Hepatoprotective activity of a complex plant extract

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SUMMARY

The article presents the results of a study of the hepatoprotective activity of a complex plant extract obtained from the following types of plant materials: roots and rhizomes of elecampane high, herb of centaury, Ural licorice roots, rose hips, hawthorn fruits, under the conditions of a model of tetrachloromethane hepatitis. It was found that the course administration of per os extract at a dose of 300 mg / kg to white nonlinear rats with carbon tetrachloride damage to the liver has a hepatoprotective effect, to some extent surpassing the effect of the comparison drug Carsil. The results of the studies showed that during the pharmacotherapy of toxic hepatitis with a plant extract, the levels of activity of enzymes - markers of the cytolysis syndrome, clearly decrease in the blood serum, Significantly decrease in these conditions and manifestations of cholestasis syndrome. The pharmacotherapeutic effect of the extract in case of damage to the organs of the hepatobiliary system is due to the presence in it of a complex of biologically active substances and, first of all, phenolic compounds. The obtained research results argue the expediency of using a plant extract containing biologically active substances of a phenolic nature in the complex treatment and prevention of liver diseases.

Key words: complex plant extract, hepatoprotective activity, carbon tetrachloridehepatitis.

RESUME

The article presents the results of the study of the hepatoprotective activity of a complex plant extract obtained from the following types of raw plants: roots and rhizomes of elecampane, common grass, roots of Ural licorice, hips, fruits of hawthorn, in conditions of a tetrachloromethane hepatitis model. It was established that a course of per os intake of extract in a 300 mg / kg dose for white non-linear rats with tetrachloromethane damage to the liver has a hepatoprotective effect, somewhat superior to the effect of the comparator drug Carsil. The results of the study showed that pharmacotherapy of toxic hepatitis with plant extract clearly decreases levels of enzyme activity in serum - markers of cytolysis syndrome, manifestations of cholestasis syndrome also significantly decrease in these conditions. The pharmacotherapeutic effect of the extract in case of damage to the organs of the hepatobiliary system is due to the presence in it of a complex of biologically active substances and, above all, compounds of a phenolic nature. The results of the research substantiate the expediency of using a plant extract containing biologically active substances of a phenolic nature in the complex treatment and prevention of liver diseases.

Keywords: complex plant extract, hepatoprotective activity, tetrachlormethane hepatit.

INTRODUCTION

Liver lesions occupy a leading place in the structure of morbidity and mortality, primarily due to an increase in the number of alcohol intoxication, uncontrolled large-scale use of drugs, environmental pollution, including water and food, foreign chemical compounds [1].

In this regard, it is relevant to search for agents that can increase the liver's resistance to the damaging effects of toxins and stimulate detoxification processes [2]. Promising for the development of methods for the pharmacological correction of these conditions are herbal remedies that are distinguished by the breadth of the therapeutic effect, low toxicity and the associated possibility of long-term use without the risk of developing adverse reactions [3, 4].

The aim of the research was to determine the hepatoprotective activity of a complex plant extract.

MATERIALS AND METHODS

The object of research was a dry extract obtained from the following types of plant materials: roots and

rhizomes of elecampane high (Inula helenium L.) - 250 g, herb of the centaury common (Centaurium erythraea Rafn.) - 150 g, Ural licorice roots (Glycyrrhiza uralensis Fisch.) - 150 g, rose hips (Rosa sp.) - 250 g, hawthorn fruit (Crataegus sp.) - 200 BC

The extract was obtained by extracting individual components with 70% ethyl alcohol, followed by combining the obtained extracts. The resulting extract contains polysaccharides, flavonoids, carotenoids, organic acids, vitamins, macro- and microelements, essential oils and other natural compounds. The extract was standardized according to the amount of flavonoids. The presence of the specified spectrum of biologically active substances suggests the potential hepatoprotective activity of the obtained extract.

The work was performed in accordance with the Federal Law “On Medicines”, “Guidelines for Conducting Preclinical Research of Medicines”. The experiments were performed on 40 nonlinear male rats with an initial weight of 180-200 g. The animals were obtained from the Federal State Budgetary Institution Scientific Center for Biomedical Technologies of the FMBA of Russia and were kept in a vivarium with free access to food and water. Pharmacological studies were carried out in accordance with the "Rules for work using experimental animals", "Rules adopted by the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes" (Strasbourg, 1986), Order of the Ministry of Health of the Russian Federation No. 708n dated 23.08.2010 " On the approval of the rules of laboratory practice ”. The studies were approved by the Bioethical Commission of the VILAR Federal State Budgetary Scientific Institution (protocol No. 4 of September 15, 2015).

A preliminary assessment of the acute toxicity of the obtained extract was carried out on white outbred male mice when administered per os in the form of an aqueous solution in the dose range 25 mg - 1000 mg / kg. It was found that the administration of the extract in the indicated doses to mice did not lead to their death during the entire observation period (14 days). Only with the introduction of high doses of the extract (800–1000 mg / kg) were restrictions on motor activity, refusal of food, frequent urination in the first 3–5 hours after the introduction of the extract noted, and by 6–20 pm their behavior and appearance did not differ from intact animals.

Preliminary studies have determined experimental therapeutic doses of the extract under study, corresponding to 100-350 mg / kg of animal weight when administered per os. Basic experimentscarried out using an experimentally selected dose of 300 mg / kg, which provides the most pronounced pharmacological effect.

Determination of the pharmacotherapeutic efficacy of a multicomponent plant extract was carried out with intragastric (once a day) course application of the extract in the form of an aqueous solution at a dose of 300 mg / kg for 10 days with carbon tetrachloride hepatitis in white rats, starting from 2 days after the first injection of the damaging agent.

Liver damage was caused by intragastric administration of 50% oil solution of carbon tetrachloride to white rats in a volume of 0.2 ml / 100 g of animal weight [5]. The plant hepatoprotector Carsil was used as a reference drug at an isoeffective dose of 50 mg / kg of rat weight. Animals of the control group received water purified in an appropriate volume according to a similar scheme. The studies were carried out after 7, 14, 21 and 28 days from the beginning of the experiment. The functional state of the liver in animals was assessed by the activity of alanine aminotransferase (ALT), aspartate aminotransferase (AST), the content of cholesterol, β-lipoproteins, total bilirubin, direct bilirubin, indirect bilirubin and total protein in serum using a Clima MC-15 analyzer for clinical chemistry.

Statistical processing of the obtained data was carried out using the software package Statistica 10.0(USA). Differences were considered significant at $P \leq 0.05$ [6].

RESULTS

The effect of a complex plant extract on the course of experimental hepatitis in white rats, caused by the introduction of carbon tetrachloride, was studied. Tetrachloromethane is the most well-known hepatotoxin used to simulate liver disease. Toxic liver damage caused by prolonged administration of CCl_4, is an adequate model of cirrhotic liver damage in humans [7].

Course administration of a complex plant extract at a dose of 300 mg / kg against the background of carbon tetrachloride hepatitis has a pronounced hepatoprotective effect, reducing the severity of violations of the functional state of the liver of animals (Table 1).

Table 1

Effect of a multicomponent plant extract on the functional activity of the liver of white rats in chronic toxic hepatitis caused by carbon tetrachloride (M ± m)

No.	Basic biochemical indicators	Intact rats	Rats with experimental hepatitis (control)	Rats with experimental hepatitis with the introduction of the extract	Rats with experimental hepatitis with introduction of Carsil

one	2	3	4	5	6
7 days					
one	ALT, μM	0.68 ± 0.11	4.96 ± 0.08	3.60 ± 0.10 *	4.00 ± 0.12 *
2	AST, μM	0.41 ± 0.05	3.20 ± 0.32	2.26 ± 0.12 *	2.48 ± 0.18 *
3	Thymol test, units	1.36 ± 0.19	7.28 ± 1.12	3.78 ± 0.30 *	4.56 ± 0.50 *
4	ß-lipoproteins, units.	9.0 ± 0.25	14.7 ± 0.40	9.6 ± 0.30 *	10.2 ± 0.35 *
5	Total protein g / l	7.45 ± 0.11	6.12 ± 0.22	6.78 ± 0.19 *	6.60 ± 0.26 *
6	Cholesterol mg%	56.0 ± 2.00	108.0 ± 6.50	57.0 ± 3.30 *	78.0 ± 4.50 *
7	Bromsulfalein test,%	2.43 ± 0.30	12.90 ± 0.50	8.40 ± 0.20 *	9.00 ± 0.25 *
eight	Total bilirubin mg%	0.69 ± 0.03	11.40 ± 0.40	10.50 ± 0.63	10.80 ± 0.60
9	Direct bilirubin mg%	0.21 ± 0.02	5.38 ± 0.40	4.63 ± 0.30 *	4.90 ± 0.35 *
10	Indirect bilirubin mg%	0.48 ± 0.17	5.02 ± 0.31	5.87 ± 0.32	5.90 ± 0.40
14 days					
one	ALT, μM	0.68 ± 0.11	4.04 ± 0.18	3.04 ± 0.22 *	3.43 ± 0.12 *
2	AST, μM	0.41 ± 0.05	2.40 ± 0.10	1.88 ± 0.09 *	2.0 ± 0.18
3	Thymol test, units	1.36 ± 0.19	6.76 ± 1.00	4.55 ± 0.20	4.3 ± 0.20 *
4	ß-lipoproteins, units.	9.0 ± 0.25	18.2 ± 1.30	14.1 ± 0.68 *	15.0 ± 0.85
5	Total protein g / l	7.45 ± 0.11	6.33 ± 0.10	6.55 ± 0.12	6.80 ± 0.15
6	Cholesterol mg%	56.0 ± 2.00	123.0 ± 11.00	87.6 ± 5.66 *	87.0 ± 9.30 *
7	Bromsulfalein test,%	2.43 ± 0.30	11.60 ± 0.80	7.25 ± 0.42 *	6.34 ± 0.23 *
eight	Total bilirubin mg%	0.69 ± 0.03	4.89 ± 0.20	3.60 ± 0.20 *	3.80 ± 0.12 *
9	Direct bilirubin mg%	0.21 ± 0.02	2.48 ± 0.10	1.26 ± 0.10	1.50 ± 0.09 *
10	Indirect bilirubin mg%	0.48 ± 0.17	2.50 ± 0.07	2.23 ± 0.30	2.20 ± 0.20
21 days					
one	ALT, μM	0.68 ± 0.11	3.12 ± 0.14	2.62 ± 0.12 *	2.75 ± 0.11 *
2	AST, μM	0.41 ± 0.05	1.69 ± 0.05	1.43 ± 0.20	1.57 ± 0.12
3	Thymol test, units	1.36 ± 0.19	6.80 ± 0.10	3.21 ± 0.06 *	4.00 ± 0.12
4	ß-lipoproteins, units.	9.0 ± 0.25	15.5 ± 0.50	12.8 ± 0.40 *	14.2 ± 0.25
5	Total protein g / l	7.45 ± 0.11	6.52 ± 0.15	7.23 ± 0.14 *	7.13 ± 0.12 *
6	Cholesterol mg%	56.0 ± 2.00	101.0 ± 6.00	77.5 ± 3.70 *	75.0 ± 2.50 *
7	Bromsulfalein test,%	2.43 ± 0.30	5.80 ± 0.60	3.20 ± 0.40 *	3.00 ± 0.40 *
eight	Total bilirubin mg%	0.69 ± 0.03	1.96 ± 0.09	1.30 ± 0.05 *	1.50 ± 0.1
9	Direct bilirubin mg%	0.21 ± 0.02	0.72 ± .004	0.45 ± 0.04 *	0.50 ± 0.05
10	Indirect bilirubin mg%	0.48 ± 0.17	1.24 ± 0.10	0.83 ± 0.02 *	0.70 ± 0.07 *
28 days					
one	ALT, μM	0.68 ± 0.11	2.82 ± 0.24	1.50 ± 0.10 *	1.70 ± 0.15 *
2	AST, μM	0.41 ± 0.05	1.18 ± 0.10	0.90 ± 0.05 *	1.02 ± 0.08 *
3	Thymol test, units	1.36 ± 0.19	3.22 ± 0.33	1.56 ± 0.30 *	1.63 ± 0.30 *
4	ß-lipoproteins, units.	9.0 ± 0.25	9.6 ± 0.21	8.8 ± 0.10 *	9.0 ± 0.25
5	Total protein g / l	7.45 ± 0.11	7.15 ± 0.16	7.21 ± 0.12	7.30 ± 0.15
6	Cholesterol mg%	56.0 ± 2.00	66.3 ± 3.10	55.9 ± 2.8 *	57.0 ± 2.7 *

7	Bromsulfalein test,%	2.43 ± 0.30	-	-	-
eight	Total bilirubin mg%	0.69 ± 0.03	0.86 ± 0.04	0.79 ± 0.07	0.82 ± 0.05
9	Direct bilirubin mg%	0.21 ± 0.02	0.23 ± 0.02	0.28 ± 0.02	0.30 ± 0.03
10	Indirect bilirubin mg%	0.48 ± 0.17	0.69 ± 0.05	0.49 ± 0.03 *	0.52 ± 0.04 *

Note:
* Differences compared to control are significant at P ≤ 0.05.

So, on the 7th day of the experiment in animals receiving the studied extract (table. 1), there is a significant decrease in the activity of ALT, AST (by 27 and 29%, respectively), compared with the data in animals of the control group. Also, on the 7th day, a decrease in the indices of thymol and bromsulfalein samples by 48% and 35% was found; the concentration of β-lipoproteins - by 35%, cholesterol - by 47% compared with the corresponding indicators in the control. After 14 days of the experiment in the rats of the experimental group, the activity of ALT, AST; indices of total bilirubin, β-lipoproteins, cholesterol, thymol and bromsulfalein samples are significantly lower than those in animals of the control group. With the introduction of the extract on the 21st day of the experiment, the total protein index increased to 7.23 ± 0.14, i.e. approached the indicator of the intact group.

The results of the studies showed that on the 28th day of the study, during the pharmacotherapy of toxic hepatitis with a plant extract, the levels of activity of enzymes - markers of the cytolysis syndrome in the blood serum of white rats clearly decrease, and the manifestations of cholestasis syndrome significantly decrease under these conditions. It should be especially noted that the administration of the studied extract to rats with liver damage was characterized by a sharp decrease in the coefficient of retention of bromsulfalein, indicators of the thymol test. While in the control group, a number of indicators (ALT, AST, thymol test) indicate an ongoing pathological process. At the same time, the effectiveness of the studied complex extract in some parameters exceeded that of the reference drug.

When assessing the state of the monooxygenase system of the liver on the 7th day of the experiment with toxic hepatitis, it was found that the use of the extract in the indicated dose significantly increases the amount of cytochrome P_{450} in liver microsomes (Table 2).

A 54% increase in the key enzyme of the monooxygenase system, which is responsible for the deoxygenation function of the liver, was accompanied by a slowdown in the rate of inactivation of this enzyme due to the stabilization of membrane structures.

table 2

Effect of the extract on the state of the monooxygenase system of the liver
at experimental CCl_4 hepatitis in white rats (7 days)

No.	Animal groups	Content cytochrome P_{450} in nmol / mg squirrel	Percentage of inactivation cytochrome P_{450} by 30 min incubation	The number of MDA in μM / ml serum × min.
one	Intact group	0.79 ± 0.04	21.2 ± 2.0	3.99 ± 0.40
2	Control group (CCl_4 + H_2O)	0.39 ± 0.06	58.7 ± 1.3	5.76 ± 0.10
3	Experienced 1 (CCl_4 + extract)	0.60 ± 0.08 *	18.1 ± 0.9*	3.89 ± 0.60 *
4	Experienced 2 (CCl_4 + carsil)	0.53 ± 0.07 *	18.1 ± 1.1 *	4.49 ± 0.40

DISCUSSION

On the basis of the data obtained, it can be concluded that the studied extract, when administered as a course, has a pronounced hepatoprotective effect, due to the property predominantly stimulating the detoxification function of the liver. Under the influence of a multicomponent plant extract from the early stages of liver damage, the activity of enzymes decreases, the severity of the inflammatory reaction decreases, and lipid peroxidation is inhibited. Together, these positive changes lead to a decrease in the severity of the pathological process.

It was found that the course introduction per os extract per dose 300 mg / kg white non-linear rats with carbon tetrachloride damage to the liver has a hepatoprotective effect, superior in a number of indicators to the effect of the comparison drug Carsil. Apparently, the pharmacotherapeutic effect of the extract in case of damage to the organs of the hepatobiliary system is due to the presence in it of a complex of biologically active

substances and, above all, compounds of phenolic nature. Due to their dominant content, the inhibitory effect of the plant extract on free radical oxidation of lipids, stabilization of biological membranes with a subsequent increase in the functional activity of the liver is provided [2, 8]. The obtained research results argue the expediency of using a plant extract containing biologically active substances of a phenolic nature in the complex treatment and prevention of liver diseases.

CONCLUSIONS

1. An experimental study of the hepatoprotective activity of complex plant extract obtained from rhizomes and roots of elecampane high, herb of a thousand thousandths, roots of Ural licorice, rose hips, hawthorn fruits, under the conditions of the model of carbon tetrachloride hepatitis.

2. It is shown that the course introduction per os multicomponent herbal extract in a dose 300 mg / kg white to nonlinear rats with carbon tetrachloride damage to the liver, it has a hepatoprotective effect, superior in a number of indicators to the effect of the introduction of the reference drug (Carsil).

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Hepatoprotective activity of a complex plant extract / E.V. Ferubko, S.M. Nikolaev, K.A. Pupykina, T. D. Dargaeva // Traditional medicine. - 2018. - No. 3 (54). - S.20-24.