts not more than 6 hours a day. There is no money at the island at all. Utopia is a federative state. All the state positions are elective and the important questions are solving by people's assembly. All the religions and sects are allowed but religious fanaticism is illegal. Atheism is not encouraged, because it is unacceptable.

The main task of the officials is do not allow anyone to evade work. Crimes in Utopia are not punished strictly. People become slaves temporary when they make a useful work for society.

More is not an apologet of individual freedom. He tried to subordinate private interests to public ones. Private property is a reason of social disaster and an obstacle to the ideal society.

Tommaso Campanella presented his views in work "The City of the Sun". The city of the Sun is a beautiful and ideal state where philosophers-priests with Metaphysician on the head are dominate. It is socially homogenious state like community with simple and rational religion. There are no place for private property and family because the children are bringing up by state. Economic unit is not a family but a workshop. Campanella is against of slavery. Life in the City of Sun is more limited than in Utopia. All people are dressed at the same way, eat the same food, start working at the same time and finish it synchronously.

More's and Campanella's ideas of equality are similar. Both of them are dreaming about a state where all people are equal to each other. People at More's work are mass lost its individuality. Nobody has no chance to distinguish itself. People's opinion is not taken into account (except people's assembly). What does the state give to people in return? The state takes care of the future, guarantees fro food and education and minimal effort. It is not so little. Is a person ready to lose his identity and change it for a well-feed life?

Equality is realized in a number of Western countries that aspire to the status of rule of law. Full equality is impossible to realize, because every person is unique. Idea of full equality is not less utopian than the idea of More's state or Campanella's state.

But we can reach this ideal as it done in Western Europe and Northern America. It is equality of rights and opportunities. More's and Campanella's equality is compulsory combined with total control and freedom restriction.

There is no word about concrete people in any social utopy. Masses or social groups are objects of investigation. Personality is nothing in this utopias. People in these countries are losing the freedom of choice (except the choice of authorities), freedom of movement, their individuality, they are indicated how to live, what to wear, what to do.

State-utopia would be comfortable for admirers of Stoicism. Conscious self-restraint, which is characteristic of the Stoics, the understanding that a minimum set of requirements which provides state is enough for their life.

A great number of ideals More and Campanella are not outdated and still implemented in the modern world. These ideals are: freedom of conscience, the right to education, right to leisure, election authorities. More's and Campanella's views were advanced for their time and played an important role in the development of philosophy and social thought of the next era.

# ETHIC ASPECT OF SELF-MEDICATION PROBLEM IN MODERN MEDICINE AND PHARMACY

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XXI century is a period of pharmaceutical progress! New drugs and dietary supplements fast appear at the pharmaceutical market. Mass media is full of pharmaceutical advertisement. Evolution of the chain doctor – patient – pharmacist is a result of progress. Patients became more demanding, less contact the doctors, because it takes much money and time. That's why we have a problem of self-medication and its consequences.

This problem is widespread in our country. It is caused by such reasons as: lack of money for payment to doctor or buying some medicine, fair of job loss, because the labour market is overcrowded and it's hard to find it. That's why patients buy medicine on the advice of the pharmacist, on the basis of self-diagnosis. Any doctor and pharmacist can confirm now that it is much easier to treat a disease that has not passed in the chronic stages. In addition, some diseases can cause an emergency condition which can be dangerous for the patient's life. If atherosclerosis being treated wrong it can lead to some form of stroke which often is a reason of death.

It should be noted that this problem doesn't occur only here, but in Europe. According to the UK Office for National Statistics there are more than 600 certificates of death in a year, which were caused by the medication sold without a prescription. Agency Reuters reports that 81% of Americans use at least one medication per week.

There are many solutions of this problem. Most of experts believe that self-medication will be less if pharmaceutical advertisement will be prohibited. Others propose to establish a strict control over the pharmacies.

Summing up, I would like to propose solutions to this problem in our country. First is a healthy lifestyle of the population. Second is the spreading of information about the dangers of self-medication in form of advertisements, posters, and banners. The third is to provide public resources to treatment. This problem is actual for our country and we must remember that before taking an advice from the Internet or from a neighbor to recall an old Latin saying: "Vivere est cogitare" – "To live is to think".

# DEHUMANIZATION OF SCIENCE

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The purpose of this article is to assess the image of science in the minds of modern society. The author analyzed the concept of scientific development in the European philosophy of modern times. Based on this analysis, he made a number of theses about the modern vision of the role of science.

Modern civilization was created by science. The philosophy demonstrated of modern times the importance of science for humanity. Science appeared as a universal instrument not only to describe, but also to transform the world. The results of research had become the basis for production technologies, political power and economic success.

Scientific rationality has been presented as the only sure way to describe the world. But science has been reduced to a mathematical description of the objects of the study. Thus, knowledge can be scientific only, and science must be based on mathematics.

Positivism has made new changes in the understanding of the science. Science does not think it is devoid of humanity, longing and passion, as well as any other feelings. This is a soulless tool that creates a soulless image of the world. But is it right? Can mathematics to describe the world? This approach is naive deception, isn't it?

The modern world is faced with the phenomenon of dehumanization of science. That is what makes us go back to the ethical issues of scientific knowledge. The purpose of the scientific knowledge is to create a world for man, but not a world without humanity.

# MUSEUM OF HISTORY OF PHARMACY OF UKRAINE: ROLE AND MEANING IN THE SYSTEM OF PHARMACEUTICAL EDUCATION

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The National University of Pharmacy is the center of pharmaceutical education in Ukraine. Improvement of forms and methods of pharmacy specialists' preparation occurs constantly. Museum of history of pharmacy of NUPh plays an important role in the process of preparation of specialists of pharmacy. The decision of founding of the museum was taken at the VI National Congress of Pharmacists of Ukraine in 2005. The museum was opened on 15, September 2010. Funds of museum of history of pharmacy enumerate more than one thousand exhibits.

The museum consists of two exposition halls which present history of pharmacy, history of pharmaceutical education, periods of formation and development of NUPh. There are lectures, practice classes, scientific seminars and presentations of new scientific investigations of the history of pharmacy sphere organized by the departments of NUPh.

The museum plays an important role in career guidance. Applicants visit the museum during the public days of NUPh. The most valuable exhibits are: Pharmacopeia in German with handmade colored illustrations published in 1890, laboratory medical utensils of late XIX century, exhibits of Kharkiv Emperor's University collection of plants late of XIX century, the first rector professor M. Valyashko's weigh scales of XIX century, personal record of professor M. Valyashko. Renewing of funds and exhibitions with the help of scientists of NUPh occurs regularly. The outstanding NUPh scientists' biography fund is creating; thematic expositions devoted to professor M. Valyashko, professor D. Salo and other take place in the museum. Photo archive of NUPh which contents the materials about history of pharmacy and history of NUPh is being collecting at the museum.

# CONCEPT OF UPBRINGING OF MICHEL MONTAIGNE

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The philosophy of the Renaissance had a significant influence on the development of subsequent philosophy. An outstanding French writer, philosopher and humanist Michel Montaigne was one of the main representatives of this period. He was a son of Gascony nobleman and had left a bright trace in the history of philosophy with his major work – “Essais”. M. Montaigne got a great popularity and respect because of his independent views and strong convictions.

The aim of our work is to study such problem as Montaigne's failure from dogmatic belief in the simplicity of human nature which was typical for various theologians, philosophers and authorities' representatives of that time.

Michel received an excellent education based on methodic which was developed by his father. The main object of M. Montaigne’s investigation is the problem of man, but not as a centre of the universe (according to Pico della Mirandola’s concept), but a man as an ordinary one. Philosopher is outraged by authoritarianism and intolerance of contemporaries to the education of the young generation. “It is a suppression of freedom of thought; this tyranny of our thoughts is widespread and captured our philosophical schools and science”. In order to change the status quo, the philosopher developed his concept of education, whose main objective became to cultivate not just a specialist, but a man with a strong mind, strong-willed, generous heart. Montaigne went further than his predecessors at issues about the inner freedom and independence. He believed that it was important to take up the knowledge and to generate moral beliefs without anyone’s help. Montaigne encouraged teachers to force students to pass their knowledge through a sieve and did not impose the ideas of the student on the basis of its authority and influence. Montaigne offers a method by which the teacher explained several theories, and the student should choose the right one if he had been able to do it. If he hadn’t been able to choose the right theory – “... at least he would be doubt, which was also good, because only fools were always confident in their rightness”.

Thus, M. Montaigne’s principles of upbringing have a universal character but perhaps he didn't pay the attention for it; and a struggle with the old ideas initiated by M. Montaigne, led not only to the development of bourgeois humanism, but also to the appearance of new and more humanistic ideology.

# SECTION № 18

# PHILOLOGY

# THE HISTORY OF ARABIC WRITING: THE ORIGIN AND DEVELOPMENT OF CALLIGRAPHY

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The purpose of this article is to analyze the specifics of Arabic writing that belongs to the Semitic group of alphabetic writing, discusses the origin and development of calligraphy.

The emergence of Arabic writing dates from the first century of the Hijrah - VII century. By this time the Arabic alphabet is almost formed.

In general, because of the limited information to date precisely the emergence of the alphabet is difficult, but the body of evidence still points to the pre-Islamic period of its origin.

Arabic calligraphy - an area of decorative fine arts, which incorporates elements of the pre-Islamic heritage. Characteristic calligraphy artistic language allows to refer to the field of Muslim calligraphy ornament.

You can talk about the two functions of calligraphy - art and decorative and religious-mystical. Arabic calligraphy is called "Hutt" or "hutut."

Originally Arabic calligraphy originated on the basis of the copy of the Qur'an, which is considered a creation of God, so the written word itself has received a sacred meaning.

In the early period of Islam was known two main types of Arabic script: monumental and italic.

Monumental relies on the use of straight lines, it majestically, while italic used in everyday vernacular records, becoming the basis for handwriting "nash".

In Arabic writing decided to allocate six basic calligraphy: "kufi", "Soultz" and "naskh", "talik" ("Persian"), "Divan" and "Rick".

In contrast to European literature, Arabic texts are written from right to left. The basis of the calligraphic inscriptions constitute strict geometric principles and precise proportions, depends on the clarity of labels and beauty line.

The basis for drawing up the rules of proportion is the size of the letter "alif", the first letter of the Arabic alphabet, which is a straight vertical line.

The unit of measurement in Arabic calligraphy is considered the point, the main work item master.

In point calligraphy has a square shape, and size of the square depends on the angle of inclination of the pen tip and the degree of pressure of the master.

Calligraphic pen, called Tomar, consists of 24 hairs ass. It is important, as the pen tip is cut off; it depends on the preferences of the master, national traditions and the type of applied text.

Thus it is seen that the value of writing inherent in the very religion - Islam.

# LEARNING ENGLISH WHILE TRAVELING

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*When traveling, do not know English, you begin to understand what it means to be born deaf and feeble-minded.( Philip Buvar)*

We propose to study language by wandering. Interested in shades of English in the world, we invite you to our tour .

USA

The Statue of Liberty was France's gift to America. It was designed by the French sculptor Bartholdi and presented to the USA in 1886. The Lady in the Harbour stands 151 feet tall, weighs nearly 225 tons and has a 35-foot waist.

The Hollywood Walk of Fame comprises more than 2,500 five-pointed terrazzo and brass stars embedded in the sidewalks along 15 blocks of Hollywood Boulevard and three blocks of Vine Street in Hollywood, California.

Roosevelt Island is a narrow island in New York City's East River. It lies between the island of Manhattan to its west and the borough of Queens to its east, and is part of the borough of Manhattan. Running from Manhattan's East 46th to East 85th Streets, it is about 2 miles (3.2 km) long, with a maximum width of 800 feet (240 m), and a total area of 147 acres (0.59 km2) . The Roosevelt Island Operating Corporation estimated its population was about 12,000 .

Canada

The Montreal Botanical Garden is a large botanical garden in Montreal, Quebec, Canada comprising 75 hectares (190 acres) of thematic gardens and greenhouses. It was designated a National Historic Site of Canada in 2008 as it is considered to be one of the most important botanical gardens in the world due to the extent of its collections and facilities.

Thousand Islands National Park (established 1904) is located on Hill Island in the Thousand Islands Region of the Saint Lawrence River. The park consists of 21

islands plus many smaller islets. It is Canada's smallest national park with a total area of 9 square kilometres (3.5 sq mi). Much of the park is only accessible by boat. The Frontenac Arch Biosphere Reserve, in which the park is located, is known as being one of the highest areas of biodiversity in Canada.

Jasper National Park. Offering visitors a more laid-back mountain experience - with equal options for adventure, discovery and relaxation. As one of Canada’s oldest and largest national parks, established in 1907, Jasper was once seen as an island of civilization in a vast wilderness. More recently, it has become a popular getaway from urban life, and a special place to reconnect with nature.

New Zealand

Baldwin Street, in Dunedin, New Zealand, is considered the world's steepest residential street. It is located in the residential suburb of North East Valley, 3.5 kilometres (2.2 mi) northeast of Dunedin's city centre. A short straight street a little under 350 metres (1,150 ft) long, Baldwin Street runs east from the valley of the Lindsay Creek up the side of Signal Hill towards Opoho, rising from 30 m (98 ft) above sea level at its junction with North Road to 100 m (330 ft) above sea level at the top,[2] an average slope of slightly more than 1:5.That is, for every 2.86 metres travelled horizontally, the elevation changes by 1 metre.

Madagaskar

The Mozambique Channel is a portion of the Indian Ocean located between Madagascar and Mozambique. It was a World War II clashpoint during the Battle of Madagascar. The channel is approximately 460 km (286 mi) The channel reaches a depth of 3,292 m (10,800 feet) about 230 km (143 mi) off the coast of Mozambique.

The Comet moth (Argema mittrei) or Madagascan moon moth is an African moth, native to the rain forests of Madagascar. The male has a wingspan of twenty centimeters and a tail span of fifteen centimeters, making it one of the world's largest silk moths. Although endangered in the wild due to habitat loss, the Comet moth is being successfully bred in captivity.

**DIFFERENT "FINNISHES":**
**PUHEKIELI, KIRJAKIELI JA STADIN SLANGI**

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One of the curious things about Finnish is that there are essentially two parallel languages: the spoken language or **puhekieli,** which follows one set of grammar rules and rules for sentence construction, and a related but different language called **kirjakieli** used only in formal written settings such as books, magazines, letters, and in certain formal spoken settings such as in formal speeches, and semi official communication media such as news broadcasts.

Spoken Finnish has its own grammar rules which are in some ways similar to, but in other ways different from the forms used in the formal written language. The spoken language has different rules for verb formation, and there are many differences in the formation of words.

The most distinctive features of spoken Finnish are in ***pronunciation***: 1) the word-final *n* is mutated into a glottal stop /ʔ/, orthographically represented by an apostrophe: *Isä*/ʔ/*än* ← *isän ääni* "father's voice"; 2) the final vowel in standard written Finnish is dropped: anteeks**i** (*sorry* in formal Finnish) - anteeks (*sorry* in colloquial Finnish). 3) Vowel clusters and diphthongs: word-final vowel clusters ending in /ɑ/ or /æ/ have much variation in dialects of Finnish. They assimilate especially in Helsinki, where only the resulting chroneme marks the partitive in many words: *puhun suomea — puhun suomee* "I speak Finnish", *pitkiä — pitkii* "(some) long (things), An /eʕ/ or /eæ̯/ cluster also appears in many adjectives: *pimeä — pimee* "dark", colloquial deletion of /d/: *tiän* for standard *tiedän* "I know", *viiä* for standard *viedä" "to take away", lyyä* for standard *lyödä* "to hit", *ruuat* for standard *ruoat ~ ruuat* "foods" (singular *ruoka*). 4) The final consonant sandhi. It improves the rhythm of speech and allows the speech not to "get stuck" to word boundaries, and because of this, may be heard even in the formal language. When a word ends in a stressed mora, which ends in a vowel or an omittable consonant, the consonant beginning the next word is doubled and it connects the words. The two words end up being pronounced with auxiliary stress is on the syllables beginning the words: "Now it arrives! You go first": a) Nyt se tulee! Mene sinä ensin. (standard); b) Ny se tulee! Mee sä ekaks. c) Nysse tulee! Meessä eka. If the consonant cannot be omitted without ambiguity, this does not happen. For example: Menetkö sinä ensin? Meeksä/meetsä ensin? = "Will you go first?" The meaning would change, if the consonant was omitted: Mene sinä ensin. Meessä ensin. = "You go first."

***Grammar*** has also some featured differences: *Personal pronouns* are contracted: "Did he mistake me for you?" has these forms: a) *Luuliko hän minua sinuksi? b) Luuliks se mua suks?* c)*"Luulikse mua suks?"*.

Verbs are formed slightly differently in **puhekieli**. The first main differences are that the first person plural forms are generally in the passive form seen in the written language, i.e. "Me mennään kahville" ("Let's get some coffee." Literally, "We go to coffee"). The second main difference is that sounds elide. In other words, parts of

words disappear. For exmple, the present forms are: (minä) olen **mä oon** *I am;* (sinä) olet **sä oot** *You are;* hän on **se on** or **hän on** *(S)he is;* (me) olemme **me ollaan** *We are;* (te) olette **te ootte** *You all are* (plural) *You are* (formal singular); he ovat **ne on** *They are.* Whereas the negative will sound as follows: en (minä) ole **emmä oo** *I am not* et (sinä) ole **et sä oo** *You are not* hän ei ole **ei se oo** or **hän ei oo** *She is not* emme ole **me ei olla** *We are not* ette ole **te ette oo** *You all are not* (plural) *You are not* (formal singular) he eivät ole **ne ei oo** or **he ei oo** *They are not.*

Numerals: kuutonen (number six) (→ kutonen), seitsemäinen (number seven) → seiska, kahdeksainen / kahdeksikko (number eight) → kasi / kaheksikko, yhdeksäinen / yhdeksikkö (number nine) → ysi / yheksikkö, kymmenen → kymppi, kybä (Helsinki slang).

In everyday speech, the *-ko/kö* suffix has the *-s* clitic added, becoming *-kos/kös*, which in turn reduces to *-ks*: *olenko minä hengissä? → oo(n)ks mä hengis?* "am I alive?"; *puhutko sinä englantia? → puhut sä enkkuu?* or *puhuks(ä) enkkuu?* "do you (sg.) speak English?"; *tuliko hän jo? → tulikse jo?* (via *tuliko se jo?*) "did he/she come yet?"

Vocabulary. Finnish buzzwords: Finnish terms drawn from or imitative of technical jargon, and often rendered meaningless and fashionable through abuse by non-technical persons. *Ydinosaaminen* - core competence, *haasteellinen* - challenging, *innovaatio* - innovatiivinen innovative, *innovoida* - to innovate, *sisäinen yrittäjyys* - intrapreneurship, *ulkoistaa* - to outsource.

Puhekieli, or spoken Finnish, serves as the basis for Helsinki slang or Stadin slangi ("Helsinki's slang", from Swedish *stad*, "city"). It is a local dialect and a sociolect of the Finnish language mainly used in the capital Helsinki. It is characterized by its abundance of foreign loan words not found in the other Finnish dialects as well as by a large number of words originally borrowed from Swedish, German and Russian, but nowadays chiefly English, vocabularies. The loanwords replace some of even the most mundane Finnish-language words with foreign alternatives. However, when spoken by a native Finnish speaker, all words are inflected by the rules of spoken Finnish, and the language sounds distinctively Finnish.

The history of Helsinki slang can generally be divided into the 'old' slang (*vanha slangi*) and the 'new' or 'modern' slang (*uusi slangi*). Old slang was common in Helsinki up to the mid-20th centuryt incorporates far greater number of Swedish and Russian loanwords than the modern variation. The modern variety has evolved side-by-side with the growing influence of English-language youth subcultures starting from the 1950s. It is thus characterized by a greater influence of the English language and proper Finnish language while the influence of Swedish and Russian has declined. For instance, viitonen (number five) (*femma*), kymmenen → kymppi, *kybä* (Helsinki slang), ravintola → *rafla* - restaurant; *pirssi* - taxi; *fiude* - a car, *skruudata* - eat; *hima* - home; *spora/skuru* - tram; *dallata* - stroll, walk; *kliffa* - nice; *snadisti* - a bit; Finnish internet slang: Finnish nonstandard terms whose usage is typically restricted to internet users: *banaani* - a ban, *jonne* - a stereotypical teenage boy, *nuupi* - newbie, noob.

# PHRASEOLOGICAL UNITS IN PHARMACY

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The aim of the article is to reveal the most popular phraseological units used in pharmacy.

The methods of the investigation: phraseological identification, context analyses, comparative analyses, comparative-typological analyses.

Results. The analyses of the studied materials have shown that in pharmaceutical texts phraseological units- sustainable combinations of words which express integral value- are widely used in different fields of pharmacy.

For example, clinical pharmacy, medical chemistry, clinical laboratory diagnostics and pathological physiology and other senses that treat people or diagnose them use such phraseological phrases as symptom of feline cry – шум в області серця; head of Medusa – мережа вен в області животу; stomach "hourglass" – звуження стравоходу при вході в шлунок; a goose liver - ожиріння печінки при жировій дистрофії; a tiger heart - ожиріння серця; a ox heart - гіпертрофія серця при пороці; a Muscat liver - ущільнення печінки, нагадує мускатний горіх; a marble pallor - характеристика кольору шкірних покривів новонароджених; a cannon rhythm - перший тон, що вислуховується над верхівкою серця; chest shoemaker - стан, при якому нижня частина грудини втиснула усередину; sound "cracked pot" - перкуторний звук над легенями.

The analyses of the studied materials have shown that pharmaceutical marketing and management, organization and economics of pharmacy, commodity pharmacy goods often use the the following phrases: pink collar worker – робітник у сфері продажу; bust one's buns – старанно працювати; bumped up – отримати надбавку до зарплати; a cold call - без попередньої домовленості; to axe someone – звільнити з робочого місця; back to the drawing board – почати все з початку; back to the salt mines – повернутися до тяжкої роботи; blue collar worker – людина робітничої професії.

The analyses of the studied materials have shown that there are many phraseological units used to express pharmacist's attitude to the patient or describe the human's state. For example, if a person is healthy and physically fit, the most popular phraseological expressions are used such as to be as fit as a fiddle, to be bursting with health, to be safe and sound. If the person is very ill, the next phraseological units are used: to be riddled with one's disease, to be living on borrowed time, to be in a bad way. If the person is dying, we use the following phrases: to be beyond help or to meet one's maker. But if the person is near the death, we can use the phrases to be on one's last legs or to be at death's door.

Conclusions. So, phraseological units are often used in pharmacy and its fields. They are unique in their own way and used for different purposes.

# THE COMMUNICATIVE APPROACH IN TEACHING OF PROFESSIONALLY ORIENTED READING OF FOREIGN LANGUAGE TEACHING IN UKRAINIAN HIGHER EDUCATION

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The purpose of teaching language for specific purposes shall be to achieve the level sufficient for their chosen specialty and its practical use in the future professional activity. The purpose of the article is to clearly highlight the main trends in exposing contemporary problems of teaching foreign language for specific purposes and to emphasize the achievements in this area of knowledge. Especially important is the professionally oriented approach to teaching a foreign language at non-linguistic universities. Thus this approach involves the formation as students' capacity to foreign language communication in specific professional and scientific spheres and situations, as well as the ability to extract the necessary and relevant information of a professional nature by reading specialist and scientific literature in a foreign language. Methods: We examine the result of generalizing personal and colleagues' professional teaching experience as well as analysis of the data on teaching methods of Russian / Ukrainian language as foreign language for specific purposes. Professionally oriented training provides professional focus not only on educational content, but also the activities of developing professional skills.

Results: to use for foreign language classes tasks that introduce the basic concepts of specialty, along with the development of communication skills to the teaching of reading specialized texts of scientific and professional character, annotation and abstracting of the reads to extract and concise the information in specialty. Taking into account the linguistic factor, training materials for the reading based on the scientific texts should be complete, integrated, etc.; to be available in content and scope; to be organized according to a gradual build-up of difficulties, to be gradually increased in volume and to use different genres. Further research in this direction could be the creation of the basic selection and organization principles for scientific and technical texts according to the factors considered above.

# KNOWLEDGE OF ENGLISH AS A PROFESSIONAL ABILITY OF PHARMACIST

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If you are a student of pharmacy you must know that to be a good expert and a successful worker you should never stop learning and working on yourself. We know that work in our sphere demands on encyclopedic knowledge and exact terminology as well as clear conversational skills. In nowadays, scientific works and professional terminology are published in English and it is more than 90 percent (three-fourth) in some fields. Pharmacist will not be able to understand the words and expressions without knowledge of pharmaceutical English terminology because English for pharmacist differs from traditional English substantially. There is no doubt that the knowledge of pharmaceutical English is separate skill for the professional chemist. The main problem consists of that students are offered to master for short term classification of pharmacological groups for medicines, their application, classification of diseases and symptoms, and without basic knowledge of English it is impossible. In other words pharmacists who constantly improve the qualification or plan to work, for example, in clinics and the pharmaceutical companies must achieve high level profound knowledge of English.

The first thing that needs to say is knowledge of medical English this is a possibility to continue education abroad. Besides it gives the chance to visit various medical conferences on actual medical topics. By the way employers are very interested in it. Moreover work in the international pharmacological sphere means active cooperation with English-speaking colleagues, doctors and health workers of various professions. Knowledge of medical English and English for pharmacologists can be one of the major factors which will influence the decision of the management to accept for employment in foreign or international clinic, the prestigious medical, pharmacological or research center. The first opinion guarantees the correct start and a reference point for further work.

The pharmaceutics prefer precision . representative of this profession should following to rules of the English grammar, the correct construction of sentences, it isn't allowing multiple interpretation of the phrase, should have found of terms' knowledge, phrases and set expressions, a medical slang, possession of pharmaceutical terminology.

The public migratory service notes that now lives in Ukraine more than 247 000 foreign citizens on a constant basis and more than 71 000 foreigners — is temporary. Foreigners have the right to ask for the emergency medical help in any state and municipal establishment of the health care of Ukraine. I wish to draw your attention to the fact that one pharmaceutical institution (a drug store or pharmaceutical point) in Ukraine serves 2264 men by calculations for the end of December, 2012 , it is obviously that account must be taken of the English-speaking population. Sure possession of English medical terminology will give advantage of reception of foreign patients. It is especially actual for pharmacists and the other workers of the health living in big cities. Of course in small towns only compatriots come for medical assistance. But if the clinic or a drug store, for example, is private, it also works in common with insurance company, and service of foreign patients inevitably. These are all rather weighty arguments for the positive decision in a question, whether health workers should learn English.

During several centuries English gradually got the status of international language today. About 90 countries of all globe accepted English as the second state, in many countries its studying is obligatory. Global cultural, scientific life is possible only thanks to English, as to a peculiar channel by means of this language it is possible exchange of experience, information, achievements. Once the knowledge of English was an intelligence sign, a luxury element. Today it is prime necessity, whatever purposes faced you: free orientation in Internet space or career development which is actually impossible without knowledge of English today. Learn foreign language with pleasure – and any discussions with foreign partners will not be terrible for you!

# SPECIALIZED CHEMICAL TERMINOLOGY IN MODERN SCIENTIFIC LITERATURE ON THE SYNTHESIS OF NOVEL COMPOUNDS

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Nowadays integration and consolidation processes play the key role in the development of science. That's why it is vitally important to share our own unique research findings and learn more about foreign investigations in the area of your scientific interest as well. Anyway, it's almost impossible for modern scientists to work without proficiency in foreign languages, especially in the English language, due to its international status.

Thus, there is a wide variety of different scientific journals printed in English. For example, 'Chemical Abstracts' (Easton, 1907), 'Tetrahedron' (L.-Oxf.- N. Y., 1957), 'The Journal of Organic Synthetic Chemistry' (Tokyo, 1943), 'The Journal of Organometallic Chemistry' (Amst.,1963), 'The Journal of Heterocyclic Chemistry' (New Mexico, 1964) are well-known to chemists all over the world.

Specialized chemical terminology is always used in articles of such journals. The main problem for our scientists is that ordinary dictionaries are useless or even harmful when scientist attempt to understand the message of a certain text correctly. Therefore, we examined the most common mistakes and difficulties in the translation of specialized chemical terminology.

The lexical problems listed below are mainly connected with: names of chemical vessels, different methods of synthesis and analysis of obtained compounds.

For example, the phrase 'under reflux' means the process of heating a liquid in such a way that any vapor is liquefied and returned to the stock. The term 'yield' is common for the full amount of the obtained product. However, the English – Russian and vice versa translations are very often incorrect in this cases.

In addition to that, the names of chemical vessels such as different types of flasks and funnels are also frequently confused.

Moreover, there is also a problem with synonyms in foreign articles. Our scientists misuse such terms as 'substance', 'material', 'matter' and 'stuff'; 'solvent' and 'environment' etc. These mistakes then lead to misunderstanding and incorrect scientific decisions.

Thus, the importance of the English language for modern scientists is obvious. It is the improvement of our foreign languages skills that is absolutely essential both for the self-development of Ukrainian scientists as well as its overall scientific progress.

# PARALLEL BETWEEN THE ANCIENT STUDENTS AND MODERNITY

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Vagants or holiards are "traveling people" in Western Europe in medieval times who composed poems, sang songs and recited prose in the squares of cities and at various meetings. The word "Vagant" comes from the Latin "vagari" - wander. Another term "holiard" derived from "Goliath" (the devil).

Among the large number of anonymous vagant poems there are songs whose authors are known. But their names are vagant: Primate (Elder) Orleans, Arhipiyita (poet of poets) Cologne, Walter Shatylonskyy.

Many examples of vagant poetry are found in the so-called “Buranskyy collection” discovered in 1803. "Cambridge songs" is considered to be the oldest collection of ancient vagant works.

Travelling students try to show the people that vagancy - is the norm of life, rather "odd", but not negative, just the opposite. They feel good in this undefined, uncertain state, and they oppose it to satiety and mustiness of ordinary settled life.

Vagants believed that people should be brave enough to fall in love with freedom vigorously. Life should be spent cheerfully, their lives should please God, and priests’ false rejection of secular joys was highly unlikely to please him.

In the university vagants begin to contradict with themselves: they want to be intellectuals, but do not want to learn, they want to be in the team, but do not follow its rules. They often drink. These headlong actions (as they thought) helped them to worship God. It sounds strange, but this is the explanation: Bacchus - the god of wine, how is it possible to honour him without drinking the divine drink?

Vagants are young and cheerful and that’s why love is fun and game for them. In order that they treat love seriously and connect some future plans with it, you need

vagants to have stability; love could be afforded only by the rich. Vagants were left to tear out happiness from their destiny in pieces.

They recount in details all the sins they accuse this world of. It is believed that vagants are the institution, brotherhood, and sometimes even a sect.

This is a very difficult question. They are students and they call themselves brotherhood for fun, but when it comes to the general definition of who they really are it all comes to the idea that they are enemies of the priests.

How loudly vagants declared that they welcomed all and their house was the whole world. From that we can conclude that they considered all people friends, the only condition was pure soul. Students considered wine the way of communication with God, guide of art work, and tried to attract more people to that "way of salvation."

If considering "friends" vagants had a list of applicants, for “enemies” it was much easier. Vagants know and actively fight with them. Knights are at the top of the social ladder, they are noble and honourable, they have power and wealth. They are rebuked with numerous wars, destruction of homes, death. Their profession is a murder and that, according to the Bible, is a deadly sin. They are believed to protect the population, but according to vagants, it’s only worse for people.

The enmity with the priests looks like the struggle between different social groups, competition existence. In fact vagants proposed the new structure of the church, arguing it by sinfulness of the former one.Vagants accused priests of the absence of mercy. The students wanted to show that they were different from all the other priests and willing to help a neighbour, even without money.

Hippie ideology is closely intertwined with the ideology of vagants. Hippie literally promoted free love and life here and now, without obligations and thinking about tomorrow. You can observe similarity to vagants who just could not make plans for normal relations and long bonds, due to the nomadic lifestyle and lack of money. Hippie encouraged drug usage to expand human consciousness, vagants worshipped drunkenness and debauchery. A typical disrespect of the material values - all of these qualities can be found both in vagant poetry and hippie’s works.

# ANALYSING OF THE ENGLISH LANGUAGE RESEARCH PAPERS AS AN IMPACT OF SCIENTIFIC AWARENESS TO POSTGRADUATE STUDENTS

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English is the language of science and postgraduate students need to master it to progress in their scientific career. More than three-quarters of scientific papers today are published in English — and in some fields it is more than 90 percent.

The existing realities require postgraduate students to have a deep knowledge of the latter not only in native language, but in English as well, since the visibility of scientists in the world academic environment is only possible if the publications in the leading peer-reviewed journals are in English. One of the main types of the English course for postgraduate students at the Department of Foreign Languages of the NUP is an analysing the English language research papers, focusing specifically on reading and writing for research. The materials for this type of work can be found in international citation databases, such as the Scopus and the Web of Science. These databases where leading academic publications are indexed, and their study may give an idea about the current state of a particular scientific field. Furthermore such type of work leads each postgraduate student to analyze the article in his/her scientific field, collecting information for future research from competent sources. While studying the structure of a research paper it is necessary to analyze its typical language elements inherent in scientific texts. They may include: high lexical density and terminology, quantitative predominance of nouns over verbs, non-personal constructions.

Also reading scientific texts helps postgraduate students learn to take notes which is the first step to writing a research paper. Ability to take notes involves the ability to highlight the main ideas in the text and reproduction them in different way from the author's one. The developed skills may assist students in making a review of relevant research papers, citing their authors and referring to them. All these make up the initial research skills.

Considering the globalization and internationalization processes which are affecting the system of higher education nowadays, the solution of problems such as building the capacity to conduct scientific research competently and reasonably as well as the ability to report on its results in English, will make a significant contribution to the development of PhD works of postgraduate students.

# COMPARATIVE STUDY OF RUSSIAN AND UZBEK LANGUAGES

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At the present time remains extremely urgent problems of contrastive linguistics. Linguistic Encyclopedic Dictionary defines contrastive linguistics as a field of research of general linguistics, intensively developing with the 50s of the 20th century. The purpose of this research is a comparative study of Russian and Uzbek languages to identify their similarities and differences at the level of grammar. To the methods used in our study we add methods of description and comparison. Material is the grammatical structure of the two languages studied on the synchronic section.

As is known, the Russian language nouns have grammatical categories of gender, number, case, animation of inanimate. Nouns in Uzbek language have categories of number, case, accessories, certainty, uncertainty and face-nonperson. Thus, the most contrasting in Russian and Uzbek languages are the categories of gender and face-nonperson, which largely determine the specificity of lexical and derivational systems of these languages.

Essentially the fact that the Russian language main way of expressing grammatical meanings is flexion, which is absent in the Uzbek language. In addition, the Russian language is widely represented, and no comprehensive Uzbek derivational affixes.

During our research, we came to the following results: for the Uzbek language with the determinant of "economical use of unambiguous affixes" is characterized by a few ways. For the Russian language a determinant of "maximum use of multi-valued affixes" characterized by the presence of numerous ways.

In summary we can draw the following conclusion: Russian and Uzbek languages are genetically unrelated and typologically contrasting: Russian language belongs to the Slavic languages; it is the language of inflectional type. Uzbek belongs to the Turkic language family (Chaghatay or Eastern subgroup); the language agglyunative type.

# IMPORTANCE OF ENGLISH IN THE PROCESS OF PHARMACISTS' TRAINING

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Today, it's impossible to imagine our life without English language. Children from an early age begin to learn this language, and even first-formers already can read and translate English texts. More language schools are opening now, also there is a great progress of tutoring, and studying program becomes more intense with English, French and German lessons. Every day we are faced with a huge number of English words. There are: names, and signs, songs, movies. Also, there is a lot of borrowing words in our language. Slang phrases filled our everyday speaking. Thus English is becoming an integral part of our daily lives.

It's not a secret that today an important criterion in hiring a new person is a quite good knowledge of foreign language. Prestigious firms and companies want to see in their ranks educated and well-rounded employees.

So, quality, fluency of English is very important for the future specialist. No matter what industry he has studied in, and where he is going to work, more attention should be paid to the development of their knowledge of a foreign language.

The theme of this thesis concerns the importance of English in the pharmacy. Future pharmacists must know this language at an advanced level, to know a great number of English names of drugs, to be able to speak freely in professional language and competently read and write prescriptions.

Difficulty in learning English for pharmacists is a huge number of terms of different specificity. Even learning all subjects in their native language, students receive a lot of new information every day, and it is so hard to remember everything. New terms, concepts, definitions, processes barely fit in the minds of young pharmacists. It is important to help students make learning not only useful and necessary, but also enjoyable and fun.

Let's imaginelearning process in which parallel with the study of vocational subjects, the students studied the aspects of translation into foreign languages of all the terms and concepts. If in studying pharmacology we can compare English words with the names in Russian and Latin, to make an analogy, it is possible for the same time to prepare not only competent specialist but a pharmacist, able to work in both Ukrainian and US pharmacies.

This approach to teaching a foreign language will allow to prepare the student for the great opportunities of working abroad without wasting of time. We are able to give a chance to realize themselves in prestigious foreign firms and loudly declare that a particular institution is able to give the world literate, comprehensive specialists. English opens the door to a huge and exciting world in which you will find a lot of opportunities and prospects. Let us enter into this world literate and ready for its requirements. The future of pharmacy in the literate and educated pharmacists!

# UZBEK

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Uzbeks were formed by mixing of ancient Iranian settled populations with the nomadic Mongol or Turkic tribes who conquered the region in the period between XI and XV centuries. Uzbek is part of the Turkic group. In addition to the language of Uzbekistan is widespread in Tajikistan, Kyrgyzstan, Kazakhstan, Afghanistan and Turkmenistan.

The formation of Uzbek literary language covers three historical periods: the ancient Turkic language, old Uzbek and modern Uzbek language. In the 15$^{th}$ c., thanks to the efforts and work of the poet Alisher Navoi, old Uzbek language became united and developed a literary language, norms and traditions that have survived until the end of the 19$^{th}$ century.

In Soviet times, the Uzbek script has undergone several reforms spelling: until 1927 used the Arabic alphabet, in 1940 - the alphabet, created the Cyrillic alphabet. In 1993, the Uzbek was officially transferred to the Latin alphabet. There are 26 letters and 3 letter combinations. No grammatical category of gender: no agreement in gender, case and number. It is mandatory negotiation subject and predicate in the face, but not necessarily in chisle. In Uzbek there are 6 cases: nominative, genitive (attributive), dative (of the guide), accusative (acts as a direct complement), local (expresses place or time of an action, name acts as circumstances), starting (expresses the subject on which (through which the past which, by means of which) takes effect)).

A specific feature of the Uzbek language is agglutinative structure, which means that the derivation in a given language is carried out by agglutination - accession to the root or base of the word affixes, each of which is unambiguous and has its own grammatical meaning.

In phonetics, grammar and vocabulary strong influence of Persian language. Most Arabisms in the Uzbek language borrowed by Persian.

In the 20$^{th}$ century in Uzbek literary language there was a tendency towards democratization rules whereby it became easier and more accessible.

# THE NECESSITY TO USE ENGLISH FOR THE DEVELOPMENT OF SIENCE

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Necessity of obtaining scientific information requires knowledge of many languages, the number of which is growing. Therefore need in international language of science, seems to me obvious. Language, which will be the second for everyone and one for all. Needless to say, I believe as international language of science most rationally to accept English because it is the most widespread language in the world now. It is language to which first of all scientific works and their summary is transferred, reports are written and pass their discussion on the international congresses.

There is no doubt that by means of English free exchange of information between language collectives is possible. Pharmacists around the world can communicate fluently in English, without feeling any language barrier. Due to its informational content and laconicism in the last 50 years, English has become the language of international communication. **Latin, some time – German, now – Shakespeare's language, played earlier this role**. Therefore, the pharmacist is obliged to own it; differently it will hopelessly lag behind!

The modern science knows no limit. There is an intensive exchange of scientific information, joint researches are conducted. Formed a powerful contingent of our scientists who work in research and educational institutions outside Ukraine. The highly professional activity they make the significant contribution to development of world science and at the same time influence a condition of scientific and educational process in Ukraine. I will give some examples in confirmation of this tendency from biology, discoveries in which (for example, connected with genetically modified organisms) cause alarm in society and demand for the assessment of competent highly qualified specialists.

I cannot say about scientific cooperation of National institute of a cancer within bilateral agreements with foreign scientific and medical institutions and the organizations. Cooperation of area of experimental and clinical oncology with

biomedical institute of Clemson University (USA) In particular, to carrying out the scientific researches connected to the creation of cancer vaccines based on dendrites cells and their clinical application. As well as cooperation with Cavendish Laboratory of the Cambridge University (Great Britain). The aim of cooperation is the joint research in the direction of the magnetic nanotherapy malignancies.

On a number of examples of successful scientific contacts, indicate joint publications in scientific journals. Fundamental works by our young scientists S. Komarnitsky, M. and L. Borisyuki, M. Kolomiyets on biotechnology, genetics, were published in November issue of the Plant Physiology magazine which has one of the highest scientific ratings now. The most important was to be published in English. If you publish the text in Russian, and you will read only in Russia**.** Undoubtedly, such contacts promote support of scientific researches in our country and can be one of real opportunities of improvement of a situation in our science.

It is not less important that we have opportunity to adopt experience of other countries. For example, the lack of a national formulary system in health care Ukraine creates many problems that hinder the effective development of the industry. The British National Form (BNF) has the leading role in evidential informing on maintaining rational pharmacotherapy in Great Britain and many international experts consider it as a world sample of the regulating documents of national scale.

The British national form is issued about 30 years. Its structure is used as a basis in many European countries. The official system allows defining accurately amount of medicines that are constantly used in medical practice, called the formulary list, that considerably simplifies procurement process of medicines, provides rational drug therapy, and so forth.

The basic principle of official system is use of drugs with the proved efficiency of their action at a certain pathological process. In comparison with other countries, experience of Ukraine on the way of introduction of official system the insignificant. For the first time in Ukraine, the regional medicinal form was published in Zhitomir area (1999). It is advisable to use the experience and knowledge of the country in creation of own forms.

Thus, it is possible to tell with confidence that English is one of the most perspective languages for development of science today, makes it possible to unite our knowledge.

# STUDY OF IDIOMS AS A HIGH LEVEL OF FOREIGN STUDENTS INTEGRATION

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Idioms are common to all languages, but in every language they have their own special form of expression. This is explained by the fact that idioms have more complex grammatical and lexical-semantic structure, in which the formation of a much greater degree of extra linguistic factors is involved. All this enables to assume those idioms are linguistic phenomenon in which most clearly reflects the national identity of the language. It's only by a comparative study of two or more languages that we can exactly establish the difference of their phraseological systems. Needless to say, that the closer the compared languages, the more we discover similarities in their idioms.

Let's establish a comparison of some French and Russian idioms. For example, "to be cruelly deceived" is translated in Russian by the idiom ‹‹попасть пальцем в небо›› and in French - «prendre des vessies pour les lanternes» (literally "to take bladders for lanterns"). Similarly, to express the idea that you cannot judge a man by his appearances, Russian people use *«встречают по одежде, а провожают по уму»* and the French - *«L'habit ne fait pas le moine»* (literally *"Clothes do not make the monk"*). These idioms obviously express the people's ethno-psychology and therefore they are by different. From the foregoing, it is clear why most of phraseological unities are literally untranslatable, they are translated into other languages by using idiomatic elements, often built on other images. But this is not always the case. In the study of phraseology foreign audience is always interested to know the cause of this or that idiomatic unity, due to the peculiarities of the culture of studied language's carriers. The most interesting aspect of the study of phraseological units is searching for linguistic parallels. It is easier to remember idioms that are completely or almost completely matching not only by their meaning, but also by the words forming them. For example, those two idioms are matching in Russian and French: *«Acheter le chat en poche»* in Russian *«покупать кота в мешке» («to buy a pig in a poke»)*, «*faire bonne mine à mauvais jeu»* in Russian *«делать хорошую мину при плохой игре» («to have a good face on a bad game»), «il faut battre le fer pendant qu'il est chaud»* is translated in Russian by *"куй железо пока горячо " (« strike while the iron is hot ").*

Many French idioms are derived from the Bible. For exemple *«Rendre à César ce qui est à César»* translated into Russian *"Кесарево - кесарю" ("Give back to Caesar what is Caesar's").* The word "Caesar" in ancient Rome meant "king". It was from him that has been formed the Russian word "царь". Also from the Bible according to the Gospel of Luke chapter 4 verse 24 *"Nul n'est prophète chez soi"* translated in Russian by *"Нет пророка в своем отечестве" ("There is no prophet in his own country").* According to the biblical story, when Jesus, famous for his preaching, returned to his homeland, to Judea, where he met there quite incredulous. "A prophet is honored everywhere, said the son of God, except in his own country ..." Now we use these words, when we see how people sometimes do not know how to appreciate the merits of close relatives or compatriots, and prefer giving honor to outsiders.

# COMPARISON OF RUSSIAN AND UZBEK LABOUR PROVERBS

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Created at different times, under different circumstances and situations, Uzbek and Russian wise sayings carry the essence of the life of every people, their actions, principles and behaviors, and much more. Comparison of Russian and Uzbek proverbs shows how common is the vision of the world, related to various situations in life, which, in turn, promotes understanding and rapprochement between people. On the other hand, proverbs help to better understand the national character of the people, their interests, customs, way of life and traditions. In this paper we set goals and objectives: 1) Select the most relevant and to analyse synonymous proverbs, reflecting the relation of man to work in Russian and Uzbek languages; 2) Trace the change attitude to work, recorded in the language of proverbs in both languages; 3) Based on the content of proverbs, to identify and describe the attitude of the Russian and Uzbek man to the core value of labor; 4) Justify the ethno-cultural content of Russian proverbs about work, based on their relation to the Uzbek proverb relevant topics.

There is a thought common to all nations, but in every nation they expressed in their own way, taking into account the ethnographic, geographic features, customs, mentality, etc. Thus, all the nations of the world have respect for good human qualities: hard work, humility, honesty. In the comparison of Russian and Uzbek Labour proverbs found some absolute synonyms: Дело мастера боится – Иш устасидан қурқади; Куй жедезо пока горячо – Темирни қизиғида бос; Что посеешь, то и пожнёшь – Нима эксанг, шуни ўрасан; Больше дела, меньше слов – Кўп гапнинг ози яхши, оз гапнинг сози яхши; Кто не работает, тот не ест – Ишламаган тишламас; Один с сошкой, семеро с ложкой – Бировлан омоч билан, еттовлан чўмич билан and others. In the Uzbek language it was noted that there are some synonyms of lexical variants of Russian Labour proverbs: Сегодняшнюю работу на завтра не откладывай – Бугунги ишни эртага қўйма (in Russian language: Не откладывай на завтра то, что можно сделать сегодня); Цыплят осенью считай – Жўжани кузда сана (in Russian language: Цыплят по осени считают); Глаза трусливы, руки отважны – Кўз қўрқоқ, қўл ботир (in Russian language: Глаза боятся – руки делают); Не смотри на красоту, а смотри каков в работе – Ҳуснига боқма, ҳунарига боқ (in Russian language: Не смотри на лицо, а смотри на дело/ или /Не тот хорош, кто лицом пригож, а тот хорош, кто на дело гож) and others.

Every culture has keywords that reflect the core values of the people who are native speakers. They form in the minds of the representatives of a culture specific mental structures - concepts that contain a value people's ideas about this recognition

of reality. The concept of "work" is the most fundamental in the ethnic consciousness of the two nations, as evidenced by quantitative predominance of proverbs with this concept:

| Russian | Uzbek |
|---|---|
| 1. Труд кормит, а лень портит. | 1. Мясо ишака поганое, но труд его честный. |
| 2. Труд – дело чести, будь в труде на первом месте. | 2. Под трудом лежит счастье. |
| 3. Воля и труд дивные всходы дают. | 3. Дерево листвой красно, человек – трудом. |
| 4. Ум и сердце в работу вложи, каждой секундой в труде дорожи. | 4. Человек трудом велик, река – половодьем. |
| 5. Зеркало человека – его труд. | 5. Весна реку разливает, труд человека прославляет. |
| 6. Кто любит труд, того и люди чтут. | 6. Труд для умного – слава и честь, а глупому – горе и страдание. |
| 7. Без труда не вытащишь и рыбку из пруда. | 7. Друзья познаются в беде, людей узнают в труде. |
| 8. Кто труда не боится, того и лень сторонится. | 8. Труд – в молодости, отдых и блаженство – в старости. |
| 9. Какие труды, такие и плоды. | 9. Труд приносит удовольствие. |
| 10. Уменье и труд всё перетрут. | 10. Золото проверяется в огне, человек – в труде. |
| 11. От трудов праведных не нажить палат каменных. | 11. Осёл силён своим трудом, кабан силён своими зубами. |

Conclusion: 1.Base and unifying factor in Russian and Uzbek proverbs of labor is the age-old wisdom of the people, boundless love for his native land, the fruits of which appear as a reward for their hard and dedicated work. 2. Almost every proverb exactly conveys the basic idea verbatim or in other ways, revealing the content of the agricultural traditions, the use of specific tools, a special relation to one or the other professions. 3.Main are Russian and Uzbek proverbs - approval of the love of labor and denial of idleness, laziness; respect for the native land, its culture and traditions, advance planning the right kind of work without making mistakes, predicting a successful outcome in accordance with the specified time and general cultural data, exposing the vices and virtues of education. 4. Study the vocabulary of Russian proverbs of labor in comparison with the Uzbek proverbs allows to revive communication in Russian, Russian to make it more vivid, colorful, imaginative, adequate to available culture-forming conditions.

# IMPORTANCE OF THE B2 ENGLISH LEVEL OF FOR THE INTEGRATION INTO THE INTERNATIONAL SCIENTIFIC SOCIETY

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Requirements for young scientists each year are changing and becoming more adapted to the world level. Like never before knowledge of the English language becomes relevant.

In general, the scientific life of the world "runs" in English. This language is an essential component for communication academics, doctors and young scientists around the world. Due to the general globalization and demand for English as in everyday life and as in scientific communication, at this date Higher School can't exist without one of the important components, which is fluent English, as it is a common "international" language of scientific articles, international conferences, symposiums, seminars, grant programs, training and the language of culture. Study of international experience and exchange of scientific developments, information exchange occurs only through the use of English. According to the new requirements for the title of associate professor and professor, any candidate for the degree required to speak English, as it is the key to self-education and self-development.

At the moment, from modern scientist is required: their own to find scientific original sources and assimilate scientific information to acquire the necessary knowledge and be competent in solving practical problems; ability to self-assess problems and find effective variants to solve them by using modern technologies and methods; ability to generate new ideas and take a creative approach to solving problems; communicate and establish relationships in different social groups, use Internet technologies and use the Internet resources.

Knowledge of the language allows us to cooperate with other high school Ministry of Health and MES of Ukraine, with high school in Europe and around the world for collaborative coordination of activities, increase of competitiveness of the scientific staff and improving their skills, educational mobility, allow for a dialog and linkages with the scientific community around the world, combine efforts in solving different global issues, exchange of experience and counseling graduate and doctoral students in research, raising the educational level of students.

Learning language is a long and difficult process, requires the full commitment and as mental as well as financial spending. Language proficiency opens up new possibilities in achieving goals.

# SOME PECULIARITIES OF THE RUSSIAN LANGUAGE

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The interdependence of foreign languages teaching and cross-cultural communication is sure to be indisputable. Cultural peculiarities of different communicators might hinder the process of cross-cultural communication. So, at the present stage one of the main tasks of foreign languages teaching is treating the target language as the real and fully functional communicative means. A widely educated professional needs a language not only as the means of production, but also as a part of the culture of the people who speak this language. The above mentioned provides for wide-ranging language proficiency. The basic principles of the new directions for the language proficiency are: learning the language functionally, in terms of using it in different spheres of society life; generalization of the vast theoretical and practical experience of teaching language for specific purposes; validation and elaboration of methods of foreign languages teaching as the means of communication between professionals; foreign languages acquisition against the background of social, cultural, and political life of nations that speak these languages; development of a model of training for teachers of foreign languages, specialists in international and intercultural communication.

Russian language is a Slavic language. It was formed in the 14$^{th}$ century, when the Old Russian language was divided into Russian, Ukrainian and Belarusian. Slavic languages are still keeping many Indo-European antiquity, as in grammar and in vocabulary. This ancient heritage makes Russian language so complicated, but interesting!

There are many interesting verbs in Russian language. For example, verbs “есть” and “дать” with their derivatives. As you know, they have a completely specific system of conjugation forms: “Я ем, дам”, “ты ешь, дашь”, “он ест, даст”. Or, the verb "хотеть", which is conjugated in singular form according to the first type ("хочешь, хочет"), but in plural – according to the second one : ("хотим", "хотите", "хотят"). "Бежать" – "бежим", "бежите", but "бегут" (mixed conjugation).

There are insufficient verbs in Russian language. For example: "победить". Он победит, ты победишь, а я... победю? побежу? побежду? How to say correctly? You have to use a replacement construction "я одержу победу" or "стану победителем". Because this verb has not I form in singular form, so this verb is insufficient.

The verb can be insufficient because of the sense. Let's take such as “вызревать”. We can say that “фрукты вызревает”, but can we say about ourselves “я вызреваю”, “мы вызреваем”? It would be senseless, and therefore, all personal forms except III form will be impossible. Personal forms of this verb can be at least in singular and plural forms, but “светает” is always in singular form. We know the verb "светать" has past tense, future tense and infinitive. But there is one verb in Russian language, that has only one form: “неймётся”. It has no any other tenses, and even indefinite form.

# SHAKESPEARE`S WORDS TRANSFORMATION TO NOWADAYS

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The research of Shakespeare`s masterpieces is topical because it will help us to find out the words investigated by him and the role he played in forming modern English. The aim of our research is to analyze Shakespeare's plays, to find out words made by him and to prove his influence to the development of the English language. Shakespeare was a poet, playwright, and actor, widely regarded as the greatest writer in the English language and the world's pre-eminent dramatist. In his works there are more than 2,200 words, which have not encountered in writing earlier. Shakespeare experimented with word-formation by combining some lexemes together, adding suffixes and prefixes. Due to these operations new shades of meanings or words with other meanings have appeared. As the English bard not only made up the words, but coined them there is an expression "words *coined* by William Shakespeare ".We even do not suspect that most of usual for us words have first been written in Shakespeare's compositions. There are some examples of words he created.

The word «ADDICTION» was first written in" Othello":

*"It is Othello's pleasure, our noble and valiant general, that, upon certain tidings now arrived, importing the mere perdition of the Turkish fleet, every man put himself into triumph; some to dance, some to make bonfires, each man to what sport and revels his* ***addiction*** *leads him." – Herald*

A very widespread word «ADVERTISING» is from Shakespeare's comedy "Measure for measure":

*"Come hither, Isabel.*
*Your friar is now your prince: as I was then*
***Advertising*** *and holy to your business,*
*Not changing heart with habit, I am still*
*Attorney'd at your service." – Vincentio*

Nowadays we hear everywhere the word «FASHIONABLE» which was first written in "Troilus and Cressida":

*"For time is like a* ***fashionable*** *host that slightly shakes his parting guest by the hand, and with his arms outstretch'd, as he would fly, grasps in the comer: welcome ever smiles, and farewell goes out sighing." – Ulysses*

How will our modern society exist without the word «MANAGER»? It was first mended in "A Midsummer-Night's Dream":

*Where is our usual manager of mirth?*
*What revels are in hand? Is there no play*
*To ease the anguish of a torturing hour?" – King Theseus*

It could be concluded that William Shakespeare affected a lot on the English language, but of course, just because the first written instances of these terms appeared in Shakespeare's scripts. It doesn't preclude the possibility that they existed in the oral tradition prior to his recording them.

# PHONOSEMANTIC FEATURES OF RESEARCH OF UKRAINIAN FOLK NAMES OF PLANTS

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Phonosemantic is the area of linguistics that studies the coordination between the meaning (semantics) of words and their pronunciation (phonetics). The sounds of language not only contain certain information and influence the emotional state of a person, but also carry the hidden images.

This research is the first attempt to investigate the phonosemantic features of the Ukrainian folk names of plants. The problem of our research is the absence of experimental base for research of specific Ukrainian phonosemantic, as such researches require generalization of the reasonable questioning of plenty of respondents to define the phonosemantic specific of the Ukrainian letters. The phonosemantic features of the Ukrainian ethnically conditioned folk names of plants have become the object of study.

The scientists have investigated, that the psyche of a person is being influenced by both semantic maintenance of speech and its sound registration. In the middle of the 1970-th a soviet linguist, doctor of philological sciences O. P. Zhuravlyov conducted a number of researches on this subject. In the book «Sound and sense» he remarks, that sounds cause for us the alike proof and general for all associations with non-sound properties. They can be «good» and «bad», «large» and «little», «rough» and «tender», «light» and «dark» and so on. On the whole 25 different scales are used for description.

While researching the Ukrainian folk names of plants we leaned against experimental data of soviet scientist O. P. Zhuravlyov, and also tried to find out if there is the accordance between botanical description of plants and their phonosemantic features. We have empirically defined, that phonosemantic descriptions of letters, included in the folk name of plant, usually does not contradict each other (although there are exceptions). Obviously, it testifies the unchance of choosing the letter. However, the original appearance of plant often differs from the features provided with the phonosemantic analysis. Hence, we can draw the conclusion, that the theory of O. P. Zhuravlyov requires further working out and verifications.

# YOUTH SLANG

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During determination of relevance of carrying out this type of research, before us such purpose appeared: acquaintance with the general concepts which at the high level open subject of a slang; to investigate and light in work of the sphere of use of slengizm, origins and their short historical data. To carry out the statistical analysis and collecting lexical material for the dictionary; to analyse and reveal lexical units of a slang which are borrowed from a wide range of medical and pharmaceutical vocabulary that at the moment are in the broad use modern scientifically and technologically integrated society.

Subject of research: use youth of slang, medical and pharmaceutical vocabulary

It is necessary for achievement of problems of work: to carry out literary information search in a slang subject, for the best understanding of this lexical sphere, to examine features of collecting and processing of statistical data, for definition of the environment of carrying out research, to carry out search of slengizm for drawing up the dictionary of slengizm of Ukrainian, to analyse medico-pharmaceutical vocabulary which became current in everyday life as a slang.

Relevance of research is shown that society isn't too informed on value of these or those lexical units, some words lost the true value and got new, people forget about it.

The slang is words which often are considered as violation of the rules standard language. These are very expressive, ironic words serving for designation of subjects about which speak in everyday life. Slang words take an important place in the standard of speech, they can be enlisted in lexically stylistic educations. Such words are inherent in informal conversation of people who are connected by a certain community of interests. The slang inherent in various groups of people also plays an important role in the individual's life. Now only certain linguists research this question. Layer of slang youth vocabulary is made in many respects by neologisms which are formed and change together with changes of society. It should be noted that some scientific jargons carry to a slang, thus, without allocating them as independent lexical group, and a slang define as special lexicon, and, used for communication of groups of people with common interests.

Conclusion: after acquaintance with thematic literature some experimental actions were carried out: collecting quantitative information for further understanding of a subject immense earlier and definition of audience for carrying out further experimental actions; collecting lexical material for the dictionary. In work was carried out, the analysis of slang words which are collected in the dictionary that is presented in appendices and it was revealed: the considerable volume of the words used in the daily speech is a lexical volume of medico-pharmaceutical branch. The these results which are carried out in work can be applied to further researches in similar branches.

# WHERE CAN I GET A JOB WITH A DEGREE IN PHARMACY?

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**Introduction.** Specialized education –is an obligatory condition for working in the pharmacy business. There are two ways to get it. The first one is to go to a pharmaceutical school or college - at the end of training you receive a diploma and certificate of the specialist, which is issued automatically, without additional education. The second one is to go to the Faculty of Pharmacy in the Medical Institute - the graduates receive the diploma of a pharmacist, attend internship, after which become owners of a specialist certificate giving the right to work.

**The topicality.** The topicality of this work is due to the fact that there are many opportunities at this time for the graduates of the University of Pharmacy to start their careers, and we outline the most important ones.

As a rule, a druggist can be seen in a pharmacy or at work in a pharmaceutical enterprise. But it's far not all of workplaces, where druggists are needed. Let us enumerate the basic places from them:

1. Certainly, a pharmacy. A druggist can release medications and other commodities that are on a counter in a pharmacy. Besides, a druggist in a pharmacy can perform other work: to prepare medications and powders or analyze the composition of medications.

2. Pharmaceutical enterprises. They cannot operate without narrow specialists such as druggists. In general most workers of pharmaceutical enterprises graduated from institutions of higher learning or medical college, i.e. have pharmaceutical education.

3. Laboratories (control-analytical, judicial, etc.). In a control-analytical laboratory a druggist can hold any position - from a laboratory assistant to the manager of a laboratory. Druggists sometimes work in judicial laboratories, getting position of judicial chemist. Another variant of employment is a laboratory of perfume plant.

4. Managers of pharmaceutical companies (pharmaceutical representatives). Today it's one of high-paying positions for those, who got corresponding pharmaceutical education.

5. Own company. Druggists and pharmacists have a right to open own firms or companies. Mostly pharmacists open own pharmacies or business.

**Conclusions.** At present a pharmacists, in addition to possessing skills of the profession, must know the modern sales techniques and basic principles of marketing. Shortage of personnel causes increased concern about young professionals. Network pharmacy gladly take for work senior students, offer them a flexible schedule, create their own corporate programs of vocational education and training, provide training on various topics - from the study of new pharmaceuticals and ending with the psychology of behavior and work with the client.

# METAPHOR IN ECONOMIC TERMINOLOGY

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Determination of unknown through known is one of the most universal methods of cognition of reality. Metaphorisation in this river-bed becomes the way of thinking, and productive variant of creating new terminological connections at the same time. Economic terminological system is until now being actively developed. We, the future economists, are deeply interested in the question of potential of scientific metaphor in our domain, in particular at implementation of nominative function (i.e. naming of different economic phenomena).

The object of our research is metaphorisation as the means of cognition of the world and scientific nomination. The subject is the scientific metaphor (binary terminological combinations) in economic sphere. The actual material has become the edition of the «Dictionary of the economist» (After the release of S.M. Goncharov). We have identified 86 metaphorical binarms, among those are «escape from money», «money injections», «frozen account» and other. Complex approach has been used in the research, in particular, such methods, as descriptive, supervision, comparison and method of semantic-component analysis.

For the studied metaphorical binarms the transference on the basis of functional likeness of two phenomena is typical. From the position of morphology the most frequent construction is *adjective* + *noun*, less frequent are *noun* + *noun*, *participle* + *noun*, *verb* + *noun.*

The practical value of the research consists in the fact that its results can be drawn at the lectures of «Ukrainian Language (of professional orientation)» for the students of economic specialities (for example, while study of the topic «History of development of Ukrainian terminology. Terms and top-level names in the scientific speech. Methods of creating terms»).

# ARABIC LOAN WORDS IN THE RUSSIAN LANGUAGE

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Borrowing – an integral part of the operation and the historical change of language, one of the main sources of replenishment vocabulary. The result of this process is language appears and lays down some foreign language element.

Russian language was influenced by the different languages at different times. Anglicizes, Gallicisms and Germanisms are traditional linguistic borrowings. According to researchers, Arabisms that have traditionally been considered among Orientalism, occupy a significant place among the borrowing in the lexical system of the Russian language (I.Y. Krachkovskii, A.E. Krymsky). Arab borrowing (Arabisms), by which we mean the word originally of Arab origin, directly or indirectly borrowed Russian, attracted the attention of a number of linguists (T.P. Gavrilova, I.I. Ogienko, I.U. Asfandiyarov). Number of words that has adopted the Russian language from Arabic, is greater than 450.

Borrowed vocabulary reflects the ethnic contacts, social, economic and cultural ties between the language communities. Just as Latin was the language of scholars in medieval Europe, Arabic was the language of science to the ancient East. Some Arabic words have been borrowed Latin, and then from the Latin were in other languages.

Arabic is the source of penetration of lexical units according to the following thematic classification: flora (*шафран, хна*); fauna (*газель, жираф*); geographical features and climatic phenomena (*сель, муссон, самум*); names associated with social status (*эмир, шериф, визирь*); clothing items and materials from which they are sewn (*бурнус, атлас, халат, бахрома*); scientific terms (*алгебра, цифра, азимут, алхимия, надир*); special places for the accomplishment of prayer, various clerics (*имам, муфтий*); collection of canons of Islam and its components (*Коран, сура, ислам, шариат*); Eastern sweets (*халва, рахат-лукум*). Arab borrowing penetrated into the Russian language through the Turkic languages, Spanish, French, German and Polish. Direct borrowing hit the Russian language because of religious contacts, a Muslim religious terminology, astronomical, scientific vocabulary, fairy-tale characters, geographical and botanical terms. Some Arabisms so adapted to the Russian language, which form derived words and meanings. They are part of phraseological units.

Many borrowings under the influence of the Russian language undergo significant phonetic, grammatical and even semantic changes, adapt to the phonetic, grammatical and semantic laws of the given language. The process of assimilation may be so deep that foreign origin of such words does not feel bearers of the language and is found only through etymological analysis.

## SECTION № 19

# PSYCHO-PEDAGOGICAL FUNDAMENTALS OF FORMATION OF FUTURE SPECIALIST IN MODERN HEIS

# FORMING OF COMMUNICATIVE COMPETENCE OF FUTURE SPECIALISTS

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The question of communicative competence of specialist, assisting successful self-determination of young people in the world of labour, continuous education, interpersonality public relations, became actual, but most important - this one of basic terms of actual development and self-realization of personality. Therefore the task of educational process is forming of communicative competence as parts of professional preparation of specialist.

Lately more intent attention of scientists the problem of mutual relations of specialists began to attract in professional activity, and also mutual relations of subjects of educational process.

Researches show that about 70 different decisions, including administrative, are accepted in oral, in the process of business co-operation, effective communication.

Character of business contacts renders decision influence on efficiency of joint activity in particular educational, in case of educational process. Updating of the system educations are bound to the ideas of humanizing. It entails the change of models of educating, support is done on the personality-oriented model that traditional forms of co-operation taught and student translates on subject - subject basis. Subject experience is determined by objects, presentations, concepts, operations, receptions, rules of implementation of actions, emotional коды personality senses, options, stereotypes, that especially meaningfully for establishment of effective communications.

A subject is subject relations in pedagogical schools have features as compared to subject - by subject relations at school. These features are rich in content descriptions of subjects composition of students, single having a special purpose options receipt of profession, presence of social experience, experience of communicative activity, maintenance of communicative, material intended for

mastering in the process of co-operation, communicative competence as component of professional knowledge.

Before to examine the methods of forming of communicative activity of subjects of educational process, it is necessary to set forth, what plugs in itself such concepts, as communication, communicative capabilities, communicative abilities, communicative competence, and as they are reflected in an educational process.

The analysis of literature allowed to define the next going near formulation of communications - a report, communication, is a communication; a specific form of co-operation of models in the processes of their cognitive-labour activity is a process of exchange by information is a semantic aspect social co-operation. Thus, communication is independent part of process of communication and specific form of co-operation of subjects.

In a pedagogical process communication comes forward as a polyfunctional condition of communication and executes the row of functions: informative, motivational, social, developing, educator and other. In socially-psychological sense communication is a process of information transfer from a respondent to the recipient. For plenitude of communication it is important to know an effect are changes in behavior of person, that take place as a result of pick up a message.

Distinguish the different variants of communications. Most expandable is approach taking into account three types of results а) change in knowledge; б) change of options; в) change of behavior of recipient. Efficiency of communication is set: by а) nature of information generator; by the б) features of forms of communication and maintenance of reports; by a в) situation in that people get information. In researches distinguish the different types of communications pedagogical, business, mass, interpersonality, subject etc.

In an educational process the special attention is spared to pedagogical communication at that a teacher comes forward either directly as an information generator or as an organizer of her search.

Communication supposes the exchange of different family information, knowledge, skills and abilities during co-operation of people. Nevertheless, it is frequently necessary to run into a situation, when in the process of speech co-operation of exchange does not take place information.

# THE MAIN CONDITIONS OF UNIVERSITY EDUCATION IN THE MODERN EUROPEAN UKRAINE

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As we all know, modern society requires some sorts of degree to get successful job. A lot of people face difficulties, while trying to achieve a degree. People are different, we can't use the current educational "system" to everyone, since world is moving on, and we are no longer stuck at the 20th century. Ukraine is heading towards Europe Union, so changes must be done. First of all it will be connected with educational system. Ukraine, as a part of the Soviet Union saved a lot of good and bad things from Soviet Union. Today, the huge factor that keeps a lot of brilliant minds leaving Ukraine – is our government (or at least how they treat people who decided to go into science). Every modern European country has a grant system for perspective students, and a lot of programs for exchange students. Ukrainian educational system should be changed by the government, so it could be equal to European or American systems .

We guess, the important condition, that keeps person at the university is the motivation of having bright future and perspective job with ladder climbing. The person must be motivated to study by himself or by someone else. The second important condition – is the check of knowledge, as we understand, that most people are becoming irresponsible without pressure on them. The third factor – is the way of teaching the subject. The lecturer should intrigue students about subject, as having boring lecturer ends up at zero effectiveness The fourth factor – is the student responsibility, the person should know why he has came here and what for, since it's the huge handicap for achieving a degree. One of the biggest problem with self-learning is the learner. Innately, most human beings tend to be lazy or to start things and never finish them. It's not a secret, that a person that is not interested in his job won't do any better even with mental and economical pressure on him. That's not to say that it's impossible for someone to become successful through self-learning, but

most people lack the initiative and drive to accomplish it. This is where the university environment steps in and provides a structured format with deadlines and incentives built in to help it's students stay on task and learn the required information in a timely manner. Additionally, students that have successfully completed the rigors of university academics demonstrate their ability to keep up with an intense workload, meet deadlines, and produce quality work. Some people show themselves with scientific articles and so on they get recognized, some people don't, and its pretty much connected with people's mentality, some people are creative and have will to power, some of them just tend to follow the given orders without asking question. Those are skills that employers are looking for, adding more reason for employers to look for degrees from their applicants. The fifth one, and probably one of the most important factors, that affects achieving a successful degree is the workplace (This factor gets huge impact on the desire to continue education at the university and useful connections can increase chances of finding a good workplace).

We are living at the rise of the capitalism system and when it comes to hiring for a new job position, most employers will have to sift through hundreds of resumes. Usually, employers will use a degree to quickly filter their choices Hiring a new employee is a big risk and expense for companies as they invest time and money into training specialist for position. In order to limit the risk of this process, employers need some kind of system to prove the credentials and qualifications of the applicants. In our world today, employers use a university degree as assurance that their future employee has the background university and skills required for the position. While there is more to university than getting a degree, when it comes to getting a job, that degree will do wonders.

The sixth one is the society, as a main reason, it pressures person from childhood what he should do and shouldn't . As instance, people take this without tend to doubt in these statements. Some psychologists name it as portrait of authority.

All of the listed factors affect in a hard way mentality of future specialists and make huge impact on their life decisions, as only determined and confident person will achieve desired degree with all of its benefits.

# IMPROVEMENT OF SYSTEM STUDIES STUDENTS OF HIGHER SOLDIERY EDUCATIONAL ESTABLISHMENTS FROM FIRE PREPARATION

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The process of modern studies requires from scientifically-pedagogical workers (SPW) permanent comprehensive development and use in the educational process of the newest technologies and methods of studies.

A man gets information a few methods by means of sense-organs. She have visual and auditory perceptions of information, which require permanent perfection and training, most developed. For activation of comprehensive cognitive activity, it is possible to involve other mechanisms, for example: abstract thinking process - by the use of facilities of evidentness (virtualness) in studies; process of perception - by getting up of the emotional state; process of attention - by the individual going and bringing in near independent work; a process of memorizing is forming of reflexes of sequence of implementation of actions, due to frequent reiterations.

Coming from it, studies are after fire preparation, where material is by means of the use of the real standards of weapon and overall-gravimetric models, computers and projectors for the show of sliding seats, films or virtual programs, held with the higher coefficient of mastering.

Acquisition of strong knowledge of materiel of weapon, abilities and skills of implementation of receptions and rules of firing from her, arrived at by students on all types of employments after fire preparation, and rises on the rifle training. However, reviews from parts, which act on young lieutenants, and long-term analysis of realization of employments after fire preparation, specifies on weak theoretical and practical preparation of students.

Implementation of individual tasks gives to the student possibility in further correctly to prepare данні for firing, to check and bring a weapon over to the normal fight, promotes knowledge of materiel of weapon, receptions and rules of firing. The sequence of implementation of individual tasks, what students, must work and accounting for them, certainly by the executable code of educational discipline "Fire preparation".

On employments SPW explain personalities of implementation of individual tasks students and specify in what terms they must be worked and protect. During the 5-и years of studies every student must produce 20 practical works from which one control and two calculation-graphic.

This variant of realization of practical employments after fire preparation, gives possibility of SPW up to a point high-quality to conduct employment, and to the students consciously to promote the level of theoretical knowledge. Permanent control after the exposure of weak parties of theoretical preparation, gives possibility of SPW anymore to spare attention to the questions which not in a complete measure or in general not mastered.

However, one of problems, which for today exists in fire preparation, as to the important constituent of military-professional preparation of future soldiery specialists with higher education, there is impossibility of man to imagine the trajectory of flight of bullet in three-dimensional space, and the more so yet and influence of weather terms on her rejection. To our opinion, there is a necessity Tom for development and introduction in the educational process of complex of the educational-training computer programs.

An idea which is offered consists: at first, in creation of computer software, which will allow to study materiel of weapon, id est evidently to show her parts and order of sorting out in three-dimensional space; secondly, to create the virtual terms of firing from the basic types of small-arms; thirdly, to bring a weapon over to the normal fight; fourthly, to carry out the evaluation of level of knowledge and abilities of students, by means of the electronic testing.

Except that, it is important to mark that the complex of the educational-training computer programs also must contain a background paper from history of creation of weapon; theoretical material, for the study of structure of weapon; auxiliary material is for scientifically-pedagogical workers taking into account the modern requirements of leading documents; a task and examples of their implementation, sliding seats and video films, are from corresponding themes.

Such approach carries system character of methods of studies which will promote :

- to upgrading of realization of lessons;
- to the best mastering by the students of bases and rules of firing, to the increase of level of knowledge of materiel and ballistic data of small-arms, acquisition of hard practical skills of dataorigination for firing.

# FORMATION HEALTH SAVING COMPETENCE IN THE TRAINING PROCESS FUTURE PHARMACIST

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Objective: To identify the role disciplines “Life safety” and “Labor protection” for health and safety future pharmacists.

Why educate for health, safety and well-being? World Health Organisation (WHO) defines health as ‘a state of complete physical, mental and social well-being’. Modern pharmacy companies that place heavy demands on the health and safety specialists as well as to the employees about their qualifications in the areas of personal security. For future pharmacists the education focus will be on social and professional skills promoting the concept of health, safety and well-being at work, and in life in general.

Results. Students should play an active role in the health and safety aspects. They feel ownership of their environment and how it is managed and feel motivated to play their part in safety and health at future profession. Ensuring the health and safety has always been a serious issue for professionals in all areas. Major directions aimed at creating a culture of safety and competence in the field of personal, social and environmental security are formulated in the concept of national education policy. An individual's ability to use the knowledge and skills to ensure safety in the area of professional activity is the main purpose of training. Profession of pharmacist is socially responsible because it is aimed at preserving and strengthening the health and disease prevention. Formation of health saving competence is carried out in the health disciplines such as “Life safety” and “Labor protection”, which main criteria indicators of safety work, from the points of view of health preservation are considered:

- Sanitary-hygienic (rational illumination, dust in working zone air; increased or reduced temperature air; increased noise level, etc.)
- Organizational-technical (regime of work and rest; monotonous character of work; ergonomics. rapid change of production processes, information etc.);
- Psychological (neuropsychic overstrains: mental overstrains, overstrains of attention and analyzers, psychological and emotional overloads).

Conclusions. Disciplines “Life safety” and “Labor protection” enables acquisition of the skills, knowledge and attitudes necessary to ensure competency in all aspects of work, including health and safety, necessary to prepare pharmacists in accordance with international standards.

# RESEARCHING OF PHYSICAL PREPAREDNESS OF STUDENTS-PHARMACISTS

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Current healthcare reform provides improvement of pharmaceutical education for the purpose of training, which would meet new international standards, both from the standpoint of view of profession training, and from the point of view of physical health.

Analysis recent studies of the level of earning capacity and health of students, has shown that to improve the health of students, it is necessary to use the means of physical culture and sports, aimed at improving the development of their motor skills. However, the health benefit from exercise requires a system of organizational measures and regular monitoring of main indicators of the body: physical development, functional state of the respiratory, autonomic and cardiovascular, nervous systems of students.

High level of academic workload, more than 30 hours per week, its uneven distribution over days and weeks, not well-arranged organization of extra-curricular activities — all this have a negative influence on the indicators of the functional state of the organism pharmacy students.

Necessity of the pedagogical supervision for health pharmacy students justified in our work. Morphological and functional parameters have been studied, based on which the adaptation indicator was defined, and the level of physical health and physical condition of the examined was found. The study involved 20 guys and 80 girls, students of National University of pharmacy. The definition of anthropometric indicators showed the presence of deviations in the operation of the major systems of the body pharmacy students that in the future may adversely affect the professional activity of employees of pharmaceutical establishments; the number of indicators that characterizes the physical development of the person, namely life index, is significantly below established standards; assessment of adaptive capacity showed intense adaptation mechanism, 79% of men and 44% women. Establishing the level of physical health surveyed showed a significant percentage of such students, which level of health corresponds to the lower-middle and low level: men are revealed 52%, and among women — 73%.

The difference in the assessment of adaptive capacity of the body of men and women is noticeable. Low level of physical development of girls can be explained by the higher sensitivity of the female body to environmental factors: complex socio-economic, climatic and geographical conditions in the area, as well as low physical activity of girls.

We think that correcting this negative situation rests in the physical education of students. Through measures — namely, the competition among students shows athletes, visiting competition as fans, which aimed at positive attitude towards physical education, the formation of students' motivation to healthy lifestyle and achieve high athletic performance.

# PEDAGOGICAL CJNDSTIONS OF THE INTRODUCTIONS OF THE INTRODUKCTION OF INTERACTIVE LEARNING IN THE PROCESS OF PROCESSIONAL TRAINING OF NURSES

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Today in the education system of Ukraine, as elsewhere in the world, increasing attention is focused on viewing and changing objectives, content, forms and methods, tools, and generally the whole organization of the educational system in accordance with the requirements of the time. The search for new forms and techniques of the discipline "Nursing" in modern conditions of reforming the system of higher education phenomenon is not only natural, but necessary. Online training should be aimed at the formation of a strong personality, possession of knowledge, skills, and practical skills. These conditions are met by the use of interactive teaching methods, which constitute a system of rules of productive interaction between those who are learning, mastering new skills, acquiring new knowledge and the opportunity for self-realization.

Modern study of the research problem in the training of Junior specialists in the medical College give grounds to ascertain the presence of conflicts between: rapid accumulation of scientific and pedagogical knowledge and their assimilation of future health workers; the integrity of specific tasks on the formation of the individual employee health and fragmented training at the medical College; the need for the use of interactive methods.

The purpose of this research is to substantiate theoretically, to develop and experimentally verify pedagogical conditions of the introduction of interactive teaching methods in the process of professional training of nurses.

To date, interactive teaching methods help nurses to solve problems, to solve problems, to find solutions to critical situations. In addition, they stimulate

the process of interpersonal communication, help establish a favorable psychological climate in the group, largely makes the learning process more efficient and productive

T. Wolfovski emphasizes the importance of interactive skills as those that provide a harmonious and creative occurrences of the individual in social life. Given the role of interactive skills for personal development, you can merge them into two groups.

Surveys, questionnaires, interviews with students indicate that the use of the above-mentioned interactive teaching methods enhance cognitive activity of students and contribute to high-quality training of future tutor, personal development, and develop highly motivated to learn and develop professional skills. It is important to note that in the process of a business game formed the consciousness of belonging of its members to the team; together is determined by the degree of their participation in the work; the relationship of the parties in addressing common challenges; collectively discusses issues that forms the severity, restraint, respect for others, care to other participants in the game.

Thus, the introduction of interactive teaching methods in the preparation of nurses in teaching professionally-oriented disciplines in Nursing at the medical College improves motivation, also helps promote critical and creative thinking. The advantage of online learning is that the students apply all levels of cognition (knowledge, comprehension, application and evaluation).

Interactive learning involves the interaction of students of the educational process in order to jointly deal with educational issues, understanding. In the interactive learning apply many techniques that help teaching, learn new material, are used to test students ' knowledge. They help in research, creative, cognitive activity of students. The use of interactive teaching methods involves the following ideas: namely, that the activation of cognitive activity of students; updating reference; individualization of the educational process; to provide an opportunity to students comprehend the importance of the knowledge to use them in practice.

# CONDITIONS OF TRAINING COLLEGE STUDENTS EDUCATIONAL MOTIVATION

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Currently, the efficiency of vocational education is topical. Among the contemporary issues of pedagogy, which require primary consideration, the problem of cognitive activity and students' creativity development is complex and multifaceted. Therefore, one of the promising areas is the development of students' educational motivation.

Motivation of educational activity is a complex psychological phenomenon, controlling which in the learning process requires keeping its structural organization and dynamism. Educational motivation is a special kind of motivation characterized by a complex structure, one form of which is internal and external motivation. Stability, the relationship with the level of intellectual development and nature of training activities are significant characteristics of educational motivation.

Students' professional motivation is especially important for successful mastery of future medical profession. Professional motivation acts as an internal driving factor in the development of professionalism and personality, as only through its high formation level, the effective development of professional education and personality culture is possible. In this regard, a student after getting the specialty is included in the activities of health workers - professionals, but today there is the lack of the proper training needed to the professional implementation of this activity.

The researches in psychological and educational sciences have already shown that the high level of motivation and students cognitive interest to the subject is the essential condition of perception efficiency, memorization, comprehension of educational material and its subsequent using in professional situations.

Psychological and pedagogical studies have shown that student's motivation, his perception, memory, attention and thinking efficiency have significantly increased in the circumstances where:

- teaching and control methods are varied. Constant changing of cognitive activity types, their forms, especially in the condition of positive emotions, makes

cognitive process interesting, exciting, diverse, and therefore more effective for a student.

- a teacher takes measurements and evaluates the students' relation to the discipline and methods of working with learning material (pilot survey);

- students are systematically familiarized with learning objectives at each class;

- students are regularly informed about the teaching techniques (especially at practical classes while mastering clinical skills);

- educational literature is chosen so that the studied material could influence the student's emotions and feelings (future patients empathy perception development);

- learning process is provided with a sufficient number of problematic tasks, clinical problems and situations that stimulate student's mental activity;

- the process of mastering object active transformation by the student is organized;

- targeting students both to their own learning activities methods and to future nurse professional activity is provided;

- targeting students on independent knowledge acquisition, the development of the internal demand for self-development is provided;

- the possibility to exercise self-control and self-esteem stimulating student's consciousness and activity is provided;

- support of success is provided;

- confidence in the interpersonal communication between teacher and student in terms of cooperation and partnership based on dialogue, that provides mutual understanding, is made.

Based on the material given above, we can make the following assumptions:

Firstly, the motivation of medical college students' educational activities is the subject to the definitions and characteristics common in psychological and pedagogical literature, but it has its own characteristics. These features are determined by more conscious professional orientation of future nurses training.

Secondly, activities motivation will be more stable and higher in students using the conditions given above as necessary training tools.

# FORMATION OF PROFESSIONAL SKILLS AND KNOWLEDGE IN THE FUTURE NURSES

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Analysis of scientific conferences and publications nurses in psychological and educational information sources indicates the urgency of solving the problem of formation of professional qualities and skills of future health care setter.

Therefore the main task of training future nurses is to train qualified personnel with a high competitive level of formation of professional knowledge, abilities, skills and creative thinking.

Analysis of the duties of nurses to determine the structure of their professional activities. Thus, the range of professional nursing duties varied and includes issues of medical diagnosis, perform medical procedures, emergency care to patients of nursing, resolving health and medical and social issues and more.

The process of training nurses involves mastering a significant amount in terms of skills and practical knowledge, skill and performance of each action should be extremely high. It makes extensive use of algorithmic technologies in the training of future nurses.

Based on the structure of the nurse and approaches to classification algorithms in training future professionals of discipline «Nursing» encouraged to develop: first, standards of learning and practicing action levels: skills and solve professional problems; Second, create algorithmic instructions of varying degrees of complexity and synthesis, such as: simple algorithms, complex, composite and complex practical problems, as well as their professional skills algorithms and algorithms of the total solution based on theoretical and practical training and testing professional tasks.

The use of this approach in the formation of professional abilities and skills will help the quality of training competent nurses.

# THE FORMATION OF THE BASIC PROFESSIONAL SKILLS OF FUTURE SPECIALISTS FOR FOOD INDUSTRY

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The National strategy of education development in Ukraine for 2012-2021determined

that Ukraine's integration into the global community requires continuous improve-ment of the national education system , the search for effective ways to improve the quality of educational services, testing and implementation of innovative pedagogical systems, modernization of the educational content and its organization adequately with global trends and requirements of the labour market ensuring the continuity of education and training throughout the life.

Nowadays we have an urgent need to understand the status and problems of profess- sional training of specialists in all spheres of public life. Because the qualification and professional skills of the employees have a direct impact on the production rate, the formation of spiritual values of the society.

The food industry is one of the largest and most important industries of Ukraine. The state of the economy and security of the state, the development of internal and external markets, and the standard of living depend on the level of its development and operation stability.

A high-quality training of specilists able to meet the growing needs of consumers and manufacturers in the industry is necessary for further development of the food industry and ensuring the profitability.Today dramatic changes associated with the extension of common forms of work organization for food enterprises,the improvement of the structural- logical scheme of functioning and in the circuits of production and technological processes of production, with the introduction of new quality control systems are observed in food industry.Contemporary conditions for the existence of food companies on domestic and foreign markets demand a high level of professional training for a specialist of food industry.

Modern specialists of this sector of the economy should have an appropriate level of knowledge in the disciplines of professional and practical training, professional and practical skills, which in turn will be an important basis for professional decision of specific production situations in the food industry, as well as to the attainment of the highest degree of professional experience - professional skills.

Professional training is the result of the teaching profession in higher education institutions (HEI)

The level of competence is a measure of how well or poorly professional training was implemented. In this context we note that in section 1, article 1 of the current Law of Ukraine "On higher education" the essence of the concept of competence is defineded.

Namely, competence is a dynamic combination of knowledge, skills and practical skills, methods, professional, philosophical, and social qualities, which determines a person's ability to successfully carry out vocational and further training activities and is the result of learning at a certain level of higher education.

Based on the Industry standard of higher education, namely, educational qualification characteristics of Junior specialists in the areas of training 6.051701 "Food technology and engineering"we define that competence is an integrated feature of personality traits, the result of preparing the graduate to perform activities in certain professional and personal-social domains (competencies), which is determined by the required volume and level of knowledge and experience in a particular field.

In other words, competence is a certain set of competencies.

So, to become a qualified technician-technologist a future professional should master the socio-personal, general scientific, instrumental, general professional and technical-professional competences

The formation of the respective competences takes place in the process of acquiring various types of systems skills on the basis of relevant knowledge and practical skills.

Given the above, we propose to analyse all innovative technologies to choose the way to attain the above competencies.

For this, we think that Processing and Food Industry College of Petro Vasilenko KNTUA should reconsider the structural-logical scheme of training of young specialists for food technology to determine the trajectories of the phase-specific activities on the formation of basic professional skills of future specialists

On its basis adequate structural-logical scheme of academic disciplines (especially the disciplines of professional and practical training) should be created.

It means - going from the general to the particular.

Thus ,all given above will provide an opportunity to define clearly what competencies should be formed in the future specialists during each particular lesson in a specific academic discipline.

# PLANNING AND MANAGING OF SELF-STUDY OF STUDENTS-PHARMACISTS

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Humanitarian significance of physical culture is to create sustainable motivation for a healthy lifestyle, developing students ' needs for physical self-improvement. The contribution of physical education in higher education should be providing students with all aspects of knowledge about the scientific foundations of physical culture and healthy lifestyle, as well as in mastering the system of practical skills, ensuring the preservation and strengthening of health, mental wellbeing and improvement of its psycho-physical abilities and personal qualities.

Self-study, physical exercise, sports; tourism should be an obligatory component of a healthy lifestyle of students. Independent study students contribute to better assimilation of educational material, can increase the total time of exercise, accelerate the process of physical perfection, are one of the way to promote physical culture and sports in the life and leisure of students.

Self-study can be carried out in all conditions, at different times and include tasks carried out by the teacher or self-made program. This form of training each year is becoming more popular. Specific directions and organizational forms of self-study depend on gender, age and health status, level of physical and functional training involved. There are **three basic forms** of self-study: morning hygienic gymnastics, exercises during the study day, separate training sessions.

Students in the planning and conducting self-study should be remembered that during the preparation and passing tests and examinations intensity and amount of self-study should be somewhat reduced, giving them, in some cases the form of leisure. With planning separate training session’s total training load, varying with the waves of mental stress on training sessions throughout the year, every year must have a tendency to increase. Manage self-study sessions is to determine the state of health, level of fitness, sports readiness involved at each time interval training and in accordance with the results of this determination to adjust various aspects of employment in order to achieve their maximum efficiency.

Objective assessment of the state of working gives the application of various tests.

The final accounting is carried out at the end of the period or at the end of the annual cycle of training sessions. This account involves compiling data of health and fitness, as well as data volume training work, expressed in the time taken to perform the exercises and the number of miles runs track and field, cross-country skiing and swimming varying intensity with the results shown in sports. On the basis of this comparison and analysis adjusted plans training sessions for the next annual cycle.

# IMPROVEMENT OF TESTING PROCESS OF STUDENTS IN MEDICAL UNIVERSITIES

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Critical need to review content and form of educational process and current knowledge assessment system has appeared during the reforming of educational system, i.e. creation of European system under the conditions of political, social and economic transformations. The results of educational researches prove that control and assessment of knowledge are essential component of educational process. It is implicated with studying of material, its understanding, consolidating and application.

Continuous improvement of educational, methodological and organizational work by generalization and distribution of advanced experience, prevention, finding out and removal of disadvantages in the organization and management of academic activities is a main objective of control in higher educational establishment.

Educational process requires system monitoring of students' work during the academic year. Thus, control purpose is also stimulation and increasing of students' motivation towards regular self-work, increasing the objectivity of students' academic performance rating.

Different special tools are used to ensure technical support of students' academic performance rating. This comprises of tools for group control – computer control-teaching complexes, which realize ideas of programmed education. Combination of efficient management by cognitive process and systematic computer control of success contributes to increase quality of educational process.

Computer-based testing gives an opportunity to realize main didactic foundations of leaning control: individual character of test and evaluation of

knowledge; systematicity of control; principle of thematicity; differentiated estimation of students' performance; identity of teacher's requirements to students.

Discipline «Medical chemistry» for specialist training in the speciality «General medicine» is pre-requisite subject. Studying of medical chemistry on the medical and bioorganic chemistry department is carried out during I and II semesters for first-year students of KNMU.

We use different forms of current control of students' knowledge during the training course on the subject «Medical chemistry». Every practical lesson students' knowledge is estimated according to the several criteria: done home-work, answers on obligatory questions, results of written control and also oral interview with teacher. To improve studying of students at home and assimilating what they read, we have developed computer program «CONTROL». This program includes tests of forming type for students' self-work on the subject «Medical chemistry».

To stimulate students' self-work we proposed electronic forms of test for 18 terms of practical lessons. Using this electronic variants students can work bringing the computer technology in the room for self-work on medical and bioorganic chemistry department, in the library, at home etc.

Testing program for self-work on «Medical chemistry» is composed in such manner that student should think logically, and not just try to guess the correct answer. Thanks to tests student can not only prepare for practical lesson but answer the questions of current control and pass informative modules on «Medical chemistry» successfully.

Program «CONTROL» has diagnostic character, focused on detection of failure cause made by students, and on identification the reasons of skill gaps.

Thus, stressing the need of students' self-work for every practical lesson we have propossed computer program «CONTROL» on the subject «Medical chemistry». This program helps to get higher effectivity at educational-cognitive activity of prospective physicians and increase level of qualitative and absolute success in studuing on «Medical chemistry».

# INTRODUCING PARTIALLY RETRIEVAL INDEPENDENT WORK OF STUDENTS OF MEDICAL COLLEGE

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The updated modern National Strategy of educational sphere reformation leads to the implementation of effective approaches to independent student's work as a leading form of the learning process.

The purpose of these materials is to highlight the features of introducing partially retrieval independent student's work (ISW) in teaching professionally-oriented disciplines "Microbiology, Virology and Immunology with Microbiological Diagnosis" in a medical college.

According to the classification proposed by P. Pidkasyst, the following types of ISW should be distinguished: those that are to be performed on samples (reproductive); by reconstructive variation; partial search (heuristic) and creative research. Partially retrieval ISW is associated with resolution of specific issues and problems outlined in lectures, seminars, laboratory works, workshops and provides partial activity construction in the new situation, meaning the organization of productive processes of students' minds. The analysis of psychological and educational researches can define effective teaching methods that allow to organize partially retrieval ISW. Among such are: role-playing, the case method, creating mental maps, the project method and so on.

The purpose of the Case (from English "case" – situation) is to analyze, by the joint efforts of students, the learning situation (case) and work out its practical solution, after – to evaluate the proposed algorithms to resolve the situation and choose the best option in the context of the problem. Types of Cases: illustrative learning situations, learning situations with the problem formation, learning situations with independent formation of the problem, applicable exercises.

In the process of ISW on the basis of KBMC № 1, the teachers of the course "Microbiology, Virology and Immunology with Microbiological Diagnostics" implemented the case-method. Students received schemes of microbiological diagnostics, special parts of films and video materials, professional medical journals with characteristics of modern diagnosis methods, prevention of diseases. The

students were given the task to carry out an independent analysis of documents and act as experts so that in their future careers they would act more carefully and responsibly while diagnosing diseases.

It is important to note that the resolution of situational problems in medical colleges is possible both during classroom time and during extracurricular organizations of ISW. Each student solves a situational problem by him/herself, offers the suggestions for its solution, which are presented for a group discussion.

The research results and works by T. Byuzen are put into the basis of creating a mental (intellectual) card, or intelligence card. Intelligence Cards were created by the researcher as a tool which can help use both hemispheres of the brain to form educational competence of students. Intelligence cards (mental cards) are a method of graphic expression of perception processes, processing and storing information, creative tasks, an instrument for memory and thinking.

Our experience of organizing ISW at the Medical College shows the effectiveness of implementing the method of compiling mental cards (intelligence cards) and students' work in the form of pairs with the use of "everyone teaches everyone" method. While studying the topics "Non-cellular Forms" of "Microbiology, Virology and Immunology with Microbiological Diagnostics" discipline, the students created mental cards, taking out opinions, facts and arguments from the information provided by the teacher; choosing the symbolic images to express the main idea of the lesson's topic.

An effective method of partially retrieval ISW organization is to attract students to develop a role play of the discipline that is under study or training to participate in it. Role play by V. Ortynsky's definition is a real situation simulation within a specially created problematic situation. It is a method of active learning which leads to achieving specific tasks, structuring the system of business relations among the participants.

Thus, the introduction of partially retrieval ISW in teaching the professionally-oriented discipline "Microbiology, Virology and Immunology with microbiological diagnosis" in medical colleges allows to increase students' motivation to learn, build health education of a future specialist's thinking, encourages students to independent acquisition of knowledge and skills, is a factor of the full development of creative and intellectual personality traits.

# THE ESSENCE OF PERSONALLY ORIENTED APPROACH AND PEDAGOGICAL CONDITIONS OF ITS IMPLEMENTATION IN TRAINING OF FUTURE BASKETBALL COACHES

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Modern pedagogic directs teachers to organize educational process by taking into account individual requests, demands of society and the state, which updates the necessity of studying the features of implementation of personally oriented approach in higher education institutions.

The purpose of these materials is to highlight the essence of personally oriented approach and pedagogical conditions of its implementation in training future basketball coaches.

In modern science scientists use terms «personally oriented education», «personally oriented teaching», «personal approach», «individual approach» along with the concept of «personally oriented approach», which are associated with the embodiment of humanistic paradigm in the educational environment of Ukraine.

In understanding the essence of the concept of «personally oriented approach» scientists and researchers differ in opinion with their views, seeing it as the principle or method of influence, skill and form of communication. Most teachers connect the personally oriented approach wich the embodiment of the principle of naturalness.

V. Stepanov defines the personally oriented approach as a methodological direction in teaching activities, which allow sensure and maintain self-expression, self-development and self-organization of personality and development of its individuality by using support of a system of interrelated concepts, ideas and ways of action.

We use the next definition when we define pedagogical conditions of personally oriented approach: pedagogical conditions is a set of objective opportunities, circumstances and actions of pedagogical process, which is a result of a selection, design and use of elements of content, methods, and organizational forms of the educational process to achieve the goals (K. E. Kostiuchenko).

During the introducing of the personally oriented approach in training future basketball coaches, the teachers of professionally designed courses should build their activity based on the principle of humanizing education.

In order to implement the personally oriented approach in teaching professionally directed disciplines it is advisable to steer the purpose of training into the formation in students the main groups of competencies (professional, instrumental, general, social and personal).

It is better to prefer active and interactive teaching methods, a combination of traditional and non-traditional forms of organization of educational process during organization of educational work with students in Universities.

The development supporting lectures and criteria for evaluation of students by teachers, the use of individual consultations in the process of teaching, the use of differentiated tasks for independent work of student during individual and group work, as well as non-traditional types of lectures, practical classes and seminars, for example: lectures press conference, lecture-provoking, lecture-discussion, seminar workshop (including the use of didactic games), self-organizing workshop, seminar-consultation seminar tour, workshop conducted using the method of «round table», practical classes with elements of training, etc.) is very useful for the introduction of personally oriented approach in stating of professionally designed courses.

Efficient work of teacher in University, who introduces the personally oriented approach, is determined by his ethics teaching and pedagogical tact. The interest in sport, a tendency to pedagogical work, efforts for continuous improvement, a deep belief in the great social significance of sport, a sense of responsibility for the quality of his activities will help the growth of the authority of the teacher who takes part in the formation of future coach personality.

Thus, the analysis of pedagogical literature on the topic of study allows to indicate that the personally oriented approach is based on the principle of naturalness which should be taken into account both in the activity of teacher and in creating educational and theoretical plans and programs; recognition of identity and personality by the main subject of the learning process, identifying and structuring the subjective experience of the personality, its directed development in the learning process.

The creation of personally oriented environment; providing professional and meaningful internal motivation; diversifying forms of training sessions; creating the situation of success; consideration of the individual characteristics of the student are to be considered as pedagogical conditions that influence the implementation of personally oriented approach in training future basketball coaches.

# FORMATION OF SOCIO-PSYCHOLOGICAL CLIMATE IN THE STUDENT GROUP

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Today the problem of optimization of socio-psychological climate in the student groups is relevant in higher school. Attitude to learning and cognitive activity and future profession, the atmosphere of scientific research, moral and professional qualities of the personality are formed in the student group.

Favorable climate experienced by each student as a condition of relationship satisfaction with his friends in a group of teachers, their studies, its process and results. This improves the mood of the student, his creativity, positive effect on the willingness to learn in this team, to apply their creative and physical strength for the benefit of themselves and others.

Unfavorable climate individually experienced as dissatisfaction with relationships in the group, conditions and content of teaching. This affects the mood of the student, his health and activity, an indicator of the results in the learning process and on his health.

Different aspects of optimization of socio-psychological climate in the collective have been the subject of study both domestic and foreign scientists such as V. Antonyuk, A. Glotochkin, O. Zotov, E. Kuzmin, A. Makarenko, N. Mansurov, O. Moroz, G. Mochenov, B. Paryigin, K. Platonov, L. Sventsitskiy, V. Semichenko, V. Shpalinskiy and others.

Socio-psychological climate is the qualitative aspect of interpersonal relations in the student group, which consists of feelings, needs, motives, evaluations and students' readiness to react in a certain way on the words and actions of others. The climate is an indicator of relations "individual - group", which are largely created by members of the group.

Socio-psychological climate in the student group is formed from the first day of its creation. First-year students don't join already existing groups, but create their own, albeit on the basis of traditions that exist in a higher educational institution. The students' collective passes a number of stages of unity in further development. One of the most difficult and responsible stages in life of each individual student is the

period of adaptation to new conditions of education and accommodation. At this time students poorly understand the conditions of higher school life and study, they are not able to interact with each other, to coordinate their efforts when performing educational tasks that leads to a big waste of energy, causes fatigue and generates the distorted view of the difficulties of educational and cognitive activity. The atmosphere of cooperation in group is based on the responsible and initiative relation of students to learning activity, to mastering future profession.

Climate of the student group is under the influence of a number of factors:

• individual and personal (temperament, character, abilities);

• interpersonal (cooperation, mutual aid, style of communication, etc.);

• public (political situation, economic situation, standard of living, organization of learning cognitive activity, etc.);

• technical, sanitary and hygienic (equipment of classrooms, provision of educational and scientific literature, elaboration of training programs, etc.).

The combination of all these factors affects the formation of socio-psychological climate in the student group, determines the role, status and leadership processes. Some students become leaders; others experience difficulties in group dynamics, staying as outsiders for some time. If the group for such students doesn't become reference, they can compensate for their low status by participation in other groups, more personally significant for them on a course, faculty or outside educational institution.

The basis for formation of socio-psychological climate is a learning cognitive activity, life and leisure of students. In their joint activity motives of formation and development of students arise and become stronger, aimed at achieving high results in their studies and social work.

The formation of socio-psychological climate in the student group requires an understanding of the psychology of personality, age characteristics of students in a higher educational institution, their emotional state, relationships with each other, features of individual and collective learning activity.

The psychological climate of the student group is a powerful incentive of learning activities for each student. Not participating in the group forms of learning activity, they do not master the most important social and psychological competencies required for today's professional.

# ACTIVE TEACHING-LEARNING METHODS IN PREPARING INTERNSHIP DOCTORS

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One of the major problems facing the high school is improving the quality of specialists training. Medical interns should not only get some knowledge in accordance with the programs of academic disciplines, acquire research methods and skills to use that knowledge. But also, they should be able to independently acquire new scientific information. During training, they must be prepared to meet any patient and any pathology. Therefore, the "emancipation" of interns and teaching them necessary practical skills and logical clinical thinking is the most important task of teaching.

Among all the modern pedagogical technologies, special attention should be paid to active methods, especially during seminars and practical classes. For example, one of the most common and effective training methods with medical interns' cognitive activity stimulation is the concrete case analysis. This method develops critical thinking and the ability to analyze life situations or professional tasks. It helps in combining theoretical knowledge with practice, in forming skills of alternatives assessment under uncertainty, shapes accurate express the point of view and argue it. Case method shapes skill to solve complex problems, which is important for future professional practice.

Enough effective method of acquiring practical knowledge and skills, in our view, is the "business game". This method is directed at optimizing professional thinking through learning algorithms, professional skills by means of programmed instruction. Business game forms a professional activity model, which is the highest form of didactic games in preparing a doctor. The meaning of educational simulation game is to raise a practical skill error-free differential diagnosis of clinically similar diseases, rapid and accurate diagnosis and optimal treatment of the patient as soon as possible.

Skill of work with the received information and motivation to active search for diagnostic information in accordance to executable role appear in preparation for the business game. Medical intern acquires skill of his behavior control, learns to adequately perceive and analyze different opinion. Advantages of business game among other learning methods lies in the fact that it develops the ability to find and work with information, can significantly intensify creativity of interns, makes it possible to learn on their own and others' mistakes, but only simulates the real situation in future practice.

Thus, the use of pedagogical techniques and, in particular, active learning methods in training future specialists allows successfully develop professionalism, stimulate and enhance cognitive activity of internship doctors, to achieve a high degree of autonomy.

# PHYSICIANS' PROFESSIONAL COMPETENCE FORMATION BY MEANS OF INNOVATIVE TECHNOLOGIES

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Competence approach in training with higher education is an approach that underlies the new paradigm of higher education. This approach provides mapping learning outcome in the form of competencies and comparability of requirements for qualifications within the European space through competence system.

A professional competency is a set of defined qualities and behaviors of specialists who demonstrate possession of knowledge, abilities, skills, professionally important qualities necessary for carrying out their professional activities.

In our opinion, basic conditions of the physicians' professional competence formation process in conditions of university ought include: adherence to the principles of education; development of guidelines and scientific and methodological support for teaching and educational process based on a systems approach; ensuring vocational motivation of students; implementation of educational activities of students based on their individual characteristics; providing professional identity formation of future doctors; establishing creative and subjective environment which make conditions comfortable for training activities.

Ensuring a high level of physicians' professional competence is possible due to the synthesis of pedagogical achievements, combination of traditional and advanced forms and methods with modern efficient educational innovations. While implementing innovative technology, teachers set goals to identify patterns of interaction between students, teachers, content, forms and methods, tools and sources of learning. In this approach, pedagogical technology is an organizing of educational process that envisages a system of actions and interactions of all its elements.

Therefore, the use of modern innovative educational technologies makes it possible to take into account the individual typological features and abilities of students, to develop creative inclinations and help in learning professional skills, in opening up and realizing future professionals. Implementation of innovative educational technologies in teaching process enables significant improvement of students' academic results while mastering new material.

The prospect of future researches is in finding the optimal combination between traditional models of forms and methods aimed at acquiring professional skills with innovative educational technologies which facilitate formation of professional thinking and personal development for future physicians.

# FINLAND'S EXPERIENCE IN TEACHING FOREIGN LANGUAGES

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The Ukrainians are suppossed to master foreign languages in the process of Ukraine's integration into the European world. In this respect the experience of Finland in the sphere of language learning seems to be useful. Thus, the aim of the present paper is to highlight Finland's system of education approaches to foreign languages teaching useful in our country.

To start with, the Finnish find that they are rather skilled in foreign languages, 77% in comparison with the European average of 44%. In particular, 70% of the population can speak more than one foreign language, 47% at least two languages and 23% even three foreign languages. Thus, it may be noted that in Finland the foreign language skills are above the European average and it is the country to follow the example.

It is needless to say that language education is compulsory at every school level. Moreover, Finland is strong in the methodology of language teaching. International methodology trends, such as communicative language teaching (CLT) and intercultural communicative competence (ICC) are widely known in this country and are also researched and developed further. International programmes and student exchange programmes have become increasingly popular nowadays. The significance of language knowledge as part of professional competence is understood by 72% of adults that say they would need more language education.

Language immersion and CLIL ('Content and Language Integrated Learning') have also been developed. More recently, practitioners and researchers in this area have been found to favour the term (CLIL) to describe the form of instruction which is considered a means by which to implement a plurilingual approach to education. Preference for CLIL can be found because the term allows for the movement of both language teachers become more involved with content, and content teachers to become more involved with language. This is particularly the case in Finland in which CLIL involves both language and content specialists. Thus, the acronym CLIL is used to refer to a type of method which may lead to the development of plurilingualism in mainstream education.

Finland also does well in terms of educational equality, the training of teachers is well organized and it is the responsibility of communes to organize education. There are projects that try to develop and diversify the education of foreign languages and the methods used in education: "Kimmoke" and then "Kieltenopetuksen kehittämishanke".

That is why a decision has been made that in upper-secondary schools a new course will be added as it would be necessary – not only to write but also to speak a language. Until now the matriculation examination has only been about the written language skills.

# THE VALUE ATTITUDE FORMATION OF FUTURE ECONOMISTS TO THE PROFESSIONAL ACTIVITY IN THE CONTEXT OF THE SOCIAL AND ETHICAL MARKETING CONCEPT

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The current state of the national economy and the appearance of the concept which aims at combining the consideration of the interests of producers, consumers and society as a whole are caused by a gradual increase in the maturity of the market economy, strengthening in it the regulatory framework and the appearance of modern socially oriented market economy.

The consideration of the production planning process from the standpoint of social and ethical marketing as an institutional tool of market economy regulation allows to reconcile the interests of businesses entities both in the internal and external environment of the company.

The factor accelerating the introduction and use of corporate social responsibility principles declaring the voluntary decision of enterprises and organizations and their staff to participate in meeting the needs of society, promoting the increase of its prosperity and harmony is the direct training of future economists, which should be aimed at the acquisition of professional values and value attitude to the profession.

Thus among the professional values of economists the following ones have been distinguished: basic values (good, spirituality, humanity, truth, morality, tolerance, etc.); values-qualities (analytical thinking, initiative, independence, consistency, practical intelligence, determination, diligence, commitment, etc.); the values of social interaction (altruism, responsibility, recognition of customers rights, business activity, kindness, emotional stability, concentration, communicative, honesty, collegiality, etc.); the personality-reflective values (meaningful moral and professional position, introspection, self-regulation of professional behavior, awareness of their professional duties, etc.); the pragmatic values shown up in the attitude to money.

Solving the outlined problem will contribute the formation of competitive advantages in terms of the national market according to the coordinates “product-service”, “price-toll”, “advertising-consumer”, “client-service”, “team-microclimate” etc. which expands the area of further scientific research.

# THE IMPLEMENTATION OF MODERN EDUCATIONAL TECHNOLOGIES IN THE TERMS OF ARCHITECTURAL COLLEGE

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In terms of socio-economic changes taking place in modern society, the problems of professionalisation of a personality become particularly important. Intensive development of modern educational technologies affects the quality of training of the specialists, whose qualifications are primarily determined by their professional qualities.

Professionalism of the future architect strongly depends on the knowledge gained during the study of special subjects in higher education institutions. Modern globalization processes in various professional fields in which practical application of knowledge learned by students in higher education institutions will happen, require of young professionals the usage of advanced, innovative and flexible techniques and skills in their work. The latter can be learnt only thanks to the successful combination of both traditional and innovative teaching methods.

The method of teaching is an optimal combination of technologies, methods, techniques and training aids that are used in order to organize the educational process, so it is the way of managing of cognitive activity of students, which should perform training, educational and developmental functions. Integration of innovative pedagogical technologies in teaching subjects is an effective process of improvement of students' knowledge level.

The activity of teacher of special subjects is various and connected with the constant necessity to anticipate, predict and plan various aspects of his activities. It is a creative process that has its own rules and its technology, because the content of professional training of specialists defines the methods and means of their teaching.

Heuristic teaching methods that involve students not only to master, and to look for the knowledge might be reflected in training programs.

Modern didactics, while treating education as a process of transmission and mastering of knowledge, skills and methods of cognitive activity accordingly considers system of principles, namely: scientific principle, the principle of availability, the principle of connection of study with life, the principle of consciousness and activity of students, principle of clarity and others.

In terms of architectural college, the projected technology of learning, implementation of which is based on the use of the method of projects as one of the most progressive methods of teaching in higher school becomes mostly widespread.

The method of projects comes forward as an important component of productive education and is an effective, non-traditional way of organization of learning activities through active methods of action (planning, forecasting, analysis, synthesis, synthesis, simulation) aimed at implementing of personally oriented approach and interactivity.

Advantages of the method of the project are that during the project activity combination, integration of active and interactive teaching methods takes place on one hand, and on the other hand - actualization, integration of acquired knowledge and skills takes place.

Therefore, the analysis of different approaches to improve studying of subjects in universities shows that there are many innovative methods of learning, which greatly stimulate students to productive work, thereby enhancing the quality of their professional activities in the future.

This technology is also used in organization of control and evaluation of achievements. The use of project technologies allows to implement active approach in learning.

Thus, the project activity of students provides a priority of objective and socially relevant knowledge and skills that will fit the paradigm of personally oriented education, because these knowledge and skills allow youth to become successfully realized lifelong in professional activities.

# THE ROLE OF EMOTIONS IN THE REGULATION OF STUDENTS' EDUCATIONAL AND COGNITIVE ACTIVITY

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It is hard to overestimate the role of emotions in the life of every person. While performing its functions (signal, adaptive, estimated, communicative, regulatory, and motivating etc.) emotions affect not only human behavior, but also the educational and cognitive activity.

Different approaches of the emotional sphere in the training activities and relation of emotions with psychic and cognitive processes have been the subject of study of many researchers: L. I. Aidarova, G. O. Ball, O. V. Dashkevich, V. V. Davydov, K. Izard, D.B. Elkonin, S. D. Maksimenko, P. M. Jacobson, O. Ja. Chebykin, etc. "Emotion is a complex psychological state that includes three separate components such as a subjective experience, a physiological response and a behavioral (or expressive) response" (Hockenbury & Hockenbury, 2007). Therefore, in psychological dictionary, the concept "emotions" is to be construed as a personality's evaluative relation to the environment, with the personality's needs that encourage activities. Emotions vary in quality characteristic (positive, negative), morality, their dynamics, the external expression and awareness. For example, negative emotions unlike positive ones reinforce the guideline for the perception of details and help their rigorous analysis, while the positive ones lead to the neglect of the details, but reinforce the focus on globality (I. M. Andreeva, 2009). A number of researchers have studied the emotions that arise during learning activities. A significant study of emotions in training has been conducted by O. J. Chebykin, who concluded from his experiment that the following emotions are encountered most frequently: interest, boredom, insult, surprise, doubt, fear, enthusiasm, pleasure, delight, joy, frustration, interest, anger, fear, etc. Interesting is the fact that emotions of fear during phase of mastering and using the studied material have been recorded in students who get good grades. According to K. Izard, "an emotion is something that is experienced as a feeling that motivates, organizes and directs perception, thinking and actions".

In addition, there is a view, which does not deny much the motivating force of the emotions, but clarifies its origin. Therefore, it is indicated that an emotion has no motive force, but human needs have, that emotions depend on the needs and function as "an internal mirror" (Je. D. Khomska, 2005). S. L. Rubinstein has a similar thought: an emotion is a subjective form of needs (motivation) existence. Psychological understanding of the human condition includes the concept of positive and negative emotional state, the internal tension, the nature of emotions (feelings, affects). After all, a person's emotional life consists of a diverse content: emotions reflect its evaluative attitude to certain conditions that facilitate or prevent activities (e.g. fear, anger), to specific achievements in it (joy, sorrow), to existing or potential situations, etc. This knowledge of a student's psychic state allows to find ways of communicating with him, matching his momentary mood, and thus to avoid misunderstandings and conflicts.

This study does not exhaust the complexity of the problem. We plan the further studying of emotional regulation of students' educational and cognitive activity.

# CORRELATION BETWEEN GROWTH-WEIGHT AND FUNCTIONAL INDICATORS OF ORGANISM STUDENTS NPhaU

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Physical Education (PhE) is a compulsory subject for all students off full-time study forms of higher education in Ukraine. The main goal of PhE is health promotion and development of physical qualities of students, without which neither effective training, nor the successful work after graduation. Methods for assessing the physical condition and health youth include the definition of their physical development, functional and physiological condition of the body and their comprehensive assessment.

Correlation method (CM) based on the fact that the physical development of various body parts and functional characteristics are interrelated. This connection can be positive or negative.

Objective: To investigate correlation between growth-weight and functional indicators of the organism of girls-students during physical education classes.

Achieving objective of the work happened if performed following tasks:

1. Study and analysis available to us literary sources.

2. Conducting observations of the content compulsory and self-study physical education of girls full-time study forms.

3. Determination relation between growth, weight and body functional indicators of pharmacy students by the method of correlation.

The following conclusions were made based on the analysis of survey materials:

1. There is a connection between growth-weight and functional analysis of the body of students which is in the range of R = 0,7-0,9.

2. Body mass index (BMI) should be used for accurate objectification body mass.

3. Students are encouraged to use the International Classification of body weight in the practical work of physical education.

4. Self-consumption of drugs and herbal ingredients for weight loss is undesirable. Their use can be cause a number of side effects that are a danger to human health and life.

5. The aim for gradual and slow reduction of overweight - a sharp weight loss itself causes metabolic disorders with the accumulation of fat in the liver.

# NON-TRADITIONAL TEACHING METHODS IN TRAINING SPECIALISTS IN MEDICAL AND PHARMACEUTICAL PROFILE

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Higher school has gained considerable experience in professional training of future specialists in the University over the centuries. Many teachers have investigated a variety of teaching methods (I. M. Paraplatin, C. K. Dyachenko, V.A. Slastion and so on), thus, there are different views on the effectiveness of these methods in the learning process. There is no consensus on this issue. Students looking for new teaching methods and analyzes the traditional order to achieve a high level of education. In particular personality-oriented pedagogy to the forefront puts non-traditional approaches to the learning process in a modern high school.

Actual purpose of training and education is the creation of personal potential future specialist medical and pharmaceutical schools, education of its ability to adequate activities in the forthcoming substantive and social situations, and content - everything that achieves this goal. Success of training depends not only on what is assimilated (learning content), but also on how to assimilate, individually or collectively, in authoritarian and humanistic terms, based on attention, perception, memory or full personal potential human, with reproductive or active forms.

Transition to non-traditional teaching methods, which are known to many years, allows us to activate the role of the student, not to limit by studying in the class, to encourage independent work and creative activities. However, the most of the teachers still use traditional approaches in the real process of learning

Analysis of the described problems allows us to identify some non-traditional methods in the training of specialists medical and pharmaceutical profile which allow optimizing the learning process.

Active and interactive learning, which based on the solution of specific professional situations and focused on clinical and scientific problems, have successfully used in many medical and pharmaceutical Universities in the world, such as Great Britain, Germany, Australia and others. The basis of selection and application of non-conventional methods is analysis of specific case studies, ie, situational problems. Their application contributes to the formation of clinical thinking in students, encourages creative, professional discussion, significantly stimulates and fosters a sense of satisfaction from their work.

Quite effective methods and forms of educational work is real and virtual tours in health care, business games, the method of "brainstorming" method of investigation of specific cases, the method of incident and others. Principle of clarity implemented with excursions where training future professionals directly acquainted with the studied objects and phenomena, specific future profession. The excursions allow to improve science education and to strengthen its relationship with life and practice. The game is especially important role in the clinical training of future pharmacists and medical professionals, because it allows responding more adequately to complex, unfamiliar cases when dealing with patients. Student has the opportunity to rehearse these cases. Brainstorming demonstrates knowledge of students wish is they represent in the form of ideas for the solution of professional problems or situations. Study of specific cases provides the opportunity to direct an active studying of situation, allows the participant to quickly assess the situation in terms of the ongoing pressure (in terms of human relationships), decisions taken in stressful circumstances; practical situation apply to the theory and intuition to solve problems.

So, non-traditional teaching methods in the preparation of future specialists in the medical and pharmaceutical profile increase interest in studying. A change methodological and psychological approach to teaching of professional disciplines allows us to optimize the studying process and to prepare qualified health care professionals.

# CARDIO-TRAININGS: ESSENCE, REQUIREMENTS FOR THE ORGANIZATION

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Cardio-training is a cardiovascular workout system that helps to increase your lung capacity. This is beneficial complex work, in which the main source of energy is the oxygen enters the blood from the lungs. This is beneficial complex work; the main source of energy is the oxygen which enters the blood from the lungs.

The goal of cardio-training is to strengthen the cardiovascular system, increase endurance, burn fat, reduce the risk of heart attack and diabetes, as well as improving overall health and making your stress level less.

The main types of cardio-trainings are running, walking intensive, jogging, all active kinds of sports such as skiing, skating, soccer, swimming and all athletics. Exercises increase endorphin levels in the blood, so people who lead an active lifestyle, usually do not feel depressive; they rarely get under the stress and do not suffer from insomnia.

Cardio-training is recommended to maintain the tone and to improve health (1-3 times a week) for losing weight and drying (3-5 times a week) at a set of muscle mass (1-2 times a week). During a workout, you should drink water. It delivers nutrients the body cells, where the muscles and internal organs especially need during exercises.

Intensity of cardio-training determined by the pulse. Therefore, before the training you should clarify rates of your heart. To determine the upper and lower heart rate limits you have to subtract your age from 220. If the resulting number is multiplied by 65%, we obtain a lower allowable limit, and multiplying by 85% - the top.

If you are new in cardio-training, it would be better to start with a mode of 50% of your maximum heart rate. In order to burn fat, suitable intensity of 60-70% of maximum heart rate. The optimal duration of sessions of 30-60 minutes. Shorter trainings are not so effective.

The human body was originally designed for motor activity, so a returning to the natural destiny will significantly improve objective health indicators.

# ADDITIONAL SECTION № 20

# THEORETICAL AND EXPERIMENTAL PATHOPHYSIOLOGY

# SELENIUM DEFICIENCY AND MALE INFERTILITY

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The World Health Organization defines infertility as the inability of a sexually active couple (at least three times per month), not using contraception, to achieve pregnancy within one year. About 15 % of sexually active couples are infertile and male factor infertility contributes to about 50 % of the infertility cases. One of factors leading to infertility in men is deficiency of micronutrients.

Selenium (Se) is an essential trace nutrient for humans and animals. Se discovered by Berzelius as early as 1817. Plant foods are the major sources of Se most countries throughout the world. The amount of Se present in the plant material depends upon the concentration of Se in the soil of that region as it varies by region. In some northern regions of Ukraine Se decrease in soil is marked.

Se deficiency has been linked to reproductive problems in many animals. Se is required for normal testicular development and spermatogenesis in rats and supplementation with Se to improve reproductive performance at them. Low sperm production and poor sperm quality including impaired motility with flagella defects localized primarily to the midpiece has been a consistent feature in Se deficient animals.

Se, in the form of selenocysteine, functions as the catalytic center in the active sites of at least 9 human enzymes, including 4 glutathione peroxidase antioxidant enzymes (protective role of oxidative stress, present in spermatids which becomes a structural protein comprising over 50 percent of the mitochondrial capsule in the mid-piece of mature spermatozoa), 3 iodothyronine deiodinases involved in thyroid hormone metabolism (provides synthesis of testosterone).

Main role in testicular function is corroborated by the observation that, in mild deficiency, Se is preferentially retained in testis. With progressive Se deficiency pathogenesis it is presented morphological alterations of spermatids and spermatozoa. Extreme deficiency results in the complete disappearance of mature germinal cells. Low concentrations of seminal plasma Se may be harmful to male fertility. It is established, that serum Se lower in men with oligozoospermia and azoospermia than in healthy. Supplements with Se has been associated with positive effects on male infertility, which appear synergistic when used with other antioxidant. Optimal dosing appears to be between 100 and 210 μg on day.

Thus, Se is essential micronutrient for male reproductive system and Se deficiency associated with infertility.

# DYNAMICS OF LEVEL OF GLYCOSYLATED HEMOGLOBIN IN BLOOD OF RATS WITH EXPERIMENTAL DIABETES MELLITUS TYPE 2

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It is known that the main criteria for compensation of diabetes mellitus (DM) are fasting glucose, postprandial blood glucose and glycosylated hemoglobin (HbA1c). In this case, one of the main risk markers for development and progression of long-term complications of diabetes is glycosylated hemoglobin (HbA1c).

Glycosylated hemoglobin is a compound of hemoglobin with glucose which is formed in a result of nonenzymatic chemical reaction of hemoglobin A, contained in erythrocytes, with blood glucose. Glycosylated hemoglobin reflects glycemia over an extended period of time (1-2 months) - average half life of red blood cells. HbA1c concentration is directly proportional to the mean blood glucose concentration in healthy people and is equal to 4.6% of the total hemoglobin. In diabetic patients this index can be 2-3 times higher.

The aim of this work was to study the dynamics of the concentration of HbA1c in rats on a background of experimental DM type 2 in different periods of observation.

Diabetes reproduced by intraperitoneal administration to rats with streptozotocin (Sigma, USA) at a dose of 65 mg/kg against the background of protective effect of nicotinamide. Blood glucose was determined by glucose oxidase method, content HbA1c - colorimetric method. And it was expressed as a percentage from total hemoglobin. Testing was performed on the 7th, 15th and 30th day after the administration of streptozotocin.

As a result of the study it was found a significant breach of carbohydrate metabolism. As evidence of this was increase in basal glycemia on the 7th day of the experiment by 2.7 times comparing with intact animals. Settled state of moderate hyperglycemia persisted throughout the experiment. On the 7th day, HbA1c levels did not differ from that of intact rats. On the second term of test was observed only a slight tendency to increase the concentration of HbA1c by 14%. However, on the 30th day of research on the background of a stable level of glucose there was a significant rise in HbA1c content in the blood by 76% that reflected a prolonged state of hyperglycemia.

Thus, elevated level of the end product of HbA1c glycation on model of DM type 2 induced by streptozotocin, was directly proportional to the glucose content in the blood of rats and was found already on the 30th day of the experiment.

# ANTIOXIDANT PROPERTIES OF A NEW COMBINED AGENT GLIKVERIN IN TERMS OF CHEMICALLY INDUCED ABSOLUTE INSULIN DEFICIENCY

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Over the last years scientists proved the leading role of lipid peroxidation processes (LPP) in pathogenesis of diabetes mellitus (DM) type 2 and in development of vascular complications. This is an evidence for using of antioxidants in pathogenetic therapy of DM. New combined agent Glikverin, developed in NUPh, contains known antioxidant quercetin and α-glucosidase inhibitor voglibose. It has an antidiabetic action on experimental models of insulin resistance. Given the gradual depletion of insular apparatus at progression of DM type 2 as a result of oxidative stress and the subsequent appointment of insulin, it made sense to investigate antioxidant activity of Glikverin on model of DM type 1.

The aim of this study was to investigate the antioxidant properties of Glikverin on a model of absolute insulin resistance in rats induced by alloxan. Alloxan was injected subcutaneously once at a dose of 150 mg/kg. Glikverin (50 mg/kg of quercetin+0.02 mg/kg of voglibose) was injected in preventative and and therapeutic mode intragastrically daily for 14 days in order to model diabetes and during next 35 days. Reference agents quercetin (50 mg/kg), voglibose (0,06 mg/kg) and metformin (200 mg/kg) were administered in the same mode. The intensity of lipid peroxidation proceses was determined in homogenates of the liver by content of diene conjugates (DC) and TBA-reactancts. Antioxidant system (AOS) was evaluated in terms of reduced glutathione (GSH) and catalase activity.

The results showed that the induction of diabetes leaded towards significant increase of DC and MDA in liver homogenates of rats. In addition, in the control group we observed decrease in catalase activity and pool of GSH.

It is established that Glikverin prevented the development of oxidative stress caused by alloxan: there was significant reducing of the amount of DC and MDA-reagents in liver homogenates comparing to control group. Restoring GSH and catalase activity increase up to intact animals suggest activation of AOS. Regarding antioxidant action Glikverin was significantly superior to metformin and voglibose and was similar to reference agent quercetin.

Thus, the results show antioxidant properties of Glikverin in terms of of absolute insulin deficiency. These properties are realized by inhibition of lipid peroxidation and increased antioxidant protection.

# RESEARCH REGENERATIVE PROCESSES IN THE ORAL MUCOSA WITH EROSIVE AND ULCERATIVE STOMATITIS

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To investigate the regenerative processes in the oral mucosa of rats with erosive and ulcerative stomatitis without treatment and the application of new dental gel "Lizostom." The experiment was conducted on 30 white rats weigh 180-200 g. All animals were divided into 3 groups: 1-st - intact control; 2-nd - rats with experimental erosive and ulcerative stomatitis (untreated control); 3-rd -rats with erosive and ulcerative stomatitis, which three times a day on the affected area applied gel "Lizostom" with lysozyme hydrochloride. To reproduce the experimental erosive and ulcerative stomatitis on mucous gums of the upper jaw on both sides and at the bottom - in the area of transitional fold, alternately rubbed over 8 min 4% solution of sodium hydroxide. Mitotic index was determined by cytological preparations gingival mucosa.

Experiments have shown that a day after the application of chemical burns of the mucous gums, all animals developed severe erosive and ulcerative stomatitis. In this case there was congestion, edema of the gums, serous raids. In the area of transitional fold lower jaw were 3-4 erosion. In the area of the upper jaw formed ulcers diameter of 2-3 mm. The general condition of the animals was decreased physical activity and decreased interest in food. One day after ulceration, mitotic activity maximum in the experimental group of animals was 92,3±1,82. In intact animals, the figure was 10,4±1,36. On the 7th day of the experiment a decrease in mitotic index to 31,8±1,76 in the experimental group of animals that coincided with a visual improvement of mucosal inflammation intensity and partial epithelialization of ulcers. In the future, the number decreased mitosis and almost returned to normal values after 21 days the experiment. In animals treated with dental gel with lysozyme hydrochloride, visual improvement of mucosal observed on the third day, and normalization mitotic index was held on the 15th day.

In the experimental erosive and ulcerative stomatitis is a significant increase in mitotic index - one of the criteria regenerative processes of the mucosa, which correlates with the severity of clinical signs of disease. The use of new dental gel "Lizostom" in experimental erosive and ulcerative stomatitis accelerates regenerative processes in the oral mucosa and reduces recovery.

# EFFICACY OF THE SUBOCCIPITAL METHOD OF INJECTION OF AUTOLOGOUS STEM MESENCHYMAL CELLS IN EXPERIMENTAL ISCHAEMIC STROKE

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**The purpose of the research** was to study in an experiment on animals a possibility of creating a model of ischaemic thromboembolic stroke, identical to the natural phenomenon, and analyse prospects of using cell therapy for elimination of the above stroke.

**Materials and methods.** Bits of the brain of 3-month-old intact male Wistar rats (n = 254) weighing 160-175 g with modelled ischaemic stroke and cell therapy (CT) against this background served as material for this research. During the whole experimental cycle the animals were kept in standard conditions of climate control (t= 19-21°C; 300 lc) at the vivarium of Kharkiv Medical Academy of Postgraduate Education of the Ministry of Health of Ukraine. All rats were differentiated into 3 groups: intact control (1$^{st}$ , n=50), modelled stroke (2$^{nd}$ n=102) and cell therapy (3$^{rd}$ n=102).

Animals of the 1$^{st}$ experimental group were not subjected to any experimental influences (ischaemia factors, cell transplantation). Rats of the 2$^{nd}$ group underwent modelling of ischaemic stroke, identical to the natural phenomenon, by surgical injection of emulsion of barium sulphate (II) into the right common carotid artery. For the research purpose, animals of the 3$^{rd}$ group were injected a suspension (3.5-5 x $10^5$) of autologous stem mesenchymal cells (ASMC) by means of suboccipital (SO) penetration of the occipital cistern. The observation lasted 14 days. Male rats were taken out of the experiments (on the 1$^{st}$, 3$^{rd}$, 7$^{th}$ and 14$^{th}$ days) by overdosage of amphetamine anaesthesia.

The results were assessed histologically. For this purpose bits (0.5 x 0.5 x 0.5 cm) of the brain of rats were fixed in 12 % formaldehyde (pH = 7.0-7.2), dehydrated by passing through graded alcohols with increasing concentration (from 30° to the absolute), and embedded with resins (paraffin/celloidin). The resultant blocks served for making sections (h = 10-15 mcm). These were stained with haematoxylin and eosin, impregnated with silver nitrate by the Cajal method and iron hematoxylin by

the Regaud method. Morphological analysis (x 300; x 400; x 600; x 1,350) was carried on with help of Lieca microscope (Germany). The results, received in the experiment, compared with those in the intact control.

**Results**. The first day of observation was considered as negligible for obvious reasons (overcoming of the haematoencephalic barrier by cells and hence impossibility to trace the fate of migrating cells). The 3rd day of experiment obviously proved tracking of transplanted cells, having demonstrated a high activation of local reparative-regenerative processes in the cerebral matter.

After SO injections of cells we observed appearance of gliomesodermal cysts (the paracentral lobule, anterolateral areas of the superior temporal lobe), an insignificant number of microvessels (arterial and venous, lymphatic branches also) in close proximity to damaged areas, in the region of walls of the lateral ventricles and of the third one as well as homo- and heterogeneous clusters of ASMC.

In cases of SO transplantation a limited number of ASMC concentrated on the level of vessels of ventricular plexuses, medial cerebral artery and its separate branches. On the 7th day of observation the volume of cysts insignificantly increased; the damaged areas served as a background for the appearance of a glial scar and a marked increase in the number of microvessels and their branches. The number of polygonal cells increased. Their population was separated from the adjoining structures with layers of gliomesodermal cells, whose structure vaguely resembled that of epithelial cells. (The origin of the latter cells was indicated by their typical geometry, structure of cytoplasm, nuclear-cytoplasmic ratio).

SO transplantation autologic stem mesenchimal cells resulted in accumulation of a limited number of cells in the ependyma, cortical part and appearance of a ramified vascular network in the sites of injection injuries of structures. The numbers of cysts and scars remained as before, their volumes increased insignificantly. The similar picture was observed on the 14th day of experiments.

**Conclusions.** The use of SO transplantation in case of experimental modelled ischaemic thromboembolical stroke facilitated a high activation of reparative processes in the cerebral matter, a reliable reduction in the volume of cysts and scars against a background of activation of angio- and sinaptogenesis, reparative processus elimination of thromboembolism, stasis, destruction and degeneration regions, necrosis zones.

The use of ASMC on the intact brain did not cause their differentiation into neurons, but, on the other hand, did not preserve their cytological properties unchangeable either. Therefore the use of the SO route of injection of ASMC can be regarded as one of effective methods for intervention of ischemic stroke.

# CYTOLOGICAL ANALYSIS OF BLOOD OF DOMESTIC DOGS WITH BABESIA INFECTION

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**The purpose** of the present research was to study the degree of Babesia infection in domestic dogs by results of cytological analysis of their blood smears. **Materials and methods.** Blood smears (Wright's staining, the author's modification, 2014) of domestic dogs (n = 11) of both sexes with Babesia infection at the age from 3 months to 6 years served as the material for the study. The preparations were fixed during 1-2 seconds with 96 % ethyl alcohol. Then warmed (t = 36.0 ± 2.0)°C commercial matrix solutions of eosin, azure and methylene blue were applied one by one. The smears were rinsed (1-2 seconds) in distilled water and dehydrated. The procedure ended with short-term drying in a diffused stream of warm dry air (Samsung house fan, power 220 W). **The results** were compared with intact control. As result of the analysis of blood smears it was found out that against a background of orange erythrocyte cytoplasm the preparation area easily revealed crimson- and red-lilac pyriform (n = 9-12…23-28 in the field of vision of the preparation), annular (n = 7-16 in the field of vision), amoebiform haemoparasites and those with other shapes (Σ=11), thereby indicating a high level of infection (81.8 %). Owing to their own chromatophilic feature, protozoan cells looked geometrically marked and clearly contrasted against a background of the saturated red-violet colour of nuclei. The developed technique of staining facilitated 1) a more qualitative analysis of ontogenetic staging (III) of Babesia (trophozoites, merozoites, sporozoites); 2) improvement of differential diagnosis of the haemoparasites with blood platelets (the latter were distinguished from cells of the causative agent by the presence of marked ovaloid azurophilic granules in the cytoplasm of young forms (Σ = 2-3 in the field of vision) and azurophilic granularity in mature forms (Σ =1-3 in the field of vision of preparations); 3) better differential diagnosis with intracellular inclusions (intraerythrocytic Cabot rings, Howell–Jolly bodies); 4) improved differential diagnosis with solid elements of sediments of used stains (the above artifacts were in a saturated dark blue or black colour and observed very seldom).**Conclusions.** By the results of the cytological analysis of blood smears it was revealed that domestic dogs with clinically detected Babesia infection had a high level of contaminaiton with parasites. In our studies this level was 81.8 %.

# SOME MECHANISMS OF SKIN AGEING

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Ageing has been defined as the accumulation of molecular modifications which manifest as macroscopic clinical changes. Major environmental factors have been recognized to induce modifications of the morphological and biophysical properties of the skin. Metabolites from ingested or inhaled substances do affect skin, which is also sensitive to endogenous hormone levels. Hormones at age-specific levels may not only regulate age-associated mechanisms but also regulate tumor-suppressor pathways that influence carcinogenesis. Understanding the molecular mechanisms of aging may open new strategies in dealing with the various diseases accompanying aging, including cancer. Factors as diverse as ultraviolet radiation, atmospheric pollution, wounds, infections, traumatisms, anoxya, cigarette smoke, and hormonal status have a role in increasing the rate of accumulation of molecular modifications and have thus been termed 'factors of ageing'. All these factors share as a common feature, the capability to directly or indirectly induce one of the steps of the micro-inflammatory cycle, which includes the expression of ICAM-1 in endothelial cells. This triggers a process leading to the accumulation of damages in the skin resulting in skin ageing since ICAM-1 expression provokes recruitment and diapedesis of circulating immune cells, which digest the extracellular matrix (ECM) by secreting collagenases, myeloperoxidases and reactive oxygen species. The activation of these lytic processes provokes random damage to resident cells, which in turn secrete prostaglandines and leukotrienes. These signaling molecules induce the degranulation of resident mast cells which release the autacoid histamine and the cytokine TNF-alpha thus activating endothelial cells lining adjacent capillaries which release P-selectin and synthesize ICAM-1. This closes a self-maintained micro-inflammatory cycle, which results in the accumulation of ECM damage, i.e. skin aging. Two factors able to induce macroscopical and molecular modifications in the skin, protein glycation and stretch, activate the micro-inflammatory cycle. Three additional factors, two external factors (electromagnetic fields and psychological stressors) and one internal factor (neuropeptides) also activate the micro-inflammatory cycles and may therefore be considered as factors of skin ageing. The most important biological processes involved in skin aging are alterations in DNA repair and stability, mitochondrial function, cell cycle and cellular metabolism.

# THE ROLE OF HEAT SHOCK PROTEINS IN PATHOGENESIS OF ATHEROSCLEROSIS

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Heat shock proteins (Hsp) or shaperons are oligomerous proteins, that help to coagulate native or denaturated proteins. They are synthesized in stress situations (therefore they are also called stress-proteins) and they are high-conservative group of proteins, that is, their structure is similar in different organisms. Cells of arterial wall product large amounts of Hsp in response to infection, fever, mechanical and oxidative stress, cytokines, heavy metals, alcohol or inhibitors of cell metabolism.

Therefore, the **aim of work** is studying of modern literature and analysis of role of heat shock proteins in pathogenesis of atherosclerosis.

**Results of work.** Found that under stress phosphorylating of small heat shock proteins Hsp27 and Hsp20 develops that influences on polymerization of actin of arterial wall. Heat shock protein 47 is the stress protein, which can be the shaperon for collagen. It is not known about its participation in pathogenesis of atherosclerosis for certain, but its localization in a fibrotic layer, regulation by height factors in parallel with a type of procollagen-1 and selective regulation by stress revealed possibility of determining stability of pre-existing plaque by Hsp47.

In recent years there were done many discoveries that allow discussing immunoinflamation mechanisms of development of atherosclerosis. Heat shock proteins Hsp60 and Hsp65 belong to the group of possible antigens for immune response. Cellular and humoral immunity to phyllogenetic conservative antigen of the Hsp60 is the triggering mechanism of development of the earliest stages of atherosclerosis. Data, which had got by scientists, show that Hsp60 contains in human atheroma and can cause damage by direct activation of macrophages. Hsp60 is the reason of inflammation cytokines formation, induction of metal-protease and low-density lipoproteins oxidation. Each of these changes affects the development of atherosclerosis. The mechanism of formation of autoimmune response to Hsp consists in an immune response for the antigens of infectious microorganism (for example, Hsp60 of Chlamydia), that cross reacts with the homologous proteins of the host organism in form of molecular mimicry.

**Conclusions.** Thus, in case of infection, organism immunity begins to be formed against Hsp60 of microorganisms. However, as a result of similarity of microbial and human Hsp60 there is a cross immunoreaction against human Hsp60, therefore autoimmune reaction that is the constituent of the infectional-autoimmune inflammation hypothesis of pathogenesis of atherosclerosis.

# ETIOLOGY OF TESTOSTERONE DEFICIENCY IN MEN

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Under physiologic conditions in men, the hypothalamus produces gonadotropin-releasing hormone (GnRH), which induces the anterior pituitary gland to secrete 2 gonadotropins: luteinizing hormone (LH) and follicle-stimulating hormone (FSH). In turn, these gonadotropins respectively stimulate Leydig cells to produce testosterone (T) and induce Sertoli cells to nurture spermatogenesis. Sperm and T downregulate their own production through a feedback loop that reduces the secretion of hormones by the hypothalamus and pituitary.

In the blood, T circulates principally in bound form, mainly to sex hormone-binding globulin (SHBG) and albumin. It tightly binds to SHBG and is not biologically available, whereas the T fraction associated with albumin is weakly bound and can dissociate to free, active T. In young adult men, only about 2% of T is in the free form, 30% is bound tightly to SHBG, and 68% is weakly bound to albumin.

Testosterone deficiency (TD) - is a clinical and biochemical syndrome frequently associated with age and comorbidities, and characterized by a deficiency in T and relevant symptoms: incomplete or delayed sexual development, secondary sexual characteristics, sexual disorders and infertility.

Etiology TD represented classification, which reflects the basic types.

1. The primary TD (disorders at the testicular level): anorchia, cryptorchidism, varicocele, orchitis, Klinefelter syndrome, XX syndrome men, XYY syndrome, testicular tumors, chronic diseases, injury testicles, radiation treatment or chemotherapy.

2. Secondary TD (diseases of the hypothalamus and the pituitary gland): Kallmann syndrome, Prader-Willi syndrome, chronic systemic illness (chronic organ failure, diabetes mellitus, malignancy, rheumatic disease, HIV infection, inherited metabolic storage diseases), congenital adrenal hypoplasia, constitutional delay of development, secondary GnRH deficiency, fractured skull, central ischemia, radiation effects in connection with treatment brain tumors, hypopituitarism, isolated LH or FSH deficiency, hyperprolactinemia, mutation receptor GnRH hormone.

3. Mixed primary and secondary TD: late-onset TD.

4. Tertiary TD (disorders of androgen target organs): testosterone insensitivity.

TD in men has a multifactorial etiology and results from testicular failure, or is due to the disruption of one or several levels of the hypothalamic-pituitary-gonadal axis.

# ZINC AND MALE REPRODUCTION

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Zinc (Zn) is a trace mineral essential for normal functioning of the male reproductive system: for testicular development and spermatogenesis.

Zn has many biologically significant interactions with hormones. Bishop and co-workers observed that Zn has a role in the production, storage and secretion of individual hormones as well as in the effectiveness of receptor sites and end-organ responsiveness. Among the most notable effects of Zn on hormone production and secretion are those related to testosterone (conversion of testosterone to 5α-dihydrotestosterone), insulin, adrenal corticosteroids and also it is irreplaceable for spermatogenesis and the development of the primary and secondary sex organs in the male.

Zn in human semen to play an fundamental role in the physiology of spermatozoa. In seminal fluid helps to stabilize the cell membrane and nuclear chromatin of spermatozoa. Other roles in male reproduction include: may have a regulatory role in the process of capacitation and acrosome reaction. The ability of Zn to reduce oxidative stress in sperm was also identified, although this was negatively associated with sperm decondensation. It is established, that Zn can counteract the oxidation by binding sulphydryl groups in proteins and by occupying binding sites for iron and copper in lipids, proteins and DNA.

Zn deficiency associated with decreased testosterone levels, gonadal dysfunction, decreases testicular weight and causes shrinkage of seminiferous tubules. The gonads are the most rapidly growing tissues in the body, and vital enzymes involved in nucleic acid and protein synthesis are Zn metalloenzymes. Zn has also been reported to be the primary factor responsible for the antibacterial activity of the seminal plasma. Zn may have a role in sperm production and/or viability, in the prevention of spermatozoa degradation, and in sperm membrane stabilization. Zn concentration in seminal plasma is known to correlate with count sperm concentration, motility and viability. Men with infertility due to an abnormally low sperm count may benefit from taking supplemental Zn in case of its established deficiency in blood or sperm.

Thus, the main aspects of zinc of male reproduction: testicular steroidogenesis, testicular development, oxygen consumption of spermatozoa, nuclear chromatin condensation, acrosome reaction, acrosin activity, sperm chromatin stabilization, testosterone synthesis and conversion of testosterone to 5α-dihydrotestosterone.

# THE EFFECT OF BIOLOGICALLY ACTIVE SUBSTANCE COMPLEX FROM *GERANIUM PALUSTRE* HERB ON THE COAGULATION PHASE OF HEMOSTASIS

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Studying the effect of the biological active substance (BAS) complex from *Geranium palustre* herb on the hemostatic system is a complicated gradual process. Preliminary it has been conducted the research of vascular platelet phase. The next stage of studying the BAS complex from *Geranium palustre* herb is investigation of its effect on the hemostasis coagulation phase. In this case the most informative screening test is a determination of activated partial thromboplastin time (APTT) and prothrombin time (PTT by Quike). APTT level is characterize the condition of hemostasis «internal» cascade: activity of factors XII, XI, IX, VIII, X, V, I, II, high molecular kininogen (HMK) and prekallikrein. In turn, PTT gives the assessment of the «external» cascade activity namely factors VII, X, V, I, II.

The aim of our research was studying of potential effect of the BAS complex from *Geranium palustre* herb on APTT and PTT levels in the blood plasma.

Determination of APTT and PTT levels was carried out on the 30 white non-linear rats weighting 160-210 g. All animals were divided in 3 groups (10 animals in every group): 1 group – animals that received 1 ml of distilled water; 2 group – animals that received BAS complex from *Geranium palustre* herb in its effective dose 3 mg/kg; 3 group – animals which were injected with reference compound – *Bursa pastoris* extract ($ED_{50}$=7 mg/kg). All research substances were administered intragastrically in the form of water solution stabilized by tween-80 for three days.

Three days later all animals were sacrificed and blood samples were taken in the volume of 3 ml. To obtain the plasma to the test tube with blood sodium citrate was previously added, after than it was centrifuged for 10 min at 3000 rpm. Determining the indicators of APTT and PTT was conducted using analytic four-channel coagulometer RT-2204 C.The findings evidence of increasing APTT level in animals that received BAS complex from *Geranium palustre* herb in 1.28 times against the control and in 1,10 times compared with reference compound. During administration the investigated extract PTT level increased in 1.14 times to intact animals and in 1.07 compared to those injected with *Bursa pastoris* extract. The results of undertaken research indicate a moderate effect of BAS complex from *Geranium palustre* herb on both «internal» and «external» ways of the first coagulation phase of hemostasis.

# STUDY THE POSSIBILITY ALLERGENIC EFFECT OF THE CREAM «DERMATOLIPOIN»

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In NFaU developed a new combination drug in the form of a cream called «Dermalipoin», it consisting from: α-lipoic acid, urea, olive oil, tea tree oil, PEG-400. Cream «Dermalipoin» is intended for the treatment of skin lesions of various origins. In accordance with procedure manual the study of a new drug should include the characteristic of the possible allergenic effect, which was the purpose of our research work.

Materials and methods: the experiments were conducted on 12 white outbread guinea pigs weighing 400-450g. To study the sensitization properties of cream used method of skin application. The animals were divided into 2 groups: 1 group – control group; 2 group – animals which on shaved skin is applied cream «Dermalipoin» once a day. Testing was performed in the 1st and 2nd phase of the skin sensitization. In the 1st phase of the skin sensitization properties were not found. Lack of sensibilization allowed continuing drawing applications to the 2nd phase. On the 20th day the testing was repeated. Noted the skin condition in the 1st hour at the place of application, then after 24 hours and expressed in points: 1 point – a point the weak hyperemia; 2 points – a point marked hyperemia; 3 points – a solid moderate hyperemia; 4 points – a solid intense and infiltration hyperemia. Furthermore, with purpose of assessment the severity of inflammation after resolution application dose was measured thickness skinfold.

Results: researches have shown that daily application of creams do not affect on the general condition of the animals. Guinea pigs were active, from the site of skin was not observed any changes in the form of congestion, infiltration, peeling, edema. Skinfold thickness did not change in the control and the experimental groups.

Thus, all dates indicated an absence of allergenic effect the cream «Dermalipoin» by cutaneous application.

# VITAMIN E AND MALE FERTILITY

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Infertility is an important medical and social problem. Approximately 15%-20% of couples of reproductive age are infertile.

For the clinician it is important to know the clinical conditions in which oxidative stress may play a role in the etiology of infertility. Excess reactive oxygen species (ROS) in the sperm or seminal plasma is known to result in oxidative damages of sperm DNA and impair sperm functions and has been linked to male infertility. Clinical conditions were found to be associated with increased oxidative stress: infections, inflammations involving the male reproductive, spinal cord injury, varicocele and smoking. Morphologically abnormal spermatozoa and leukocytes are the major sources of ROS in the male reproductive tract.

Vitamin E (VE) has been known as an essential nutrient for reproduction since 1922 when Evans and Bishop observed fetal resorption in rats fed with rancid fat.

VE are essential antioxidants that protect the body's cells from free radical damage. In vitro studies show that VE is a major chain-breaking antioxidant in the sperm cell membranes and it appears to have a dose dependent protective effect. VE is a synergist of androgens action. A few foods that can contain a high amount of VE such as: cereals, seeds and nuts, green vegetables, tomatoes, red peppers, oils, potatoes, fruits such as mangoes or papaya.

A low intake of VE was associated with poor sperm concentration and motility. The association VE intake and progressive motility was reported in Eskenazi study and Suleiman et al. study determined that VE improved sperm motility. Treatment with VE (300 mg per day) significantly decreased the malondialdehyde (a marker for lipid peroxidation) concentration in spermatozoa.

VE supplements the first line of empirical therapy for male idiopathic infertility. The therapeutic dose makes 50-400 mg per day. Usually VE supplements with another antioxidants: Vitamins A and C, L-Carnitine, zinc, selenium. Our researches have shown that the complex supplement VE (200 mg per day) with selenium (100 μg per day) in a current of two months leads to normalization of spermograms parameters in men with idiopathic asthenosoospermias (increase percentage of motility forms spermatozoids).

Thus, VE is one of the main antioxidant of male reproductive system, essential for fertility.

# PARTICIPATION OF HEAT SHOCK PROTEINS IN THE PATHOGENESIS OF AUTOIMMUNE DISEASES

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The heat-shock proteins (Hsp) – phylogeneticaly old intracellular proteins that are found in all cells with nucleus. The capacity to connect with intracellular peptides and taking part in the different cellular processes (proteins transport, antistress cells protection etc.) specifies the variability of their functions.

**The aim of the study** was the analysis of the current literature on involvement of heat shock proteins in the pathogenesis of autoimmune diseases.

**The results of the work.** Modern researches have set that the adjuvanticity of different types of Hsp is answered for actually not by Hsp, but their complexes with peptides (Hsp-peptide complex, Hsp-pc). It is shown that the Hsp can bind virtually any protein fragments, both endogenous and exogenous, both natural and model. Macrophages, dendritic cells, fibroblasts and other antigen presenting cells (APCs), with the exception of B-lymphocytes, capture Hsp-pc, isolate from them antigenic peptides and present them on the surface of immune effector cells in complex with MNS class I and II.

APC activated Hsp-peptide complexes induce activation of cellular and humoral immune responses against antigens of tissues from which they are allocated Hsp-MS, which creates serious preconditions for development of an autoimmune reaction. Activation occurs by proliferation of CD8+ cytotoxic and CD4+ lymphocytes, stimulation of NK-response. This process is accompanied by synthesis of a wide range of pro-inflammatory cytokines, especially interleukin-12 and costimulatory molecules.

**Conclusions.** Heat shock proteins can actively participate in the development of autoimmune diseases such as rheumatoid arthritis, diabetes, endocrine ophthalmopathy and other by formation of complexes with peptides.

# NEUROBIOLOGY OF LOVE

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Romantic love (RL) is a passionate spiritual-emotional-sexual attachment between man and a woman that reflects a high regard for the value of each other's person. RL is a complex social, psychological, neurobiological phenomenon, relying on trust, belief, pleasure and reward activities within the limbic processes in brain. These processes it is carried out under the control minor hormone: oxytocin, vasopressin, dopamine and serotonergic signaling. Besides, endorphin and endogenous morphinergic mechanisms, coupled to nitric oxide autoregulatory pathways, play a role.

Physiology, to “fall in love” is the first step in pair formation, involving attachment and bonding as well as romantic, sexual, parental and gender behaviors, that as a result forms lust, pleasure, joy and happiness. Stage, intense RL is associated with subcortical reward regions that are also dopamine rich. Accordingly, dopamine, interpreted here as a key step of the biologically important reward process, is a central instrument for the neurobiology of love. This seems to be particularly true with regard to the stimulating and pleasurable aspects of dopamine signaling. It is important to note that, based on new knowledge, there is a potential for endogenous morphine signaling to be part of this process. Morphine, given its reported effects and those exerted via constitutive NO release, may thus form the foundation of a common signaling among love and pleasure phenomena, including attachment behaviors.

In the period of passionate and intense love there is also a change in the sex hormones. These hormones have receptors in the brain. Testosterone in men play key role in libido, erection and ejaculation. During ovulation, a rise in testosterone increases sexual desire in women. Estrogens play role in sexual behavior in men and women.

Pheromones are chemical signals that are released by the body that can serve to attract or repel potential mates. Only recently have scientist discovered real evidence of a vomeronasal organ in human adults. Pheromones could trigger our sex drive by traveling the neural pathway that connects the nose to the hypothalamus, a region of

the brain that initiates the release of sex hormones and fuels erotic feelings and sensations.

Thus, the RL is difficult neurobiological phenomenon which underlies a choice of the marriage partner and formation of a happy family for the subsequent birth and education of children.

## ADDITIONAL SECTION № 21

# GENETIC RESEARCH: POSSIBILITIES OF USING IN THE PRACTICE OF MEDICINE AND PHARMACY

# HORMONES AND THEIR BIOLOGICAL ROLE

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The endocrine system is the collection of glands that produce hormones that regulate metabolism, growth and development, tissue function, sexual function, reproduction, sleep, and mood, among other things. Hormone levels can be influenced by factors such as stress, infection, and changes in the balance of fluid and minerals in blood. A gland selects and removes materials from the blood, processes them, and secretes the finished chemical product for use somewhere in the body.

These are the glands of the endocrine system: adrenal glands - influence the way your body uses energy, they also release a hormone called adrenaline when you are under stress; hypothalamus - part of your brain that controls hormone production by releasing different chemicals to the pituitary gland; ovaries - produce oestrogen and progesterone in women, and also release egg cells; pancreas - releases the insulin your body needs to metabolize sugar; problems with the pancreas can lead to diabetes; parathyroid - located behind the thyroid gland, they are essential for proper bone development; pineal gland - connects the endocrine system with the nervous system; produces several important hormones, including melatonin, important to sleep/wake cycles and sexual development; pituitary gland – likely the most important gland in your body, it is crucial to growth, mental development and reproduction; influences or controls the rest of your endocrine system; testes - produce the hormone testosterone; in men, testosterone maintains sperm production and bone mass; thymus - crucial to normal immune function in childhood; once a child reaches puberty, its tissue is replaced by fat; thyroid gland – located in the front of your neck, it releases hormones that control your metabolism and govern the way your body uses energy.

Once a hormone is secreted, it travels from the endocrine gland through the bloodstream to target cells designed to receive its message. Along the way to the target cells, special proteins bind to some of the hormones. The special proteins act as carriers that control the amount of hormone that is available to interact with and affect the target cells.

Also, the target cells have receptors that latch onto only specific hormones, and each hormone has its own receptor, so that each hormone will communicate only with specific target cells that possess receptors for that hormone. When the hormone reaches its target cell, it locks onto the cell's specific receptors and these hormone-receptor combinations transmit chemical instructions to the inner workings of the cell.

# ACTIVE FORMS OF LEARNING IN THE STUDY OF HISTOLOGY

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Active forms of learning - an important area of pedagogical activity in the modern university. Most often, the active forms of learning used in students of the senior courses. On the first course active forms are rarely used. The use of active learning is the most effective way to increase interest in the academic disciplines and the learning process at the university. Modern pedagogy has proven that students better understand and remember the material they studied by active methods. Developed many different methods of active learning. It is necessary to select the method that help to feel a sense of success. Such methods motivate the most. In most cases, the method chosen teachers. Participation of students in the choice of teaching methods is rational. Students must choose the learning method that is most like them.

The purpose of the study: to choose such methods of active learning histology, that are most suitable for first-year students.

Material and methods. In the group of 1st year students specialty "Laboratory Diagnostics" on the practical classes used different methods of active learning. These were the imitation game and non-game methods of active learning - a business game; pedagogical situations; educational objectives; imitation professional activities, collective thinking activity. After testing different methods students choose the best. Best methods were selected based on the results of an anonymous questioning of students.

The results of the study. In practical classes of histology at first-year students were tested several different forms of active learning. According to the results of an anonymous survey the best forms were selected. This is such forms. The Team Discussion the most difficult theoretical questions. Difficult questions selected students. Self-drawing up and decision of situational problems on the topic. Independent study of histological preparations. One student plays the role of an experienced specialist - histology, the second - the role of student. Reciprocal estimation of the level of development of theoretical material - points per lesson the student receives from his companions in the group.

Conclusion: active learning methods should be used to start at the first-year students. This increases the motivation to study both the theoretical and practical material.

# MODERN RESEARCH METHODS IN HYSTOLOGY AND CYTOLOGY

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One section of the histology - cytology. Cytology is the science about of the structure of all normal and abnormal components of cells and the changes, movements, and transformations of such components. The discipline includes cytogenics, cytochemistry, and microscopic anatomy, which involve investigations employing various microscopes, such as light, phase, interference, and electron microscopes. Cells are studied directly in living state (phase microscopy) or are killed (fixed)and prepared for viewing (embedded, sectioned, and stained) on light or electron microscopes. The birth of the modern era of cytology dates to the 1950's. The advent of new research techniques and the advances made in related branches of science stimulated the rapid development of cytology and led to a blurring of the boundaries between cytology, biochemistry, biophysics, and molecular biology.

The principal goals of modern cytology include the continued study of microscopic and submicroscopic cell structures, the chemical organization of cells, the functions of cell structures and their interactions, the ways in which substances penetrate into cells and may be isolated from cells and the role of membranes in these processes, the reactions of cells to neural and humoral stimuli of the macroorganism and to stimuli from the surrounding medium, the perception and conduction of excitation, the interaction between cells, the reactions of cells to injury, and the repair of injuries and the adaptation of cells to environmental factors and injurious agents. Cytology is also conducting further research in the reproduction of cells and cell structures, the transformation of cells in the course of morphophysiological specialization (differentiation), the nuclear and cytoplasmic genetic apparatus of the cells and of changes therein that cause hereditary diseases. In addition to the theoretical aspects, cytology is also working toward a solution of several very important biological, medical, and agricultural problems.

A number of branches of cytology have emerged, depending on the objects being studied and the methods of study used; they include cytogenetics, karyosystematics, cytoecology, radiation cytology, oncological cytology, and immunocytology. The most common uses of microarrays cytogenetics methods are for early diagnosis of congenital diseases. The use of microarrays in cancer research and diagnosis has been adopted too.

Methods cytochemistry and tsitogeneriki intensively developed. They are widely used in experimental and clinical pharmacology, in practice medicine.

# MODERN METHODS OF DIAGNOSIS OF THE ECHINOCOCCUS

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Echinococcus is chronically running across helminthiasis, characterized by destructive liver, lung and other organs of the body allergy and severe complications. The problems of echinococcus is debatable problem of modern parasitology, which is particulary actual in endemic areas. In some regions, for example in Australia, echinococcus has been entirely eliminated as a nosology. Nevertheless in other areas it is seen rather frequently, particularly in Europe and Eastern Asia and on the western coast South America. Among bogelund knocks are the most common, and occur in almost all regions of Ukraine. The aim of this study was to modern methods of diagnosis of the echinococcus.

The disease is caused by Echinococcus granulosus and Echinococcus multicularis. Last type occurs rarely, is highly virulent, and infection is usually lethal. The biotic cycle of the parasites involves the change of the host organism. Intermediate host, in which the cystic form (cysticercosis) develops, is usually a cow, ram, horse, camel and other herbivorous animals, and human as well. The endstage of development – pubescence shape is developed in another organism – dog or wolf (carnivore animal), where eggs are produced.

The main path infection is the gastrointestinal tract. Eggs or segments that contain oncosphere, having got into the digestive channel, is released from the envelope and dives into the strata of a stomach mucous membrane or small intestine and later into veins and lymphatics vessels. Some oncospheres through artery-vein fistulae get into the large circle of blood circulation and can be disseminated into any organ or tissue. Among laboratory indexes increased erythrocyte sedimentation rate and eosynophylia are observed. Serological the tests and intradermal test of Kasoni are not used now, which is stipulated by low informative value and high hazard of allergic reactions. In addition to conventional clinical and laboratory examinations are conducting a study of the immunological status with the definition of a set of indicators characterizing the cellular and humoral immunity, including the determination of the white blood cells, blood lymphocytes and their factions, and classes of immunoglobulins A, M, E, G, apply leptocythere, ultrasound, examination of the hepatic hemodynamics and other. The diagnosis is mostly established accidentally during instrumental (ultrasound, X-Ray, laparascopis) investigations of organs at arising of complications.

# IMMUNOLOGICAL FACTOR IN THE PATHOGENESIS OF TISSUE HELMINTS

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At the present stage parasites occupy among nosology one of the leading places in Ukraine and, in particular, in the Kharkiv region for the prevalence and negative influence on the human body. Immunology, which is widely developed in all areas of medicine, and in the case of parasitic diseases. Got to the host organism, parasites do a wide range of immunological reactions, which are formed according to the general principles of immune.

However, because of the difficulty biochemical, nature and mechanisms of immunological reaction in helminthes have there our characteristics. Immunity in parasitic invasions formed by the mutual activation of various immune cells. Parasites through constant variability of their antigens structure and production of suppressive factors inhibit the activity of the immune systems, helping to create immunodeficiency disorders.

The aim of this study was to analyze current scientific data concerning the pathogeneses of tissue factor immunological human helminthes.

The basis of the immune response in tissue helminthes IgE antibodies are the products and can fully activate effector cells eosiniphiles. Helminthes stimulate the synthesis of TNF-α, acute phase proteins, etc, through which formed the inflammatory process. When helminthes immune response develops in Th2 (humoral) type. Anti-inflammatory interleukins produced by Th2 Lymphocytes, eosinophiles cause enhanced proliferation (IL-5), labrocytes (IL-3, colony stimulating factor), and the formation of specific IgE and IgG4 (IL-4). Formation of immune response to helminthes depends on many factors, but mostly it depends on the state of health of the body.

The products of specific antibodies stimulate physical and functional secrets and excreta antigens forms. In stimulate doses helminthes antigens produced IgE, IgG4 antibodies that do not have complete properties. For helmint infections characterized by increasing levels of total serum IgE and eosynophylia. In the future, the development of helminthic changing its antigenical structure increases its immunogeficity, which leads to the synthesis of IgM and IgG4.

The IgG4 due to lack of their own receptors on cells, combined with receptors for IgE, blocking them for this antibody. Under the influence of IgE antibodies in

helminthes activated two types of cells that play a leading role in protecting antihelmintic. Conjugated with parasites processes considered excavation IgE and IgG4.

Eosinophils are the main effectors cells, which have antihelmintic and parasitic function by forming extracellular lysis. Eosinophils have receptors for IgE, markers of activation (CD 69 and CD 66), adhesion molecules, through which they are in contact with the vascular endothelial cell, produce and secrets IL-4, IL-5, GM-CSF, TNF-α, which leads to the formation of eosinophilic infiltration in tissues and organs.

The intensity increases with eosynophylia migration of larvae in tissue, while chronic process − the number of eosynophyles decreased. In addition to the complex IgE-antibody-antigen worms appear antibodies IgM and IgG Classes and involved in the process of cell-effectory late phase allergic response (platelets, neutrophiles, macrophages, lymphocytes). Antibodies IgG and IgM classes directly or in the forms of immune complexes fixed on the surface of helminthes its eggs, larvae, thus activating the complement system.

The most intensive synthesis of specific antibodies observed in parasites and intestinal helminthes weaving, especially during migration and molting larvae.

Thus, organ pathology in the acute stage of helmintheasis depends on the intensity of infestation and features of the host immune response. While for the development of organ lesions in the chronic stage helminthes and determined reforms superinvasion, especially the defensive reactions to taxonometrical alien strains structure, proximity metabolites elements parasitic to host tissue elements.

In the acute stage of helminthiasis is determined by the increase in the content of eosynophylia in the blood and total serum albuminum. Helminth antigens produce IL-4, IL-5. Trigger the stimulation aktivnosti Th2 populations is accompanied by increased production of IgE, IgG4, differentiation eosinophilia.

The value of the allergic phenotype in shaping the characteristics of the immune response is confirmed by a similar predominance of the activity of a population it is for Th2 allergic diseases.

Generally, the basis of the immune response in the tissue helminth - synthesis of IgE antibodies and the activation of the effectors cells eosynophyls.

Thus, organ pathology in the acute stage of helmintheasis depends on the intensity of infestation and features of the host immune response. While for the development of organ lesions in the chronic stage helminthes and determined reforms superinvasion, especially the defensive reactions to taxonometrical alien strains structure, proximity metabolites elements parasitic to host tissue elements.

# POPULATION STUDY OF SLEEP DURATION AND DREAMS IN UKRAINE POPULATION SAMPLE

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One of the most striking examples of manifestations of human biological rhythms is the sleep-wake cycle, characterized by changes in the activity of a number of physiological processes. Alternation of sleep and wakefulness is subject to the laws of the circadian biological rhythms that fit in a 24-hour time slot. It is now known that circadian rhythms are controlled by the suprachiasmatic nucleus of the hypothalamus, which in turn regulates the secretion of the hormone melatonin by the pineal gland, which is reduced in the daytime, and increases in the dark.

During the life of a man dreaming dreams is about six years, an average of two hours a day. The best way to gather information about dreams - an anonymous survey of people in groups. In the study of the population of Ukraine we used this method. The study involved 2305 people in Ukraine aged 14 to 72 years, mostly in Kharkiv and Kharkiv region, who gave informed consent for questioning. Collection of information held in view of ethical requirements when dealing with a person. The questionnaire contained socio-demographic information. Probands were 741 male and 1501 female. In the study there were 74 married couples, 105 pairs of siblings and 352 parent-child pairs, 1174 people were surveyed without a relative. Groups were formed depending on the objectives of the study.

The average age of the patients in study of sleep characteristics was 24.5 ± 0.8 years in men (s = 9.9), and in women – 25.8 ± 0.7 years (s = 12.7); sleep duration in men was 8.3 ± 0.2 h (s = 1.7), in females 8.2 ± 0.1 h (s = 1.6); the average duration of sleep in the studied population was 8.2 ± 0.1 h (s = 1.7). Mode and median duration of sleep was 8 h. In the analysis of subjective sleep duration gender differences were found.

The analysis of other sleep characteristics was done depending on gender and age. Daytime sleep was not related to gender, but was associated with age ($p < 0.05$). In the study of the speed of falling asleep it was revealed that in general 70% of the patients fall asleep quickly, 25% - slowly, and 5% were mixed in the subjective evaluation of the speed of falling asleep. Gender differences in speed of falling asleep

were not found, but it was shown its relationship with age ($p < 0.001$). In studying the symptoms of insomnia sex differences were found, but in general about 14% of the patients have sleep problems. Symptoms of insomnia were associated with age ($p < 0.01$).

Among the examined people phenomenon of recurrent dreams was present in 24% of the population. The resulting value is quite small in comparison with those of other researchers, according to which recurrent dreams may reach 50-80%. According to others recurrent dreams occur in 70% of women and 65% men. On the other hand, a small fraction of the frequent recurrence of dreams is a positive thing, because, as a rule, recurrent dreams are accompanied by a number of nervous and mental disorders. Also there was a relationship of age to the presence of frequent recurrence of dreams ($r = 0.12$, $p < 0.05$). Thus, most (about 30%) recurrent dreams occur in younger people, less often (about 14%) - in older individuals.

In the sample studied in 10% of the population there was seen nightmares. The presence of relatively frequent nightmares in the sample was related to gender. So, women nightmares occur almost 8 times more likely than men ($K = 0.12$, $p < 0.01$). A relationship between gender and their presence in dreams was found ($r = 0.12$, $p < 0.05$). Thus, 32% of men and only 16% of women do not have the features of dreams. Perhaps in the studied sample women just better remember dreams than men. Special studies in sleep laboratories have shown that at least 70% of human dreams were in color, although on average only about 25-30% of people remember their dreams have specified feature that is consistent with the data obtained in the studied sample. There is the presence of about 8% of rare dreams and deepest dreams 7%, suggesting the predominance in this part of the population of slow-wave sleep.

Thus, a sample of the population of Ukraine distribution of duration of sleep is characterized by positive skewness and kurtosis. Sleep duration weakly negatively correlated with age, regardless of gender. The presence of an afternoon nap, the speed of falling asleep and symptoms of insomnia are not related to gender. The speed of falling asleep is not related to gender, but lower among younger and older age groups, as well as among students and health professionals. Risk of developing symptoms of insomnia is higher in people of younger and older age groups. A relatively small proportion of recurrent dreams in the population was found, and their prevalence was higher in younger age groups. A higher incidence of nightmares was seen in women. The presence of the typical features of dreams in most of the population was found.

# FOOD PREFERENCES AND TASTE SENSITIVITY AND BEHAVIOURAL CHARACTERISTICS (TAKING THE POPULATION OF UKRAINE AS AN EXAMPLE)

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Food behaviour is a kind of human behaviour, and can be of an adaptive and deadaptive character. Food preferences are associated with a number of behavioral manifestations and may be a cause for occurrence of some somatic and psychopathological conditions.

The immediate aim of the research was to identify the associations of phobias and food preferences/sensitivity to the pheniltyocarbamide (PTC) within the population of Ukraine. The age of the participants was within the range of 16 to 20 years old. Taste sensitivity was studied, taking the PTC as an example. A piece of filter paper was immersed in the freshly prepared solution of the FTC, after that it was dried and cut. The stripes of clean filter paper were used as a means of control. The participants were asked to taste a strip of clean filter paper, and then a stripe immersed in the PTC. If a participant tasted the FTC as a "bitter" taste, then the phenotype of a participant was defined as a tester. Food preferences were studied in terms when the participants had equal access to food, a choice of several food categories and they were not hungry. We selected seven food groups, towards which preferences were studied: sweet foodstuffs, meat, fruit, salty foods, vegetable dishes for the first course, fast food and fat food.

Behavioral response was considered taking into account presence/absence of phobias. The interdependence of sex and the presence of phobias was examined. As a result; it was found out that there were approximately an equal number of women with phobias and without them. There were 3 times fewer in men with phobias than those who had not experienced the marked fear to any object or phenomenon. Therefore, the further analysis was performed separately for men and women. The groups to compare the participants of different sex were formed on the basis of presence/absence of phobias. The results showed no interdependence between all the studied food preferences/taste sensitivity and sex of the participants with phobias and those who did not demonstrate them.

# STATE OF CURRENT KNOWLEDGE IN PHARMACOGENETICS AND ATTITUDES TO PHARMACOGENETIC TESTING IN A SAMPLE OF PHARMACY STUDENTS

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The problem of the individual's approach to treatment is crucial in modern medicine. It is connected with the range of important discoveries in the field of molecular mechanisms of drugs action. These discoveries are related to the levels of pharmacodynamics (receptors) and pharmacokinetics (enzymes). A series of new interdisciplinary subjects appeared not so far, such as pharmacogenetics, pharmacogenomics, pharmaceutical biotechnology, etc. Thus, it is necessary to develop educational programs for pharmaceutical and medical students, as well as for specialists in advanced training, who work in the health care system.

Pharmacogenetic testing aims to determine the genetic characteristics that are important for individual selection of medicines. The consequence of such research should be to prevent potentially dangerous side effects for patients, and possibly reducing the overall cost of treatment. At the same time, even in countries with well-developed medical infrastructure the use of pharmacogenetic tests is not a massive.

The aim of the present work is to analyze the students' awareness about pharmacogenetics and their attitudes to pharmacogenetic tests.

Field investigations were used in this work. Questioning of students in Ukraine was conducted. Gathering of information was conducted taking into consideration the ethical requirements while working with a human. The material analysis based on questioning 3143 students majoring in pharmacy, medicine or biology has been carried out.

The relationship between qualitative characteristics was evaluated using the criterion $\chi^2$. Conclusions to statistic hypotheses were made at the significance level $p \leq 0.05$.

As many atypical human reactions to drugs are due to a genetic factor, it is reasonable to include the question about the possibility of pharmacocorrection for understanding hereditary conditions (diseases). The results of the study showed that the majority of the males questioned believed that it was impossible to correct hereditary diseases using drugs (51.2%). 41.4% of females thought that hereditary diseases could be treated with drugs. Nevertheless, any significant differences between peculiarities of females and males answers to this question haven't been found ($\chi^2 = 2.70$, $\nu = 2$, $p = 0.26$).

Analyzing answers to the question about the notion of pharmacogenetics it has

been shown that this concept is understood differently by males and females, and differences obtained are statistically important ($\chi^2 = 13.84$, $\nu = 6$, $p = 0.03$). Thus, 11.8% of the males and 6.4% of the females questioned have not heard anything about pharmacogenetics. 14.1% of the males and of the females 25.2% have heard about it, but do not know exactly what pharmacogenetics studies. The right answer about the notion of pharmacogenetics was given by one third of the males (37.7%) and females questioned (43.9%).

In our study it has been stated that females – future pharmacists are more progressive as to awareness of pharmacogenetics ideas. Consequently, as females are more informed about genetic peculiarities of the organism and its response to drugs, they probably will advise visitors of the chemist's to conduct these tests in future. Besides, females as a subject of the pharmaceutical market potentially more often can be consumers of its production themselves (pharmacogenetics tests), they less likely will have side effects due to incorrect treatment. In connection with this, the male population can get into potential risk group of increased frequency of atypical reactions.

In the analysis of the responses to the question of willingness to pay for conducting pharmacogenetic tests for yourself or your family members shows that 16.73% of men and 14.68% of the women surveyed are willing to pay for conducting pharmacogenetic tests in any case, regardless of cost. Just under a third of the men surveyed (31.05%) and slightly more than a third of women (38.85%) are willing to pay for conducting pharmacogenetic tests, if the cost of such a study is acceptable. Approximately one-third of male respondents (32.06%) and women (31.14%) did not consider it necessary to pay for pharmacogenetic tests under any circumstances. 20.16% of men and 15.33% of women expressed their lack of understanding of the purpose of the pharmacogenetic testing and, accordingly, also exclude the possibility of payment. Thus, about half of the population surveyed expressed readiness (conditional/full) to pay for pharmacogenetic testing.

Apart from the fact that not all respondents were adjusted positively to conduct pharmacogenetic tests, the majority held that DNA testing is generally costly. Analyzing the subjective opinion of the respondents about the possibility of holding of the DNA test, it was found that approximately ¾ of the respondents (71.81% of men and 78.62% women) suggest that the cost of such research is high.

More than half of respondents believe (60.6%) that pharmacogenetic testing should pass the entire population, regardless of gender, age and clinical status. 8% of respondents believe that pharmacogenetic tests are conducted in pregnant women. Least of all, according to the study participants, pharmacogenetic testing is necessary for the elderly (1.9%).

# DERMATOGLYPHICS AND ITS USE IN MEDICINE AND GENETICS

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Towards the end of the nineteenth century, the recognition of the importance of fingerprint patterns was gaining ground in many quarters, notably in India, Japan, Argentina and the UK. After Galton's initial pioneering work, many further investigations were undertaken to develop this fledgling science of dermatoglyphics. The scientific investigation of the hand was beginning to prove without doubt that the hand was indeed a study worthy of the finest minds and could reveal not only vital genetic and medical information about an individual but also something of the psychological uniqueness of each person. With the discovery of the significance of dermatoglyphics, the study of the hand was truly beginning to come of age. It was reading Cummins and Midlo's work that inspired LS Penrose to conduct his own dermatoglyphic investigations as a further aspect of his research into Down's Syndrome and other congenital medical disorders. In 1945, he was appointed to the Galton Chair of Eugenics at London University. Although the post had existed for some fifty years up to this point, very little research had actually been done into the genetic significance of fingerprints.

Although many important discoveries regarding the psychological significance of fingerprint patterns have been made, the main thrust of scientific dermatoglyphic research in the latter half of the twentieth century has been directed into genetic research and the diagnosis of chromosomal defects.

The current state of medical dermatoglyphics is such that the diagnosis of some illnesses can now be done on the basis of dermatoglyphic analysis alone and currently, several dermatoglyphic researchers claim a very high degree of accuracy in their prognostic ability from the hand's features. Dr Stowens, Chief of Pathology at St Luke's hospital in New York, claims to be able to diagnose schizophrenia and leukaemia with up to a 90% accuracy from the patterns of the hands alone and in Germany, Dr Alexander Rodewald reports he can pinpoint many congenital abnormalities with a 90% accuracy from a consideration of the features of the hands alone.

The modern study of the hand is thus far removed from the popular image of the soothsaying hand reader uttering mysterious incantations in an arcane language. Rather, through decades of scientific research, the hand has come to be recognised as a powerful tool in the diagnosis of psychological, medical and genetic conditions.

# PTC SENSITIVITY IN THE POPULATION OF UKRAINE

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Phenylthiocarbamide (PTC) is a synthetic compound, which by the interaction with certain human taste receptors is felt bitter in some individuals (tasters) and tasteless in others (non-tasters). Despite the fact that PTC is synthesized in the laboratory and is not found in nature, the ability to sense this substance is highly correlated with the ability to sense other bitter compounds of natural origin, many of which are toxic, such as strychnine, ricin and quinine, and some are very useful, such as grapefruit, green tea, broccoli, arugula, cauliflower, and others having in their composition compounds with anticancer activity (citrus flavonoids, polyphenols of green tea and red wine ect.). At the same time, it is essential to consider that sensitivity of certain compounds with a bitter taste, for example, goitrin, does not correlate with sensitivity to PTC, while they may be contained in the same products. A variety of gustatory senses in the population can significantly affect the eating behavior of a person and, therefore, the state of his/her health; moreover, associations may have a sex specificity. PTC is of great interest from the medical point of view since a number of associations of the taster status with human diseases have been found. Cheapness and availability of this type of testing appear to be attractive diagnostically. In Ukraine similar studies were carried out restrictedly, thus the aim of this study was to analyze distribution of the sensitivity to PTC in the sample of the population of Ukraine presented by residents of Kharkov and some other populations of Ukraine.

The study involved 533 people (78 males and 455 females) aged from 16 to 25 years. All participants of the study filled in specially designed questionnaires, which included a list of issues of the demographic and medical nature, as well as the issues related to food preferences. This study included the analysis of only the main characteristics of the respondents required to calculate the structure of the population by the genetic marker studied. The respondents were not relatives, and they largely represented the general population sample in relation to the sensitivity to PTC. The collection of information was conducted taking into account the ethical principles when dealing with a person in accordance with the Declaration of Helsinki (World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research

Involving Human Subjects). All participants of the study gave the written consent to participate in the study.

The design of the experiment corresponded to the blind cohort cross-sectional study. The relationship between the traits was determined by means of Pearson criterion $\chi^2$. The significance of differences was determined at the level of $p < 0.05$.

In relation to the demographic indicators mentioned of all trial subjects 159 people were natives of the Kharkov and Kharkov region, 348 people were natives of other regions of Ukraine and 9 people were born outside Ukraine. 466 people identified themselves as Ukrainians, 45 – as Russians and 16 – as representatives of other nationalities. 385 of the respondents had the Ukrainian father, 80 had the Russian father and 23 had fathers of other nationalities. 432 of the trial subjects had the Ukrainian mother, 60 had the Russian mother and 20 had mothers of other nationalities. All trial subjects were students of the National University of Pharmacy (Kharkov).

When studying the phenotype frequencies of PTC tasters and non-tasters the data indicating that among all the populations studied 20% of PTC non-tasters were obtained. There is a tendency of increase of the frequency of non-tasters among males compared to females (24.4% and 19.1%, respectively), however, the relationship between sex and taster/non-taster status has not been found.

Assuming that the sensitivity to PTC is not a trait by which an assortative mating exists (i.e., the population is panmictic), taking into account the monogenic nature of the trait there the frequencies of the gene responsible for the presence of (T) and the absence of (t) sensitivity to this compound were calculated separately among males and females. Based on the Hardy–Weinberg equation the frequencies of three possible genotypes (dominant homozygotes TT, heterozygotes Tt and recessive homozygotes tt) were calculated.

The frequencies of alleles T and t obtained in the male and female population under research are very close to the frequencies of the same alleles in two populations of India (Khan, T and t are 0.52 and 0.48, respectively among males, and Mir, T and t are 0.55 and 0.45, respectively among females).

Data of this study supplement the currently available information in relation to the genetic structure of modern Ukrainian cities.

In our further studies it is planned to expand the sample and study the possible associations of the sensitivity to PTC with the indices in the local population, which are significant for the state of somatic and mental health.

# GLUCOSE-6-PHOSPHATE DEHYDROGENASE DEFICIENCY AND ITS CLINICAL SIGNIFICANCE

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Glucose-6-phosphate dehydrogenase deficiency (G6PD deficiency) also known as favism (after the fava bean) is an X-linked recessive genetic condition that predisposes to hemolysis (spontaneous destruction of red blood cells) and resultant jaundice in response to a number of triggers, such as certain foods, illness, or medication. It is particularly common in people of Mediterranean and African origin. The condition is characterized by abnormally low levels of glucose-6-phosphate dehydrogenase, an enzyme involved in the pentose phosphate pathway that is especially important in the red blood cell. G6PD deficiency is the most common human enzyme defect. There is no specific treatment, other than avoiding known triggers.

Carriers of the G6PD allele appear to be protected to some extent against malaria, and in some cases dominant males have shown complete immunity to the disease. This accounts for the persistence of the allele in certain populations in that it confers a selective advantage. Most individuals with G6PD deficiency are asymptomatic. Symptomatic patients are almost exclusively male, due to the X-linked pattern of inheritance, but female carriers can be clinically affected due to unfavorable lyonization, where random inactivation of an X-chromosome in certain cells creates a population of G6PD-deficient red blood cells coexisting with normal red cells. A typical female with one affected X chromosome will show the deficiency in approximately half of her red blood cells. However, in rare cases, including double X deficiency, the ratio can be much more than half, making the individual almost as sensitive as a male.

Many substances are potentially harmful to people with G6PD deficiency. Antimalarial drugs that can cause acute hemolysis in people with G6PD deficiency includeprimaquine, pamaquine, and chloroquine. There is evidence that other antimalarials may also exacerbate G6PD deficiency, but only at higher doses. Sulfonamides (such as sulfanilamide, sulfamethoxazole, and mafenide), thiazolesulfone, methylene blue, and naphthalene should also be avoided by people with G6PD deficiency as they antagonize folate synthesis, as should certain analgesics (such as aspirin, phenazopyridine, and acetanilide) and a few non-sulfa antibiotics (nalidixic acid, nitrofurantoin, isoniazid, dapsone, and furazolidone). Henna has been known to cause haemolytic crisis in G6PD-deficient infants.

# HUMAN MITOCHONDRIAL DISEASES

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Mitochondrial diseases are very diverse conditions due to dysfunction of mitochondria, specialized compartments in virtually every cell of the body. Mitochondria generate more than 90% of the energy required by the body. Mitochondrial dysfunction depletes cells of energy causing cell damage and even cell death. Due to the high energy requirements of brain and muscle, mitochondrial disease typically affect these parts of the body causing encephalomyopathies. Mitochondria are unique organelles because they are the products of their own genetic material (mitochondrial DNA or mtDNA) and nuclear DNA. Therefore, mitochondrial diseases are caused by mutations in either mtDNA or nuclear DNA.

Mitochondrial diseases are often difficult to diagnose and therefore, it is important for patients to be evaluated at a medical center with appropriate expertise. In some cases, symptoms and signs may suggest a particular mitochondrial disease. Physical examination and laboratory tests are necessary to characterize involvement of various organs and to reach the correct diagnosis. Laboratory studies typically include: blood tests, brain MRI or CT scans, heart tests (electrocardiogram and echocardiograms), ophthalmological and neurological evaluations, and hearing tests. Elevated lactic acid (lactate) or lactate to pyruvate ratio (>20:1) in blood or cerebrospinal fluid is a common sign of mitochondrial dysfunction. Muscle biopsy is the gold-standard for the diagnosis of many mitochondrial diseases and requires specialized microscopic analyses and biochemical tests (such as measurements of mitochondrial respiratory chain enzyme activities). Finally, genetic testing of blood, urine, or muscle is performed to pinpoint the exact mutation responsible for a specific disease. The most common symptoms of mitochondrial disorders are: muscle weakness, exercise intolerance, fatigue, cognitive difficulties, and neurological problems. The current genetic advice is that fathers with mtDNA mutations are at no risk of transmitting the defect to their offspring. Maternal transmission of mutated mtDNA occurs, but the risk depends on the type of mutation and possibly the segregation of the mutation within maternal tissues. Identifying specific mtDNA mutations and investigating family members for evidence of transmission will give guidance to the likelihood of transmission through the germline. Detailed studies of large patient cohorts provide invaluable information on the risk of transmission.

# THE ROLE OF LEARNING THE HISTOLOGY DISCIPLINE IN THE FUTURE PRACTICAL ACTIVITY OF SPECIALISTS IN LABORATORY DIAGNOSTICS

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Motivation is very important for studing any academic discipline. Motivation is significantly increased if the student understands the value of professional discipline.

Histology - the science that studies the development, structure and function of tissues. Organs and tissue histology studies at the microscopic level. The main purpose of the discipline "Histology, cytology and embryo-ogiya" is the knowledge of microscopic and submicroscopic structure of cells, tissues and organs. Histology is also studying the general laws of development of living organisms. During the studying histology students specialty "Laboratory Diagnostics" learn to work with a microscope. Using light microscope, they study the structure of tissues and organs. Histology generates biological and medical thinking. Histology is needed for the study and understanding of physiology, pathology, pharmacology. After examining the histology students should learn to analyze the relationship between structure and function of tissues and organs. Students should learn to understand the normal microscopic picture of human tissue.

Material and methods. Questioning of first-year students specialty "Laboratorydiagnosis". Survey questions: what is the histology; why is it necessary for laboratory doctors; do you like histology. Questionnaires conducted at the beginning and end of the semester.

The results of the study. At the beginning of the semester the answer to the first question was given 90% of respondents. The study of histology at the beginning of the semester like 60% of the students. To answer the question of the significance of histology were able to only 10% of students. Throughout the semester, every lesson the teacher explained the purpose of the study subjects. Students and teacher understand the importance of each topic together. There were lessons-excursions to the histological laboratory throughout the semester. Then, at the end of the term the answers given 100%, 85% and 80% respectively.

Conclusion: awareness of the importance of discipline for the future professional activity increases the motivation to its study.

# PROBLEMS OF GENEALOGICAL CULTURE IN UKRAINE

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In modern society a growing need exists to create databases on genetic structure of population using both classical and DNA markers. The most acute problem consists in the creation of the so-called "referential" databases, however, the general principles of the formation of the reference population do not exist in connection with the specificity of demographic, socio-cultural, ethno-religious processes in different countries and regions. In solving various problems connected with the human heredity, there frequently emerges a necessity to obtain accurate genealogical information, including one of the most important indicators such as ethnicity. This indicator is necessary for the correct application of DNA markers in forensics, medical genetics, in dealing with ethnogenesis and human evolution issues, etc. The information about pharmacogenetic peculiarities of different ethnic groups in the multiethnic population will allow to develop recommendations on the pharmacotherapy organization for each of these groups. Accounting of the ethnicity obtains a tremendous significance at the prediction of the so-called ethnic diseases, the population frequency of which has a specific character. One more complication to the work of Ukrainian geneticists consists in the fact that the population, which is not familiar to the population-based studies, expresses incomprehension and concern about the use of the genealogical data. The deletion of the "nationality" position from the Ukrainian passport led to the fact that the majority of young people started to identify ethnicity and nationality. This situation reduces the accuracy of the scientific studies and the probability of medical genetics and other predictions.

In this study there were used the data on the records from the registry office, and 4450 questionnaires collected by the authors (in 2004-2007 and in 2014), which included information on the nationality of the proband, his parents and grandparents. According to the available data the generally valid statistics was calculated. Statistical hypothesis testing was performed at a significance level of 0.05.

The main tendency in ethnic identity in Ukraine is that young people (participants of the studies in 2004-2007 and 2014) associate their ethnicity with nationality. This phenomenon leads to the fact that at the moment more than 90% of residents of Ukraine call themselves Ukrainians, i.e. there takes place an ethnic consolidation. For example, according to the data on marriage records in 1993, there were 49.9% Ukrainians in Kharkov and almost as many Russians – 43.6%. Such a

drastic change can be explained by the change of self-definition. This result is of great importance in conducting molecular genetic studies in Ukraine. If formerly such studies contemplated basically taking biological material for DNA analysis in individuals with three generations of parents of the titular nationality, then currently it is difficult to implement such a requirement. Apparently, in the future the role of ethnicity in Ukraine will lose its value for these purposes, and Ukrainians, as an ethical group, will become more genetically heterogeneous.

Almost 90% of the population consider themselves Ukrainians in eastern Ukraine, and almost everyone – in western. In Ukraine, among persons of the titular nationality there are more females, while among males there are almost three times more representatives not of Slavic nationality. Most Russians and representatives of other nationalities are concentrated in metropolitan areas. As a rule, if a person can not define his national identity, especially if he is an offspring of the interethnic marriage, geneticists are guided by the nationality of parents and grandparents. It turned out that the informational value of these indices is not absolute, especially if a respondent is male. At the same time the questionnaires regarding nationality of 8.1% of males and 2.8% of females were not able to answer any question. It should be noted that in 2014 the amount of these people became much less: less than 1% of the population of Ukraine could not decide about their own nationality, at that sexual differences on this criterion were not identified. Unfortunately, the awareness of the relatives ethnicity of youth falls. Persons of the younger generation have more difficulties reproducing information about their relatives. Among males of the older generation (aged 36 years or more), 7.6% could not decide with their own nationality, 16.0% - with the nationality of the father and 15.1% - with the nationality of the mother. Young males (under 36 years) appeared to be less informed: 9.4% found difficulty in relating themselves to a certain nationality, 26.4% did not know the nationality of the father, 17.3% - of the mother. The same tendency is present among females: 2.1% of the older could not name their nationality, among the younger there were 3.3%. Among the older females, 6.3% did not know the nationality of the father, 8.7% - the nationality of the mother, in the younger generation - 10.8% and 11.2% respectively. From a half to ¾ of respondents did not know the nationality of their grandparents. In general, both males and females were better informed about their relatives on the maternal line than paternal, which may be connected with the fact that in the single-parent families children usually live with their mother, not the father. Most fully informed about the nationality of their parents are representatives of the rare nationalities, which is in agreement with the data, where the largest assortative mating by ethnicity is also observed among the representatives of ethnic minorities.

# FOOD PREFERENCES: COEFFICIENTS OF HERITABILITY IN UKRAINE POPULATION SAMPLE

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One of the determinants of a human health is nourishment. Quantitative and qualitative aspects of the diet play an important role both in the development and in the prevention of many disorders including diabetes mellitus, metabolic syndrome, obesity, chronic degenerative diseases, heart failure etc. With the development of human genetics the questions of possible genetic influence on eating behavior and food preferences in particular began to be studied. The majority of these studies have been carried out on twins. The interaction of genes and environment may be so complex that the consumption of nutrients, being under genetic control to a certain degree, may become an environmental factor of modification of the gene expression associated with diseases, especially, obesity. Many biological and socio-demographic factors influencing food preferences, which include age, ethnicity/race, income and educational levels, etc are described for different populations. In modern conditions the human eating behavior can modify such a purely environmental factor as an appearance of new kinds of food, such as organic, synthetic and nanofood, along with the already common products with the GMO content, nutritional and dietary supplements, functional foods, etc.

The purpose of this study was to evaluate the heritability of several food preferences among the residents of Ukraine on the basis of the correlation analysis in pairs “parent-child”, in siblings pairs and in married couples.

The questionnaires on food preferences were filled by 291 “parent-offspring” pairs (including 19 “father-son” pairs, 54 “mother-son” pairs, 34 “father-daughter” pairs and 184 “mother-daughter” pairs), 84 sibling pairs (including 7 male sibling pairs, 36 female sibling pairs and 41 opposite sex sibling pairs) and 70 marital couples. All the participants of the study were the residents of Ukraine, predominantly of Kharkiv population. Data was collected in accordance with the ethical requirements when dealing with a human as to the Declaration of Helsinki (World Medical Association Declaration of Helsinki, Ethical Principles for Medical Research Involving Human Subjects). Food preferences were studied by the method of special interviewing by putting the investigated persons under the equal availability of food options, lack of hunger and an opportunity to choose several food categories. The food groups, in regard to which preferences were studied, were as

follows: sweet – ice cream, cake, chocolate (high-calorie carbohydrate group), meat – a sandwich (protein group), fruit – an orange (cellulose and vitamins), salty food – pickles (the source of NaCl), first vegetable courses – a borsch (cellulose and vitamins, "healthy" food), fast food – chips ("junk" food containing food additives, colorings, preservatives), fatty food – sunflower seeds (the source of essential fatty acids, high-calorie food).

Methods of the study included the survey on the basis of a specially designed questionnaire, as well as classical genetic analysis and statistical analysis. Preliminary correlation analysis was performed by calculating the nonparametric Spearman correlation coefficient ρ. Genetic analysis was performed taking into account the correlation coefficients for the parent-offspring pairs (ρp) ("mother-daughter", "mother-son", "father-daughter", "father-son"), sibling pairs (ρs) ("brother-brother ", " sister-sister ", " brother-sister ") and husband-wife pairs (ρhw). The correlation coefficients between relatives were corrected taking into account the correlation coefficient between spouses. The corrected correlation coefficients between relatives were used for the component decomposition of total phenotypic variance by the formulae: $Ga = 2\rho p$; $Gd = 4(\rho s - \rho p)$; $G = Ga + Gd$; $E = 1 - G$, where G – the total genetic component, Ga – its additive and Gd – dominant components, E – the environmental component.

The majority of statistically significant correlation coefficients are recorded in pairs "mother-daughter". Thus, not high, but significant correlation coefficients are observed for preferences for meat (0.28), fruit (0.17), salty food (0.19) and the first vegetable courses (0.25). In pairs "mother-son" a significant correlation coefficient was observed only for fruit (0.39), and in pairs "father-daughter" – only by salty food (0.36). The significant correlation coefficients for five food preferences for siblings were approximately similar – 0.33-0.37 (average value). In opposite-sex sibling pairs and in female sibling pairs, a positive correlation for preferences for sweet was observed, whereas, despite the same degree of relationship, the similarity for sweet wasn't found in pairs "parent-offspring". The only kind of food preferences for which there was no relationship between all the relatives, was fatty food. The results of the correlation analysis in marital couples has shown that the negative correlation coefficients were found for spouses only for sweet food.

The moderate heritability coefficient was obtained for preferences for first vegetable courses (50%). High heritability coefficients were recorded for food preferences for meat (88%), salty food (76%) and fruit (88%). Two preferences (for sweet and fast food) presented the maximum possible heritability coefficients (100%).

# DEVELOPMENT OF TECHNOLOGY OF MANUFACTURING OF THE BIO-RECYCLED PLASTIC FILM FOR FOOD PACKAGING

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The development of effective methods of solid waste management and prevention of the environment pollution is one of the most urgent problems of modern society. In this regard, the development of manufacturing technology of packaging polymers, which are capable to self-decompose in a short time in natural environments, and thus don't produce toxic decomposition products, is one of the possible solutions to this problem.

The aim of our research was to develop the technology of production of bio-recycled packaging polymer film of corn starch with high contents of amylose. Specific objectives of the study included: assessment of the genetic diversity of maize starch fraction composition and selection of the best sources of starches with high amylose; the development and refinement of methods of creating bio-recycled packaging polymer film of high amylose corn starch; experimental verification of the technological properties of the polymer film.

Packaging materials are materials that necessary to ensure the safety of different products and raw materials during storage and transportation. The most popular packaging materials are made of paper and cardboard, and especially, polymeric materials.

It is known that as a material for packaging films production can be used a large number of synthetic polymers. Most prevalent among these is polyethylene, which is also the most common plastic in the world. Polyethylene has good insulating ability, dielectric properties and depreciation. However, such packaging films have two disadvantages. The first is that the polyethylene monomer is ethylene, which is produced from raw nonrestorable materials: oil deposits are close to be exhausted. The second drawback is the difficulty disposing of such products.

The list of raw materials for the production of bio-recycled films for food packaging comprises a broad group of natural biopolymers. However, the most suitable biopolymer for this pupose should be considered a starch. Starch is the major storage polysaccharide of cultivated cereals and its content in the grain of these cultures reaches 75-78%. The benefits of starch for the production of bio-recycled films comprise also the existence of the necessary infrastructure of starch production - plant breeding, seed production system and system of agriculture.

Starch is a complex of two copolymers - amylose and amylopectin. They differ in the degree of polymerization and location of chemical ties that bind the monomers. It is proved that the chemical structure of amylose and influences the technological features of the starch. Starches with a high content of amylopectin have low temperature of gelatinization, transparency, resistance to retrogradation, stability and high viscosity of pastes. Conversely, starches with high amylose contents form strong gels with high tensile strength and elastic structure. Namely the high amylose content starches are the best source of raw materials for the bio-recycled plastic films.

Any cereal culture that contains starch can claim to be the raw material for the production of bio-recycled packaging films. However, corn is the most suitable for this purpose. In connection with the recent establishment of the first domestic maize hybrids based on different endosperms' mutations an opportunity to develop the technology of production of bio-recycled packaging polymer films to replace imports.

The prescription mixture for the production of polymer films was composed of a gelling agent, a plasticizer and a solvent.

The role of plasticizer in the composition of the mixture consists in providing high flexibility and elasticity of bio-film. A large group of substances may be used as a plasticizer. Among these are glycerin, sorbitol, fructose, glucose, sucrose, sodium lactate, diethylene glycol, polyethylene glycol and glycerol diacetate.

The best gelling mixture is a corn starch which contains about 60% amylose. A mixture of sorbitol and glycerin in a ratio of 1:3 is a good plasticizer. The best film forming properties provide compositions of 4-7% starch, 4-7% plasticiser and of 86-92% water.

It was found that the gas permeability of high amylose maize starch film is much higher than that of conventionally used polyethylene film for packing bakery products.

The result of this study is developing of technologies for production of bio-recycled packaging polymer film based on high amylose corn starch which involves obtaining starch suspension by gelatinization in a high pressure reactor, its partial cooling, the addition of plasticizers and evaporation of the solvent at a certain temperature. The polymer films based on high amylose corn starch of different hydrophilicity, homogeneous structure, a good molding ability, a sufficiently high structural and mechanical powers, gas permeability, and degradable under natural conditions by amylolytic enzymes.

The researches were carried out under the leadership of Academician of IA Academy of Ukraine S.M.Tymchuk.

# FEARS DYNAMICS IN UKRAINE POPULATION

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Fear is an ancient natural reaction of a human being to a threat and it is also an adaptive feature, however obsessive fear can transfer into phobias. Phobias are found to be either symptom of psychical and mental disorders or a separate behavioural deviation. A polarity is typical for some kinds of fear. Fears connected with professional activities are of great interest. Some kinds of fear can be enforced under certain circumstances after they were initiated by different events, for instance, during epidemic of plague or tuberculosis, the fear of these diseases can develop into hypertrophied form. After the tragedies in Hiroshima, Nagasaki and Chernobyl, the fear of ionizing radiation consequences (radiophobia) increased, nevertheless, until the middle of the twentieth century, the study of their own body using X-rays was just a fun for many people. A certain part of population meets the fear of inexplicable and mystical phenomena ("Flying Dutchman", "black holes"), psychological influence (hypnosis, extrasensory intervention), innovations (genetically modified organisms and computer technologies) etc. Nonetheless, in spite of many studies done on fear, many questions are yet not clarified. In the former Soviet Union, research on human behaviour traits was mostly tabooed. The current research will fill some gaps on the "behavioural map" of Ukraine in relationship with fear distributions in two successive generations of residents of Ukraine.

867 residents of Ukraine, predominantly residents of Kharkov and Kharkov region participated in the study. All participants were distributed into groups of younger and older generations. The age of individuals of the younger generation was up to 35 years. The youngest one in this group was 14 years old. Individuals of the older generations were aged 36 and more. The oldest one in this group was 72 years old. 24 emotional states of fear have been studied by Ivleva-Shcherbatyh questionnaire, which was developed and validated by Russian psychologists in Slavs samples. The examined fear sources were as follows: animals, darkness, psychic disorders development, disease of relatives, street attack, communication with authorities, complications in personal life, making responsible decisions, old age, pain, poverty, uncertainty about future, exam, war, death, closed space, height, depth, adverse changes in the case of relatives' disease, the possibility of disease, sexual dysfunction, suicide, speaking in public, the possibility of aggressive behaviour with relatives. Each fear was estimated on a point scale, ranging from 1 to 10. Statistical

analysis in large groups (n>30) has been performed by parametric methods. A relationship between characteristics has been assessed with Spearman correlation coefficient. Conclusion as to statistic hypothesis has been conducted on the significance level $p \leq 0.05$.

In the population sample under study, females got more points practically in all types of situational fears (fear of animals, darkness, closed spaces, height, and depth) and in some social phobias (fear of communication with the authorities, uncertainty of future, examination, and public speech). From a biological point of view, any fear may have ancient evolutionary roots. For example, socialized xenophobia is a natural reaction of fear to strangers; "social" fear of the authorities is a biological fear typical for many species of living organisms. It is just the fear of dominant individual and the possibility of being forced out of the social ladder. Traditionally, females had less direct contacts with mentioned sources of fear, so they might have lesser adaptation to them. Females with initial greater fear degree to certain objects (predators, unknown people and others) more probably could avoid harm from the contact with them and, consequently had more chances to survive, leave offspring, and pass on these adaptive genes of higher fear. Comparing the intensity of fears in younger and older generation participants, it has been found that the most differences were recorded in females. Some differences were detected in both sexes simultaneously. A small age dynamics was detected almost in all kinds of fear both in older and younger generation individuals. In some cases, this dynamics has sex specificity; in others it has different direction, depending on the accessories for generation. All the correlation coefficients are not high even in the case of their significance. The most differences were recorded in females of younger generation. Some kinds of fear with differences between two generations were found in males and females. One kind of fear (the fear of speaking in public) was part of them. It should be mentioned that univalent conclusions about the different causes between representatives of different generations are difficult to make. The resulting difference can be either a consequence of the cohort effect (as representatives of two generations were brought up in different environment), or a consequence of development variation. For more correct conclusions, longitudinal investigations are necessary to be conducted with the same people in certain periods of time. However, due to the complexity of this type of investigation and the necessity of registering the generation, we limited ourselves to the age dynamics study within each generation separately. The fear of war in older males may be the result of the cohort effect, because either they themselves or their relatives took part in wars (World War II, wars in Afghanistan, Nagorno-Karabakh, Chechnya and other "hot" spots). Because of the absence of such experience in younger males' generation, the fear of war is less pronounced.

# SECTION № 22

# APPLICATION SHEET

# VALIDATION OF SPECTROPHOTOMETRIC METHOD OF DETERMINATION OF THIAMAZOLE AT DISSOLUTION TEST FOR THE TRANSDERMAL FORM OF THE DRUG

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Development of medicinal form as a transdermal therapeutic system requires realization of measuring of freeing of active pharmaceutical ingredient from the matrix of patch. These researches are key for the stage of pharmaceutical development for the study of dynamics of freeing of active pharmaceutical ingredient at the choice of adhesive and, also, as an important part of control of the prepared product.

In 3rd volume of the State Pharmacopoeia of the Republic Kazakhstan it is introduced the test 2.9.4 "Dissolution test for transdermal patches". This test is intended for determination of the speed of dissolution of the active substances contained in a patch. The test was conducted by the method of rotary-type cylinder. The spectrum of absorption of thiamazole in area of wave-length of 200-320nm has two maximums of absorption at 211nm and at 252nm. For the quantitative determination of thiamazole a maximum of absorption at 252 nm is used. Measuring of the optical density of solutions of thiamazole at the wave–length of 252nm in the range of concentrations from 0.005 mg/ml to 0.04mg/ml showed that the optimal concentration of test solution can be a concentration 0.005 mg\ml. At higher concentrations a range of optical density already will be outside recommendable optical density for the aims of quantitative determination.

For confirmation that analytical methodology is suitable for the intended measurement within the limits of necessary range, we conducted a research to determine the analytical efficiency of the chosen method. Validation research included proof of specificity, linear dependence, rightness, exactness in a necessary worker range. Developed methodology of quantitative determination of thiamazole was validated by the method of standard. Water was used as a solvent, taking into account the specificity of the developed medicinal form of transdermal therapeutic system.

The specificity of methodology is well-proven by absence of absorption of the placebo solutions in area of absorption of thiamazole. We are conducted the studies on 9th model's solutions for simultaneous determination of parameters of linearity, rightness and precision. A rightness and precision (exactness) are studied on model solutions, the quantitative content of the basic substances in which is defined relatively to a standard reference solution. The rightness of methodology is estimated on standard deviation of results from a truth value, exactness – from the mean value of selection. At the study of stability of solutions it is certain in the time that the optical density of solutions remains stable during 24 hours.

Investigational validation parameters of analytical methodology of spectrophotometric determination of thiamazole in the range of concentrations from 0.0025mg/ml to 0.0070mg/ml correspond to the criteria of fitness. Methodology can be used for quantitative determination of thiamazole by the method of spectrophotometry for a test "Dissolution".

# SIMULATION OF DERIVATIVES OF JUSTIFICATION FOR DIHYDROQUERCETIN «STRUCTURE-ACTIVITY»

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**Objective the work:** computer modeling of dihydroquercetin of derivatives for determining communication "Structure Activity.

**Methods of research:** Prediction of the spectrum of biological activity of the chemical compound of the structural the formula, carried out by under the program of existing instructive sampling (version PASS), which includes tens of thousands of compounds.

**The Results:** With the help of computer programs modeled around 5 modified derivatives dihydroquercetin, of practical interest from the point of view pharmacological activity. Were obtained the hydroxylated and acylated derivatives, considering variations of substitution the heterocyclic ring. Each model is was formed into separate files mol. Was conducted to search for new compounds of these derivatives, for which the manifestation of anti-inflammatory activity most likely. In particular for proposed types of derivatives of the predicted mean activity in the available literature has been found experimentally confirmed. To evaluate the results use of the proposed approach in the search for new biologically active compounds in the series of analysis dihydroquercetin testing biological activity of a large number of compounds and naturally most effective. When planning a biological research always have be taken into account, that this procedure is quite costly, therefore test a large number of compounds simultaneously, and check a wide range of pharmacologic activity in these conditions is very difficult. Although the need for similar studies, there is undoubtedly. Forecast results were analyzed using PharmaExpert. On the basis of these predictions was presented an ordered list of specific activities and the probability of activity under the signs $P_a$ − «be active», $P_i$ − «to be inactive». Accept the terms of the activity that is responsible index «anti-inflammatory activity» ($P_a$=0,717, $P_i$=0,036; $P_a$=0,612, $P_i$=0,021; $P_a$=0,578, $P_i$=0,015; $P_a$=0,525, $P_i$=0,011; $P_a$=0,509, $P_i$=0,09), was determined the probability of novelty modeled structure. In computer modulate to substantiate communication «structure-molecule-activity» given to determining the place of the attack of the substrate and the electrophilic agent used. In practice, the reaction $S_E$ with high selectivity in position of are atoms or groups, having a high electron density of molecular of orbitals. In the acylation reaction carried out dihydroquercetin charge transfer from the highest occupied orbital of the donor to the acceptor lower free orbital leads to the maximum boundary overlap of molecular orbitals. Were developed for new compounds derivatives dihydroquercetin electronic information (HOMO, EFonD, the heat of formation, orbital energies), issued by the with the program MOPAC (Hyper Chem).

**Conclusions:** based on the computed prognostic data of biological activity and reactivity, will be conducted experimental studies on the synthesis of new compounds derived dihydroquercetin.

# THE THEORETICAL BASIS OF CREATING NEW HETEROCYCLIC COMPOUNDS SERIES BASED BETALAKTAMOV

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The present level of development of science cannot predict until the creation of new chemical compounds through targeted modification of the structure of substances. Is too complex nature of the relationship between chemical structure and biological activity. The greatest success can only be achieved through a combination of theoretical and empirical ways to create new chemical compounds. All currently existing theories include elements of empirical character. It is the first period in the development of the science of one of the most effective drugs - antibiotics is associated with the empirical search for substances of various natural producers. The result of such searches over the past 60 years, opened about 50 thousand of antibiotics with different spectrum of action, but in clinical practice, a limited number of antibiotics. This is mainly due to the fact that most antibiotics do not meet the requirements of practical medicine. The search for new drugs that have a primary antibiotic activity compared to known to provide the needs of medical practice, is still solvable problem.

Thus, for the directed synthesis betalaktamidov application of new screening options that determine the relationship between chemical structure and biological activity, predicts the perfection of methods of quantum chemistry.

Independent study of the reaction of formation of new compounds with various organic radicals, ensures optimal development of methods of synthesis of individual drug groups antibiotics heterocyclic series.

**The purpose of the research** is to establish the preferred directions of chemical reactions of some compounds heterocyclic series betalaktamov with various organic radicals.

**Basic tasks of the research.**

Theoretical aspects of study the reactivity of a series of beta-lactam compounds based on quantum chemical calculations; synthesis of a number of heterocyclic compounds based on cycle betalaktamov with various organic radicals; qualitative and quantitative identification of new compounds by chemical analysis, IR, UV spectroscopy; determination of antibiotic activity of novel compounds on the basis of a number of heterocyclic betalaktamov with various organic radicals.

**The expected results**.

On the basis of quantum-chemical calculations of a number of potential betalaktamidov will be revealed in the reaction center are estimated and reactivity in the reactions of formation of new compounds with various organic radicals; will develop new methods of synthesis of heterocyclic compounds based on a number betalaktamov different organic radicals; elemental composition will set the new compounds by chemical analysis and determined on the basis of their structure by IR and UV spectroscopy; will test the antibiotic activity of new drugs in various systems of the body.

**Scientific novelty and practical significance of the work**.

A number of studies on the theoretical prediction of the relationship between chemical structure and biological for the first time will allow to predict the directed synthesis of new beta-lactam compounds. For the first time will be revealed patterns for a new approach to the creation of beta-lactam compounds. Based on this, you can create a real prototype of synthesis techniques for betalaktamidov. For the first time will be offered a theoretical justification the reactivity of a series of beta-lactam compounds on the basis of mathematical methods of calculation.

# BENZOYL CHLORIDE AS A REAGENT IN THE SYNTHESIS OF DIHYDROQUERCETIN

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In the synthesis of new derivatives dihydroquercetin has great practical significance reaction of O-acylation using benzoyl chloride. This is one of the most known reagents used in a number of carboxylic acid chlorides.

**The purpose of** this work was to determine the electrophilic properties of benzoyl chloride in the reaction of O-acylation dihydroquercetin.

**The scientific novelty** of this work is to determine the properties of the reaction of benzoyl chloride in the synthesis of new hitherto unknown compounds.

The software system HyperChem 8.0.7, MOPAC, used in this study, makes it possible to obtain semi-empirical calculation, allow to explain the mechanism of the reaction of O-acylation.

For the reaction of O-acylation determined the relationship between charges and the atoms to yield the final products. According to the data the calculations of computer simulation benzoyl chloride in the center of the attacker has a positive charge. Influenced halogen on a carbon atom of the carbonyl group forms a significant positive charge, the consequence is the activity interacting with various nucleophilic raegentami.

For this reaction, an electrophilic substitution followed the relationship between yield of final product and and other indices the reactivity of the reactants (the energy frontier molecular orbital (MO), squares coefficient expansion of frontier MO over the basis of atomic orbitals (AO), etc.)

As a result, molecular modeling molecular substances, reactive, and dihydroquercetin molecules derivative using quantum-chemical method AM1 data were obtained, confirming that, that reaction can proceed by electrophilic substitution mechanism.

In practical experiments carried out dihydroquercetin benzoylation at an equimolar ratio of reagents using triethylamine as an acceptor of hydrogen chloride liberated. As the solvent, dichloromethane was chosen. Drying the carried out using a rotary evaporator throughout the 1 hours at a temperature of 56°C.

As a result of the work done was obtained new substances in the ratios 1:1, 1:2, 1:3, 1:4, 1:5.

More precisely, the distribution of electron density in the molecules of benzoyl chloride and dihydroquercetin, we can say, negatively charged nitrogen atom in the molecule can attack dihydroquercetin positively charged carbon atom in the carbonyl group is strongly polarized of benzoyl chloride.

In this way, were first synthesized by a number of hitherto unknown derivatives on the basis of biologically active, non-toxic and relatively the available flavonoid dihydroquercetin.

In what follows, will be evaluated, that some of the synthesized compounds can be promising medicinal products.

# PRODUCTION OF THE ANTIBIOTIC BETA-LACTAM SERIES

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Semisynthetic antibiotics preparing a combined way: by microbiological synthesis receive the basic core of molecules native antibiotic 6- aminopenicillanic the acid (6-APA), method of chemical the synthesis and by partially changing the chemical structure 6-APA introduction to it or her acyl groups — novel semisynthetic preparations. The so-obtained new medications of beta-lactam series of semi-synthetic origin are characterized rather high resistance to the action pathogenic microorganisms, so they receiving is relevant.

**The purpose of the research:** creation of new model-based molecules 6-APA and acylating reagents and methods of receiving of semisynthetic antibiotics of microbial and chemical synthesis.

**Objective the work:** culture of *Escherichia coli*, natural penicillin, acylating agents (phosgene, acetyl chloride).

**Methods of research:** semi-empirical quantum-chemical method PM3 (parametric method 3), included in the software package MOPAC versions 8.

**The experimental part:** to ascertain the singularities electronic and steric structure of the first quantum-chemical modeling method PM3 new of model systems 6-APA, 6-APK-phosgene and 6-APK- acetyl chloride. Has been optimized spatial structure, calculated parameters of the electronic structure and energy characteristics of the new compounds. The character of the process of acylation molecules 6-APA acylating agents (phosgene, acetyl chloride) and show that it is orbitally controlled response. It was found that the most thermodynamically stable system is a model system 6-APA- acetyl chloride. For microbiological synthesis enzyme producer was chosen culture of *Escherichia coli*. The method of diffusion in agar was determined activity of the new antibiotic compound. Determination of the elemental composition of the newly synthesized compounds and characteristic bands in its IR spectrum indicate the coincidence of its chemical structure with the results of a number of known compounds of beta-lactam.

In this way, identifying the most stable form - 6-APA-acetyl chloride. By a combination of microbiological and chemical the synthesis a new compound is obtained, corresponding to the regulatory requirements of the State Pharmacopoeia of the Republic of Kazakhstan.

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*Scientific edition*

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