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**PHARMACODYNAMICS OF ALCOHOLIC AND AQUEOUS EXTRACTS FROM THE BUPLEURUM AUREUM FISCH.**

***Naboka О. І., Khouari S.Z., Koshevaya E.J., Glushchenko А. V.***

***National University of Pharmacy***

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Drug-induced liver injury has approximately 10 percent of adverse effects associated with pharmacotherapy. This issue is particularly important to pediatrics due to imperfect detoxification system of the liver in children.

Despite the wide arsenal of hepatoprotective drugs, the problem of effective therapy for liver disease remains unresolved. Interest in medicinal plants as a source of various biologically active substances that provide a wide range of pharmacological activity has increased in recent years [7-9]. Bupleurum aureum has long been used in folk medicine for the liver diseases treatment. This plant has choleretic, wound-healing, and tonic effect.

Alcoholic and aqueous extracts from the Bupleurum Aureum Fisch. containing flavonoids (quercetin, rutin, izoramnetyn, nartsysyn), tannins and phytosterols have been obtained at the Department of quality, standardization and certification of Institute of Pharmacy Professionals Qualification Improvement. Phytochemical analysis of extracts allowed to assume that they have [hepatoprotective and antioxidant activity](https://www.google.com.ua/url?sa=t&rct=j&q=&esrc=s&source=web&cd=1&cad=rja&uact=8&ved=0CB8QFjAA&url=http%3A%2F%2Fwww.ncbi.nlm.nih.gov%2Fpubmed%2F22701284&ei=368yVJ75MaXmyQOmtYGwCQ&usg=AFQjCNG_hQByvpN3rN7A_8TH6piVOPijZg&bvm=bv.76802529,d.ZWU) [7,9].

The aim of this study was to investigate the potential hepatoprotective and membrane stabilizing effects of herbal extracts of aerial part of Bupleurum Aureum on carbon tetrachloride-induced hepatitis in vivo.

**Materials and methods.**

Pharmacodynamics of alcoholic and aqueous extracts from the Bupleurum aureum fisch was carried out under conditions of rats’ acute experimental hepatitis, caused by tetrachloromethane.

The investigations were conducted on 46 male rats weighing 180-200 g.

The animals were daily for 4 days injected once per day into stomach by examined extracts in dosage of 5 mg/kg (for preventive purpose). The examined animals were divided into 6 experimental groups of 7 animals in each one:

1 group – intact animals;

2 group – control animals with experimental hepatitis;

3 group – animals that have taken aqueous extract of Bupleurum Aureum in dosage of 5 mg/kg;

4 group – animals that have taken alcoholic extract of of Bupleurum Aureum in dosage of 5 mg/kg;

5 group – animals, that have taken reference drug “Silibor” in dosage of 100 mg/kg.

6 group – animals, that have taken reference drug “Quercetine” in dosage of 50 mg/kg;

Tetrachlormethane was injected once intragastrically as 50 % oil solution of tetrachlormethane in dosage of 0,8 ml/100 g [2].

Bile formation and synthetic function of the liver were studied according to the guidelines [2,3].

Membrane-protective properties of investigated extracts were studied by the method of determining the spontaneous hemolysis of erythrocytes by Yager [1].

**RESULTS AND DISCUSSION.**

Results are presented in the Table 1 shows the effect of aqueous and alcoholic extracts of Bupleurum Aureum on the functional state of rat liver under conditions of acute hepatitis caused by tetrachloromethane. Intragastric administration of tetrachlormethane induced functional liver disorder of rats in the positive control group. The secretion rate and lithogenic properties of bile were significantly changed. Prophylactic administration of alcoholic and aqueous extracts of an aerial part of Bupleurum Aureum to rats significantly reduced the hepatotoxicity induced by tetrachloromethan. The maximum efficiency was found for 50% alcoholic extract of Bupleurum aureum. It was found that prophylactic administration of extract of Bupleurum Aureum to rats restores bile secretion and synthetic function of the liver (Table 1).

Results presented in table 2 show the effect of extracts of Bupleurum Aureum on the spontaneous lysis of red blood cells in rats under conditions of acute hepatitis caused by tetrachloromethane. Liver cell injury induced by carbon tetrachloride involves free radical-induced lipid oxidation, which leads to membranes disruption, functional changes in the activity of membrane-bound monooxygenases in the endoplasmic reticulum, inhibition of the transformation of xenobiotics and endogenous metabolites, decreasing in the activity of protein synthesis [6,7,8,9].

Administration of tetrachlormethane significantly disrupted the physical properties of the membranes of red blood cells, increased cell lysis by 2-fold (Table 2). Prophylactic administration of alcoholic and aqueous extracts of Bupleurum Aureum to rats reduced the lysis of erythrocytes 1.4-2.0 folds compared to a positive control.

Membrane protective activity of aqueous extract of Bupleurum Aureum was -27%, alcohol extract - 51% (Table 2). It was found that the reference drugs “Silibor” and "Quercetin" have almost the same membrane protective activity 42% and 54% respectively.

**CONCLUSION**

It was found that explored herbal extracts of Bupleurum Aureum have hepatoprotective and membrane protective properties.

Prophylactic administration of extracts of an aerial part of Bupleurum Aureum to rats restores bile secretion and synthetic function of the liver.

The maximum efficiency was found for 50% alcoholic extract of Bupleurum aureum. The examined extract of Bupleurum Aureum is not inferior to reference-preparations “Silibor” and “Quercetine”.

Table 1

**Effect of aqueous and alcoholic extracts of Bupleurum Aureum on the functional state of rat liver**

**under conditions of acute hepatitis caused by tetrachloromethane**

|  |  |
| --- | --- |
| Data | Groups of animals |
| Negativecontrol | Positivecontrol | Extracts of Bupleurum Aureum 5 mg/kg; | “Quercetine” 50 mg/kg | “Silibor”, 100 mg/kg |
| alcoholic | aqueous |
| Weight coefficient of liver, g/100g | 3,0±0,1 | 4,3±0,2 \* | 4,4±0,2 \* | 4,1±0,1\* | 4,0±0,3 \* | 4,1±0,2 \* |
| The rate of bile secretion, ml/100g×hr-1 | 1,00±0,07 | 0,60±0,05\* | 0,79±0,08 | 1,05±0,03\*\* | 0,67±0,06\*/α | 0,96±0,09\*\* |
| Concentration of bile acidsin bile, mg%/ml/100g×hr-1 | 532±35 | 353±45 | 486±61 | 728±72\*\* | 345±55 | 584±81 |
| Concentration of cholesterol in bile, mg%/ml/100g×hr-1 | 11,5±1,7 | 25,6±4,4 \* | 21,8±1,6 | 17,3±3,3 | 13,7±2,8\*\* | 15,1±1,9\*\* |
| Holato-cholesterol ratio | 51±6 | 15±1 \* | 26±6 | 55±15\*\* | 29±6 | 41±7 |

Notes: \* – discrepancy authentic concerning intact control, р≤0,05;

\*\* – discrepancy authentic concerning control pathology, р≤0,05;

Table 2

**Effect of aqueous and alcoholic extracts of Bupleurum Aureum on the spontaneous lysis of red blood cells in rats under conditions of acute hepatitis caused by tetrachloromethane**

|  |  |  |
| --- | --- | --- |
| Groups of animals | Hemolytic activity% | Activity, % |
| Negative control | 24,74±1,40 | –  |
| Positive control (tetrachloromethane) | 47,80±1,46\* | – |
| Aqueous extract of Bupleurum Aureum + tetrachloromethane | 34,87±4,42\*/\*\*/α/β | 27 |
| Alcoholic extract of Bupleurum Aureum + tetrachloromethane | 23,31±1,47\*\* | 51 |
| “Quercetine” 50 mg/kg+ tetrachloromethane | 27,76±2,57\*\* | 42 |
| “Silibor” 100 mg/kg+ tetrachloromethane | 21,82±2,95\*\* | 54 |

Notes: \* – discrepancy authentic concerning intact control, р≤0,05;

\*\* – discrepancy authentic concerning control pathology, р≤0,05;

α – discrepancy authentic concerning reference drug “Silibor”, р≤0,05

β – discrepancy authentic concerning reference drug “Quercetine”, р≤0,05

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