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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

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საქართველოს სამედიცინო სიახლენი

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ЕЖЕМЕСЯЧНЫЙ НАУЧНЫЙ ЖУРНАЛ

ТБИЛИСИ - НЬЮ-ЙОРК

GMN: Georgian Medical News is peer-reviewed, published monthly journal committed to promoting the science and art of medicine and the betterment of public health, published by the GMN Editorial Board and The International Academy of Sciences, Education, Industry and Arts (U.S.A.) since 1994. **GMN** carries original scientific articles on medicine, biology and pharmacy, which are of experimental, theoretical and practical character; publishes original research, reviews, commentaries, editorials, essays, medical news, and correspondence in English and Russian.

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3. Submitted material must include a coverage of a topical subject, research methods, results, and review.

Authors of the scientific-research works must indicate the number of experimental biological species drawn in, list the employed methods of anesthetization and soporific means used during acute tests.

4. Articles must have a short (half page) abstract in English, Russian and Georgian (including the following sections: aim of study, material and methods, results and conclusions) and a list of key words.

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3. სტატიაში საჭიროა გაშუქდეს: საკითხის აქტუალობა; კვლევის მიზანი; საკვლევი მასალა და გამოყენებული მეთოდები; მიღებული შედეგები და მათი განსჯა. ექსპერიმენტული ხასიათის სტატიების წარმოდგენისას ავტორებმა უნდა მიუთითონ საექსპერიმენტო ცხოველების სახეობა და რაოდენობა; გაუტკივარებისა და დაძინების მეთოდები (მწვავე ცდების პირობებში).

4. სტატიას თან უნდა ახლდეს რეზიუმე ინგლისურ, რუსულ და ქართულ ენებზე არანაკლებ ნახევარი გვერდის მოცულობისა (სათაურის, ავტორების, დაწესებულების მითითებით და უნდა შეიცავდეს შემდეგ განყოფილებებს: მიზანი, მასალა და მეთოდები, შედეგები და დასკვნები; ტექსტუალური ნაწილი არ უნდა იყოს 15 სტრიქონზე ნაკლები) და საკვანძო სიტყვების ჩამონათვალი (key words).

5. ცხრილები საჭიროა წარმოადგინოთ ნაბეჭდი სახით. ყველა ციფრული, შემაჯამებელი და პროცენტული მონაცემები უნდა შეესაბამებოდეს ტექსტში მოყვანილს.

6. ფოტოსურათები უნდა იყოს კონტრასტული; სურათები, ნახაზები, დიაგრამები - დასათაურებული, დანომრილი და სათანადო ადგილას ჩასმული. რენტგენოგრამების ფოტოასლები წარმოადგინეთ პოზიტიური გამოსახულებით **tiff** ფორმატში. მიკროფოტოსურათების წარწერებში საჭიროა მიუთითოთ ოკულარის ან ობიექტივის საშუალებით გადიდების ხარისხი, ანათალების შეღებვის ან იმპრეგნაციის მეთოდი და აღნიშნოთ სურათის ზედა და ქვედა ნაწილები.

7. სამამულო ავტორების გვარები სტატიაში აღინიშნება ინიციალების თანდართვით, უცხოურისა – უცხოური ტრანსკრიპციით.

8. სტატიას თან უნდა ახლდეს ავტორის მიერ გამოყენებული სამამულო და უცხოური შრომების ბიბლიოგრაფიული სია (ბოლო 5-8 წლის სიღრმით). ანბანური წყობით წარმოდგენილ ბიბლიოგრაფიულ სიაში მიუთითეთ ჯერ სამამულო, შემდეგ უცხოელი ავტორები (გვარი, ინიციალები, სტატიის სათაური, ჟურნალის დასახელება, გამოცემის ადგილი, წელი, ჟურნალის №, პირველი და ბოლო გვერდები). მონოგრაფიის შემთხვევაში მიუთითეთ გამოცემის წელი, ადგილი და გვერდების საერთო რაოდენობა. ტექსტში კვადრატულ ფჩხილებში უნდა მიუთითოთ ავტორის შესაბამისი N ლიტერატურის სიის მიხედვით. მიზანშეწონილია, რომ ციტირებული წყაროების უმეტესი ნაწილი იყოს 5-6 წლის სიღრმის.

9. სტატიას თან უნდა ახლდეს: ა) დაწესებულების ან სამეცნიერო ხელმძღვანელის წარდგინება, დამოწმებული ხელმოწერითა და ბეჭდით; ბ) დარგის სპეციალისტის დამოწმებული რეცენზია, რომელშიც მითითებული იქნება საკითხის აქტუალობა, მასალის საკმაობა, მეთოდის სანდოობა, შედეგების სამეცნიერო-პრაქტიკული მნიშვნელობა.

10. სტატიის ბოლოს საჭიროა ყველა ავტორის ხელმოწერა, რომელთა რაოდენობა არ უნდა აღემატებოდეს 5-ს.

11. რედაქცია იტოვებს უფლებას შეასწოროს სტატია. ტექსტზე მუშაობა და შეჯერება ხდება საავტორო ორიგინალის მიხედვით.

12. დაუშვებელია რედაქციაში ისეთი სტატიის წარდგენა, რომელიც დასაბეჭდად წარდგენილი იყო სხვა რედაქციაში ან გამოქვეყნებული იყო სხვა გამოცემებში.

აღნიშნული წესების დარღვევის შემთხვევაში სტატიები არ განიხილება.

Содержание:

ოპტიმალური კონცენტრაცია (5%), რომელიც არ არღვევს თერმომგრძნობიარე გელის ფორმირების პროცესს. მოწოდებული in-situ ჰიდროგელის გელწარმოქმნის ტემპერატურა არის 36.6^{0}C, ხოლო გელწარმოქმნის დრო 10 წთ. მოწოდებული ჰიდროგელი რეოლოგიური მახასიათებლებით შეესაბამება ფსევდოპლასტიკური სითხეების ვისკოელასტიკურ თვისებებს. ნანოკომპოზიციურ ჰიდროგელში შეფასებულია შემადგენელ კომპონენტებს შორის შესაძლო ურთიერთკავშირი ინფრაწითელი სპექტროსკოპიის გამოყენებით. დადგენილია, რომ ჰიდროგელსა და ნანონაწილაკებს შორის პირდაპირი ქიმიური კავშირი არ აღინიშნა. მიკროსკოპულად დადასტურებულია პოლიმერული ნანონაწილაკების ჰომოგენური განაწილება ჰიდროგელში. ნანოკომპოზიციური ჰიდროგელიდან მოქმედი ნივთიერების გამოთავისუფლების დინამიკა ორფაზური და გახანგრძლივებული ხასიათისაა. 72 სთ-ში ფოსფატურ ბუფერში და უჯრედული კულტურის არეში გამოთავისუფლდა მოქმედი ნივთიერების 64% და 78%, შესაბამისად.

მოწოდებული ნანოკომპოზიციური ჰიდროგელის ბიოთავსებადობა შეფასებულია კვერცხის მოდელზე. ჩატარებული ექსპერიმენტით დადადგენილია, რომ ის არ იწვევს სისხლძარღვების ისეთ დაზიანებებს, როგორიცაა სისხლძარღვთა ლიზისი, ჰემორაგია, თრომბოზი, ჰემოლიზი.

HEPATOPROTECTIVE EFFICIENCY OF G10 SUBSTANCE FROM ZHUZGUN PLANT IN EXPERIMENTAL TOXIC HEPATITIS

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The problem of hepatitis is one of the most significant in modern medicine, since millions of cases are registered annually and at the moment there is no tendency to reduce the incidence rate [3,19]. To attract attention to this problem all over the world, who announced the 28th of July the world Day of fight against hepatitis. It should be emphasized that close attention to the problem of hepatitis treatment is due not only to the increase in the incidence of hepatitis worldwide, but also to the increase in the mortality rate. In this regard, for practical health care, the task of finding new, effective treatments that can accelerate the rate of functional recovery of the liver or protect hepatocytes from the damaging effects of hepatotropic viruses and other pathogens remains urgent. The modern approach to adequate treatment of hepatitis involves the use of both synthetic drugs and herbal preparations that have a multi-sided positive effect [3,19].

The hepatoprotective properties of herbal preparations are closely studied by scientists in many countries [4,5,12,13]. The reason for this is their high biological activity, low toxicity and lower probability of side effects compared to drugs of synthetic origin. Biologically active substances of plants are close to the natural metabolites of the human body, they are well compatible with them. Many of them are necessary for normal life and can be used in complex pharmacotherapy of diseases of the hepatobiliary system. Plant objects can become an unlimited source for obtaining phytopreparations, including hepatoprotectors, which, ultimately, will lead to a reduction in the cost of production and release of drugs, and, consequently, to a decrease in its market price [1,14-16].

One of the most common etiological factors that cause pathology of the hepatobiliary system is the action of toxicants of various origins. Toxic liver damage is caused by an absolute increase in the body's contacts with hepatotoxic xenobiotics: household, industrial and agricultural chemicals. In addition, long-term and uncontrolled use of drugs, which is the cause of 40% of hepatitis in patients over 40 years of age, is of significant importance in the development of toxic liver damage [6,7,10,11,17]. At the same time, in most cases of drug-induced liver damage, withdrawal of the drug is sufficient to reverse the development of pathological changes [20]. However, when a long course of treatment with highly effective drugs with potential hepatotoxic effects is required, it is necessary to combine them with correctors of metabolic disorders [20], which may be plant-based hepatoprotectors.

One of the promising species in this direction is the Zhuzgun plants of the genus Calligonum L. of the Polygonaceae family. This genus includes about 150 species, most of which are distributed in the deserts of Central and Central Asia, from the Sahara Desert (North Africa) to Alashan and Ordos in China. On the territory of the Republic of Kazakhstan, this plant is found everywhere and includes about 80 species. In the laboratories of the L. N. Gumilyov Eurasian National University (Republic of Kazakhstan, Moscow, Russia). Nur-Sultan) from the Zhuzgun plant, the substance G10 was obtained on the basis of biologically active substances containing various classes of natural compounds: flavanoids, tannins, terpenoids, amino acids, carbohydrates, trace elements, essential oils, which made it possible to study it as a basis for creating a drug with a hepatoprotective effect [8].

The aim of this study is to study the hepatoprotective properties of the substance G10 obtained from the plant "Zhuzgun" on an experimental model of acute toxic hepatitis in rats and to determine its effectiveness in comparison with the official plant hepatoprotector "Karsil".

Material and methods. The experiments were performed on 70 white mongrel rats weighing 180-250 g, obtained from the vivarium of the NAO "Astana Medical University". The animals were kept and studied in accordance with the principles of the Helsinki Declaration on the Protection of Vertebrates Used for Experimental Purposes. Before and during the experiment, the rats were kept in standard vivarium conditions on a standard food regime. The work was performed in the "Laboratory of Pharmacological Research" of the Department of General Pharmacology. The experiment was conducted in accordance with the methodological recommendations of the Organization for Economic Cooperation and Development (OECD) No. 423. The study is part of the scientific work " The effect of substance G10 on the course of acute toxic hepatitis in rats (experimental study)", approved by the Local Ethics Committee of the NAO "Astana Medical University" (Protocol No. 4, dated 2019).

Characteristics of the reference drug-Karsil. The hepatoprotective efficacy of substance G10 was evaluated in comparison with the phytopreparation "Karsil" on an experimental model of acute toxic hepatitis in rats. Karsil's active ingredient is silymarin, which is a complex mixture of flavonolignans silibinin, silicristin, silidianin and isosilybin [2]. Karsil prevents the destruction of cells by toxins, drugs, and alcohol. Therefore, its main indications include prevention and treatment of the initial stage of hepatic pathology. Substance G10 and the reference drug Carsil were administered to experimental rats intragastrically through a probe daily for 7 days, 1 hour before the administration of paracetamol. The estimated dose of Karsil administered to experimental animals was 50 mg/kg. Substance G10 was used in doses of 1000 and 1500 mg/kg of body weight [18].

Creating a model of paracetamol hepatitis. Acute toxic hepatitis was modeled for 7 days by intragastric administration of paracetamol through a probe once a day at a dose of 2500 mg/kg of body weight [9]. The duration of the experiment was 14 days.

Groups of animals. To study the biochemical parameters of blood, experimental animals (n=35) were divided into groups: Group I – intact (n=7); group II – animals with paracetamol hepatitis (n=7); group III – animals with acute toxic hepatitis treated with Carsil (a reference drug); group IV - animals with acute toxic hepatitis treated with substance G 10 at a dose of 1000 mg/kg (n=7); Group V – animals with acute toxic hepatitis treated with substance G10 at a dose of 1500 mg/kg (n=7).

The dynamics of biochemical parameters of blood serum was studied by determining the level of enzyme activity of alanine aminotransferase (AlT), aspartate aminotransferase (AsT), alkaline phosphatase (ALP), as well as the content of total bilirubin. Testing was carried out on the 2nd, 7th and 14th day of the experiments. Experimental data obtained in groups II and III served as a control for determining the comparative effectiveness of using different dosages of substance G10 in animals with acute paracetamol hepatitis.

To study the morphological changes in the liver (n=35), the experimental animals were also divided into 5 groups: Group I: intact (n=7), animals received 1 ml of saline solution for 7 days; group II, animals that were modeled with paracetamol hepatitis (n=7); group III: animals received Carsil at a dose of 50 mg/kg on saline solution 1 hour before administration of paracetamol (comparison drug); group IV, animals with acute toxic hepatitis, substance G10 was obtained at a dose of 1000 mg/kg on 1% starch 1 hour before the administration of paracetamol (n=7); Group V, animals with acute toxic hepatitis, received substance G10 at a dose of 1500 mg/kg on 1% starch 1 hour before administration of paracetamol (n=7). The animals were removed from the experiment in compliance with all the necessary international ethical standards and requirements.

The material for morphological studies was liver tissue, which was extracted during autopsy and fixed in a 10% formalin solution. Further processing and pouring of the material into paraffin was carried out according to the generally accepted pathohistological method. Microscopic sections 5-7 microns thick were made from paraffin blocks and stained with hematoxylin-eosin.

The results were carried out using MSExcel application programs and using the statistical package "SPSS Statistics 20". Descriptive statistics were performed using MSExcel application packages. The data is presented as the arithmetic mean and the standard error of the average result (M±m) under normal data distribution. The presence of statistically significant intergroup differences was determined using a single-factor analysis of variance, the differences between the groups were considered significant at a significance level of $p<0.05$.

Results and discussion. In acute toxic hepatitis, the phenomena of cytolysis of hepatocytes come to the fore. The primary mechanisms of cytolysis syndrome are closely associated with a violation of oxidative phosphorylation, a decrease in energy production, and subsequent changes in the function and structure of liver cells, primarily hepatocytes. The syndrome is based on a violation of the permeability of cell membranes, their organelles, which leads to the release of intracellular enzymes into the blood plasma. Reliable indicators of the cytolytic process in the liver are indicator enzymes (AlT, AST, ALP, etc.), as well as total bilirubin. The degree of increase in their activity indicates the severity of cytolysis and ultimately allows us to assess the functional state of the liver.

Blood biochemical parameters. Analysis of the research results showed that the use of paracetamol significantly leads to acute toxic damage to the liver of experimental animals. At the same time, a significant increase in the level of ALT and AST enzyme activity in the blood serum at all follow-up periods was a reliable marker that allows us to judge the characteristic involvement of hepatocytes in the pathology.

If the ALT values in group I were in the range of 57.00-64.00 ukat/l, then in group II animals during all the study periods they significantly exceeded the initial values by 2.4, 2.8, and 2.6 times, respectively ($p1<0.001$) (Table 1).

The situation with changes in the activity of the AST enzyme was much more dramatic (Table 2).

Thus, in group I, the initial parameters of the studied enzyme varied within the following values: 19.42±4.4 ukat/l, 23.16±8.52 ukat/l and 13.16±2.52 ukat/l, whereas after modeling experimental acute paracetamol hepatitis, the level of AsT activity on the 2nd, 7th and 14th days of the study in group II was 168.51±17.62 ukat/l, 156.61±12.03 ukat/l and 154.85±15.29 ukat/L respectively. Compared with the data obtained in group I, the excess of the AST values was more than 6 and 11 times ($p1<0.001$).

Due to the fact that the cytolytic syndrome is accompanied by the destruction of hepatocytes with the release of the excretory enzyme alkaline phosphatase, it is of interest to study its level in the studied groups. When studying the data on alkaline phosphatase in a group of intact animals and a group of animals that were experimentally modeled with toxic hepatitis, an almost 3-fold increase in the level of its enzyme activity was found (Table 3). Thus, the values of ALP in group I animals ranged from 98.21±2.31 ukat/l and 100.96±2.26 ukat/l, while in group II rats the studied parameter was 3 – 3.3 times higher than the standard values for all study periods ($p1<0.001$).

Table 1. Changes in the level of ALT activity (ukat/l) in blood serum in rats with acute hepatitis during the use of substance G 10

Group / Day of research.	Intact (I) n=7	Acute hepatitis (II) n=7	Acute hepatitis + Carsil (III) n=7	Acute hepatitis +substance G10	
				1000 mg / kg (IV) n=7	1500 mg/kg (V) n=7
2	63,83±5,56	154,22±21,14 R_1<0,001	61,57±5,01 R_1>0,05 R_2<0,001	105,97±19,65 R_1<Of 0.001 R_2=0,001	77,5±of 9.71 R_2<0,05 R_3<0,05
7	58,32±4,21	166,61±a 12.03 R_1<0,001	of 66.13±7,23 R_1>0,05 R_2<0,001	78,86±25,80 R_1<0,05 R_2<0,001	amounted 61.41±3,77 R_1>0,05 R_2<0,001 R_3>0,05
14	56,71±3,62	150,57±13,3 R_1<0,001	61,31±5,62 R_1>0,05 R_2<0,001	69,82±rate of 16.07 R_1>0,05 R_2<0,001 R_3>0,05	60,43±2,29 R_1>0,05 R_2<0,001 R_3>0,05

notes: p1 - indicator of the reliability of differences in comparison with group I; p2-indicator of the reliability of differences in comparison with group II; p3-indicator of the reliability of differences in comparison with group III $P3_3$-indicator of significance of differences in comparison with group III

Table 2. Changes in the level of AsT activity (ukat/l) in blood serum in rats with acute hepatitis against the background of the use of substance G 10

Group / Day of research	Intact (I) n=7	Acute hepatitis (II) n=7	Acute hepatitis + Carsil (III) n=7	Acute hepatitis +substance G10	
				1000 mg / kg (IV) n=7	1500 mg/kg (V) n=7
2	19,42±4,4	168,51±loss of 17.62 R_1<0,001	25,71±7,2 R_1>0,05 R_2<0,001	of 28.87±6,07 R_1>0,05 R_2<0,001 R_3>0,05	of 23.21±6,9 R_1>0,05 R_2<0,001 R_3>0,05
7	of 23.16±8,52	156,61±a 12.03 R_1<0,001	of 18.31±4,6 R_1>0,05 R_2<0,001	21,59±4,1 R_1>0,05 R_2<0,001 R_3>0,05	21,77±5,50 R_1>0,05 R_2<0,001 R_3>0,05
14	13,16±2,52	154,85±15,29 R_1<0,001	of 16.13±2,26 R_1>0,05 R_2<0,001	19,4±5,34 R_1>0,05 R_2<0,001 R_3>0,05	18,24±3,71 R_1>0,05 R_2<0,001 R_3>0,05

notes: p1 - indicator of the reliability of differences in comparison with group I; p2-indicator of the reliability of differences in comparison with group II; p3-indicator of the reliability of differences in comparison with group III $P3_3$-indicator of significance of differences in comparison with group III

Table 3. Changes in the level of activity of alkaline phosphatase (ukat/l) in blood serum in rats with acute hepatitis against the background of the use of substance G 10

Group / Day of research.	Intact (I) n=7	Acute hepatitis (II) n=7	Acute hepatitis + Carsil (III) n=7	Acute hepatitis +substance G10	
				1000 mg / kg (IV) n=7	1500 mg/kg (V) n=7
2	100,96±2,26	310,57±16,71 R_1<0,001	only 114.2±of 17.48 R_1>0,05 R_2<0,001	297,14±26,48 R_1<0,001 R_2>0,05 R_3<0,001	197,57±25,14 R_1<0,05 R_2<0,001 R_3<0,001
7	116,6±3,21	366,61±of 17.03 R_1<0,001	118,1±19,2 R_1>0,05 R_2<0,001	221,71±21,92 R_2<0,001 R_3<0,001	of 123.04±9,82 R_1>0,05 R_2<0,001 R_3>0,05
14	98,21±2,31	320,7±20,37 R_1<0,001	102,54±3,61 R_1>0,05 R_2<0,001	186,7±of 16.02 R_2<0,001 R_3<0,001	111,52±12,9 p_1>0,05 R_2<0,001 R_3>0,05

notes: p1 - indicator of the reliability of differences in comparison with group I; p2-indicator of the reliability of differences in comparison with group II; p3-indicator of the reliability of differences in comparison with group III $P3_3$-indicator of significance of differences in comparison with group III

Table 4. Changes in total bilirubin (ukat/l) in blood serum in acute hepatitis in rats, when using substance G 10

Group / Day of research	Intact (I) n=7	Acute hepatitis (II) n=7	Acute hepatitis + Carsil (III) n=7	Acute hepatitis +substance G10	
				1000 mg/kg (IV) n=7	1500 mg/kg (V) n=7
2	3,83±0,47	22, and 13±0,47 R_1<0,001	9,00±1,41 R_2<0,001	12,82±1,07 p_2<0,01 R_3>0,05	13,50±of 3.08 p_2<0,05 R_3>0,05
7	of 6.28±1,54	38,48±0,45 R_1<0,001	12,13±1,26 R_1<0,05 R_2<0,001	16,81±3,9 p_1<0,01 p_2<0,001 R_3>0,05	10,36±2,70 p_1>0,05 p_2<0,001 R_3>0,05
14	8,31±2,61	a 29.08±3,37 R_1<0,001	of 11.31±1,6 R_2<0,001	10,22±2,24 p_1>0,05 p_2<0,001 R_3>0,05	was 6.77±0,7 p_1>0,05 p_2<0,001 R_3>0,05

notes: p1 - indicator of the reliability of differences in comparison with group I; p2-indicator of the reliability of differences in comparison with group II; p3-indicator of the reliability of differences in comparison with group III $P3_3$-indicator of significance of differences in comparison with group III

Similar dynamics were determined when studying the total bilirubin content in the blood serum of rats with acute toxic hepatitis. During all the study periods of the experiment (2, 7, 14 days), the total bilirubin content steadily exceeded the data obtained in the group of intact animals (Table 4). Moreover, the most pronounced hyperbilirubinemia with a significant increase in the concentration of total bilirubin, by 5-6 times, was observed on the 2nd and 7th days of the experiment. On the 14th day of the study, there was a slight decrease in the content of this metabolite in the control-2 group, however, it continued to remain at a level 3 times higher than in the group of intact rats (p1<0.001).

Together, the results obtained indicate the severity of the process of violation of the integrity of hepatocytes, which is characteristic of acute liver damage and hepatitis of toxic origin.

Results of the use of the comparison drug-Karsil. Following the design of the experiments, the effect of the official hepatoprotective drug Karsil on the course of acute toxic hepatitis in rats was studied. The results obtained were necessary for comparing the effectiveness of the substance G10 under similar conditions of its use. At the same time, it was found that the enteral administration of Karsil at a dose of 50 mg/kg to group III animals contributes to a critical decrease in the level of enzyme activity of both AlT and AsT on the specified 2nd, 7th and 14th days of the study. When compared with the data of group II, in which the experimental model of toxic hepatitis was reproduced, statistically significant differences were found (p2<0.001), thereby characterizing the decrease in the activity of the studied enzymes in the blood serum. At the same time, there were no significant differences in the studied parameters in intact rats and animals with acute toxic hepatitis treated with Carsil.

The analysis of the data on SCHF allowed us to conclude that the use of Karsil in group III contributed to the normalization of the studied parameter in all periods of observation. This was evidenced, with a high degree of confidence, first, by a decrease in the enzyme activity of alkaline phosphatase in comparison with the data obtained in group II (p2<0.001), and secondly, by a clear trend of its return to the baseline values recorded in intact rats.

A different pattern of changes was determined when studying the total bilirubin content in the blood serum of group III animals. Against the background of the use of Karsil, the concentration of total bilirubin decreased by 2.5-3 times (p2<0.001) compared to similar data in group II, but it continued to remain slightly higher than in the group of intact rats.

Hepatoprotective efficacy of various doses of substance G10. Enteral administration of substance G10 at a dose of 1000 mg/kg of weight against the background of modeling of acute paracetamol hepatitis affected the dynamics of cytolysis markers in the blood serum of experimental animals as follows: on the 2nd day of the study, AlT activity in group IV corresponded to the values of 105.97±19.65 ukat/l, which was 1.5 times lower than in group II, but continued to be higher than the values of the intact group of animals. A return to the standard parameters was observed only on the 7th and 14th days of the experiment. At the same time, G10 at a dose of 1500 mg/kg of weight, already starting from the 2nd day of the study and in the following days, showed a more pronounced positive effect on the dynamics of AlT. At the specified time, the level of AlT activity was significantly lower than in group II (p2<0.05 and p2<0.001) and practically did not differ from the standard indicators of intact animals (p1>0.05).

When studying the dynamics of the enzyme activity of AsT in groups IV and V, it was found that, regardless of the dose of the substance G 10 used, almost complete normalization of the studied parameter was observed from the 2nd day of observation, in addition, the differences between groups III, IV, V were leveled (p>0.05).

During all follow-up periods, the level of alkaline phosphatase enzyme activity in group IV, in which substance G10 was used at a dose of 1000 mg/kg, continued to be significantly higher than in intact rats (p1<0.001), with no significant differences in this parameter between groups II and IV. In addition, in group IV animals, the activity of ALP significantly exceeded those of group III rats that received Karsil.

It should be especially noted that the increase in the dosage of G10 to 1500 mg / kg of weight caused a more favorable dynamics of changes in this enzyme. So, on the 2nd day of the study, in comparison with the group of animals with acute toxic hepatitis, this indicator decreased by almost 1.5 times (p2<0.001), although by this time, in comparison with the group of intact animals, a higher level of its activity was still maintained (group

I, p1<0.05). Only on the 7th and 14th day of the study, the differences between groups I, III and V were completely leveled.

Analysis of the total bilirubin content in the blood serum against the background of the use of substance G10 in different dosages revealed a unidirectional trend of changes. It was characterized by a significant decrease in the total bilirubin content in all these study periods. Thus, in comparison with the data obtained in group II, in groups IV and V, the values of the studied parameter decreased by more than 2 times (p2<0.001). At the same time, the true normalization of this indicator occurred by the 14th day of the study only in the group of animals that were prescribed substance G10 at a dose of 1500 mg/kg of weight.

Our biochemical studies of blood serum in acute paracetamol hepatitis revealed a significant increase in the level of enzyme activity of alanine aminotransferase (AlT), aspartate aminotransferase (AsT), alkaline phosphatase (ALP), and total bilirubin, which indicates a pronounced cytolysis of hepatocytes. It was also found that the use of substance G10 in doses of 1000 and 1500 mg / kg of weight effectively eliminates the toxic effects of paracetamol and normalizes the level above the studied indicators.

However, at the same time, for a deeper understanding of the pathogenesis and nature of developing pathological processes, as well as to determine the structural basis of the sanogenic effect of substance G10, it is necessary to conduct appropriate morphological studies.

Results of morphological studies. Macroscopic examination of the liver of intact animals did not reveal any destructive changes: the liver is dark red in color, with a smooth capsule, homogeneous on the section, of the usual consistency.

In animals treated with paracetamol, there are signs of toxic hepatitis. There is cytolysis of individual groups of hepatocytes, diffuse violation of the correct beam structure of the hepatic lobule; hepatocytes in a state of vacuole and drip dystrophy; uneven hyperplasia of Kupffer cells. There are single binucleated hepatocytes (11-12 binucleated per 100 cells). Isolated granulomas are found around the damaged cells, and the lumen of the sinusoids contains lymphocytes. In the periportal tract, a productive inflammatory reaction involving macrophages, histiocytes, plasmocytes, and lymphocytes. The infiltrate penetrates into the thickness of the hepatic lobules. (Fig. 1).

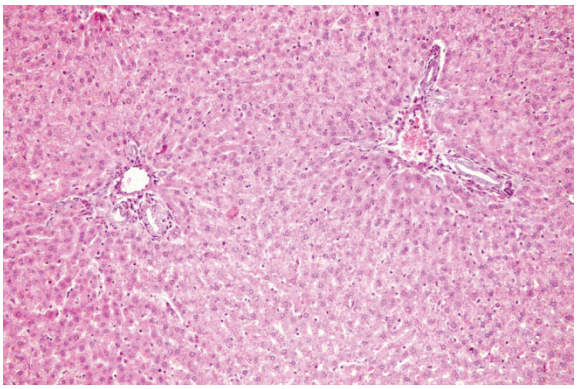

Fig. 1. Violation of the correct beam structure of the hepatic lobule in paracetamol hepatitis. Stained with hematoxylin and eosin. Magnification x160

In some areas, there is a toxic expansion of hepatocytes, diapedetic hemorrhages, focal collicvation necrosis. There are sharply dilated blood vessels (Fig. 2).

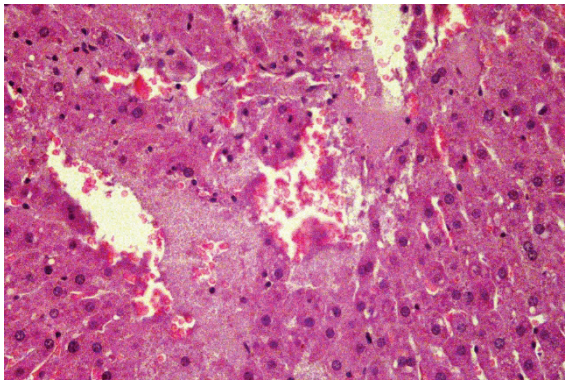

Fig. 2. Collicvation necrosis in paracetamol hepatitis. Stained with hematoxylin and eosin. Magnification x160

In the interlobular stroma, there are cellular proliferates around the vessels of the microcirculatory bed. Isolated granulomas are found around the damaged cells, and the lumen of the sinusoids contains lymphocytes. the proliferative consist of isolated lymphocytes and macrophages. Hepatocytes in a state of protein dystrophy (Fig. 3).

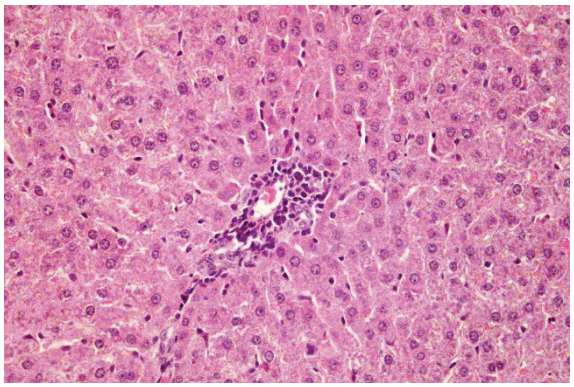

Fig. 3. Cell proliferation in paracetamol hepatitis. Stained with hematoxylin and eosin. Magnification x160

When using paracetamol against the background of the introduction of karsil, there is a decrease in the cellular inflammatory response, Kupfer cells are enlarged unevenly. The sinusoids are dilated, the fullness is less pronounced. In the hepatocytes of the centers of the lobules, signs of protein dystrophy are determined (Fig. 4).

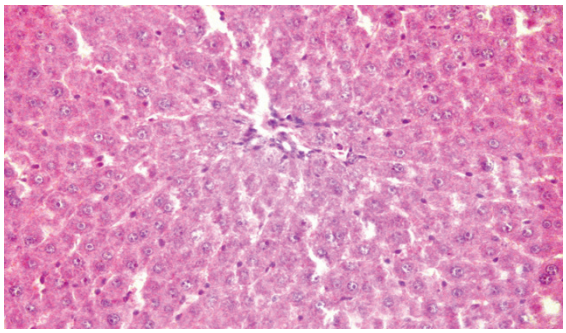

Fig. 4. Changes in hepatocytes on the background of karsil administration. Stained with hematoxylin and eosin. Magnification x160

When using paracetamol against the background of substance G 10 at a dose of 1000 mg/kg on the seventh day, pronounced

interstitial inflammation persists. There is no necrosis, there are lymphocytes in the sinusoids around the portal tracts. In the cytoplasm of some hepatocytes, there are small fat vacuoles. In the periportal tracts, there is a moderate inflammatory reaction involving histiocytes and lymphocytes. (Figs. 5-6).

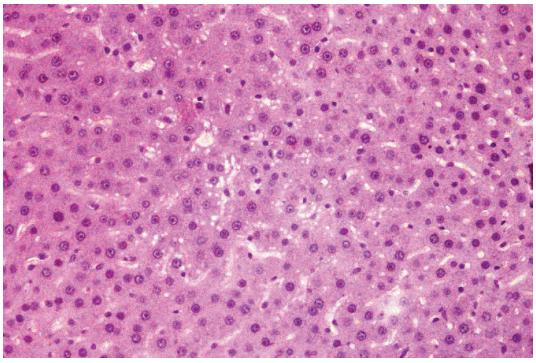

Fig. 5. Histological preparation of the liver of rats with paracetamol hepatitis on the background of substance G 10 at a dose of 1000 mg/kg on day 7. Fatty degeneration. Stained with hematoxylin and eosin. Magnification x160

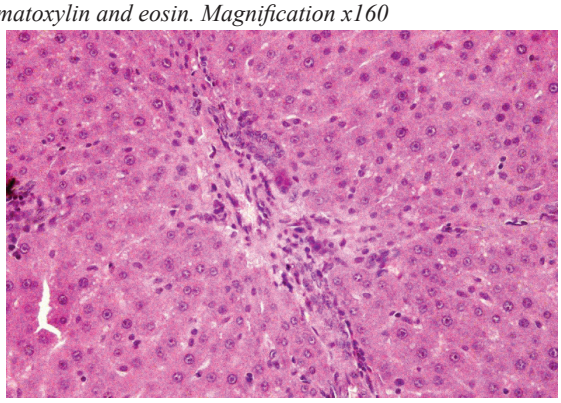

Fig. 6. istological preparation of the liver of rats with paracetamol hepatitis on the background of substance G 10 1000 mg / kg on day 7. Periportal inflammation. Stained with hematoxylin and eosin. Magnification x160

After the introduction of substance G 10 at a dose of 1000 mg/kg on the 14th day, there is an improvement. The balloon structure of the hepatic lobes is preserved, the sinusoids are evenly, moderately expanded, and contain red blood cells. The central veins are irregularly full-blooded. Single changes are noted in the periportal tracts. (Fig. 7).

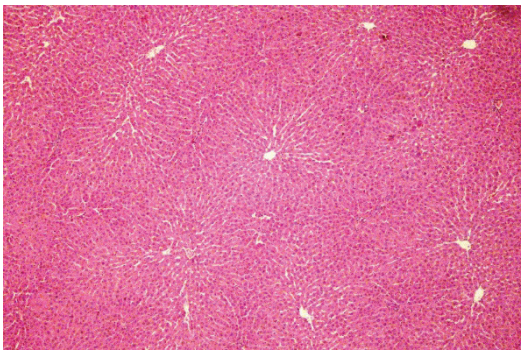

Fig. 7. Histological preparation of the liver of rats with paracetamol hepatitis on the background of substance G 10 at a dose of 1000 mg/kg on day 14. Liver lobules. Stained with hematoxylin and eosin. Magnification x160

After the introduction of substance G 10 at a dose of 1500 mg / kg on the 14th day, you can see changes for the better. There is moderate mild inflammation, no necrosis. Eosinophilic granulomas are formed in the liver lobules. (Fig. 8).

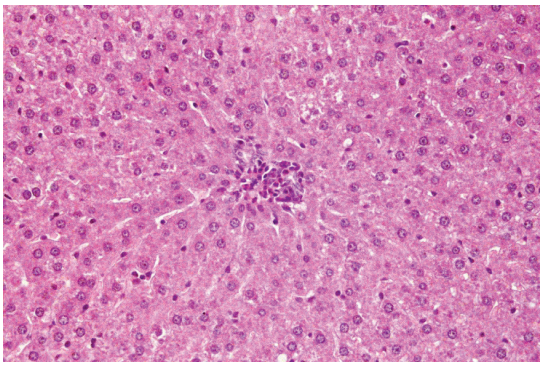

Fig. 8. Histological preparation of the liver of rats with paracetamol hepatitis on the background of substance G 10 at a dose of 1500 mg/kg on day 14. Eosinophilic granuloma. Stained with hematoxylin and eosin. Magnification x160

Conclusion. Thus, the analysis of the results of our own research allows us to conclude that the substance G10 obtained from the plant "Zhuzgun" has a significant positive effect on the dynamics of biochemical parameters of blood serum in animals with experimental acute paracetamol hepatitis.

Substance G10 in doses of 1000 mg/kg and 1500 mg/kg of weight contributes to a significant reduction in markers of cytolysis (AsT, AlT), as well as indicators of cholestasis (alkaline phosphatase, bilirubin). At the same time, a more pronounced and stable positive effect of the action has a high dosage of G10, namely 1500 mg/kg of weight, which causes an acceleration of normalization of the studied parameters, comparable to those of intact animals.

The results of pathomorphological examination of the internal organs of laboratory animals (rats) with intragastric administration of substance G10 also allow us to conclude that it has a hepatoprotective effect.

In terms of its effectiveness, the dynamics and nature of the restoration of impaired liver functions in experimental animals, the substance G10 is practically in no way inferior to the official "Karsil". However, the huge distribution area of the plant "Zhuzgun" and the presence of a large number of reserves of natural plant raw materials around the world undoubtedly determine the obvious advantages of the substance G10 over the comparison drug "Karsil". The obtained preliminary data on the hepatoprotective efficacy of substance G10 open up new prospects for further studies of its pharmacological properties.

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SUMMARY

HEPATOPROTECTIVE EFFICIENCY OF G10 SUBSTANCE FROM ZHUZGUN PLANT IN EXPERIMENTAL TOXIC HEPATITIS

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The article presents the results of biochemical studies of blood and morphological characteristics of liver changes in laboratory animals (rats) under experimental conditions of paracetamol hepatitis and intragastric administration of a new substance G10 from the «Zhuzgun» plant in various doses. The obtained data open up prospects for further studies of the pharmacological properties of the substance G10, the possibility of including it as a phytotherapeutic agent in the complex of preventive and therapeutic measures for acute toxic hepatitis.

The study of the hepatoprotective properties was conducted in the "Educational and Research Pharmacological Laboratory" of the Department of General Pharmacology of the Astana Medical University. The object of the study was the substance G. 10 from the Juzgun plant, which is a brown powder, odorless, poorly soluble in water.

The analysis of the results of our own research allows us to conclude that the substance G10 obtained from the plant «Zhuzgun» in various doses has a significant positive effect on the dynamics of biochemical parameters of blood serum in animals with experimental acute paracetamol hepatitis.The results of pathomorphological examination of the internal organs of laboratory animals (rats) with intragastric administration of substance G10 also allow us to conclude that it has a hepatoprotective effect.

The results of microscopic and biochemical studies of laboratory animals (rats) in acute toxic hepatitis with a new substance from the plant Calligonum allow us to conclude that the substance G10 has a hepatoprotective property. The obtained preliminary data on the hepatoprotective efficacy of substance G10 open up new prospects for further studies of its pharmacological properties.

Keywords: liver, experimental paracetamol hepatitis, cytolysis, substance G10 from the plant "Zhuzgun", hepatoprotective efficacy.

РЕЗЮМЕ

ГЕПАТОПРОТЕКТОРНАЯ ЭФФЕКТИВНОСТЬ СУБСТАНЦИИ G10 ИЗ РАСТЕНИЯ ZHUZGUN ПРИ ЭКСПЕРИМЕНТАЛЬНОМ ТОКСИЧЕСКОМ ГЕПАТИТЕ

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В статье представлены результаты биохимических исследований крови и морфологических особенностей изменений печени лабораторных животных (крыс) в условиях эксперимента при парацетамольном гепатите и внутрижелудочном введении нового вещества G10 из растения Zhuzgun в различных дозах.

Исследование гепатопротекторных свойств проведено на 70 белых беспородных крысах массой 180-250 г. Объектом исследования явилось вещество G10 из растения Zhuzgun, представляющее собой коричневый порошок, без запаха, плохо растворимый в воде.

Анализ результатов собственных исследований позволяет сделать вывод, что вещество G10, полученное из растения Zhuzgun, в различных дозах оказывает значительное положительное влияние на динамику биохимических показателей сыворотки крови у крыс с экспериментальным острым парацетамольным гепатитом. Результаты патоморфологического исследования внутренних органов крыс при внутрижелудочном введении

вещества G10 также позволяют сделать вывод о его гепатопротекторном действии.

Полученные данные открывают перспективы дальнейших исследований фармакологических свойств вещества G10, возможности включения его в качестве фитотерапевтического средства в комплекс профилактических и лечебных мероприятий при остром токсическом гепатите.

რეზიუმე

მცენარე ZHUZGUN-დან მიღებული სუბსტანცია G10-ის ჰეპატოპროტექტორული ეფექტურობა ექსპერიმენტული ტოქსიკური ჰეპატიტის დროს

ი.უიზბაევა, გ.აკპოლატოვა, დ.ტარჟანოვა, კ.მუკანოვი

ასტანას სამედიცინო უნივერსიტეტი, ზოგადი ფარმაკოლოგიის კათედრა, ნურ-სულტანი, ყაზახეთი

სტატიაში წარმოდგენილია სისხლის ბიოქიმიური კვლევის შედეგები და ღვიძლში განვითარებული მორფოლოგიური ცვლილებები ექსპერიმენტში პარაცეტამოლური ჰეპატიტის და მცენარე ZHUZGUN-დან მიღებული ახალი ნივთიერება G10-ის სხვადასხვა დოზის კუჭში შეყვანის პირობებში ვირთაგვებში.

ჰეპატოპროტექტორული თვისებების კვლევა ჩატარდა 70 თეთრ უჯიშო ვირთაგვაზე წონით 180-250 გ. მცენარე ZHUZGUN-დან მიღებული ახალი ნივთიერება G10 წარმოადგენს უსუნო, წყალში ცუდად ხსნად, ყავისფერ ფხვნილს.

კვლევის შედეგების საფუძველზე ავტორები დაასკვნიან, რომ მცენარე ZHUZGUN-დან მიღებული ახალი ნივთიერება G10 სხვადასხვა დოზით ახდენს მნიშვნელოვან დადებით გავლენას ბიოქიმიური პარამეტრების დინამიკაზე სისხლის შრატში ექსპერიმენტული მწვავე პარაცეტამოლური ჰეპატიტის დროს. ვირთაგვების შინაგანი ორგანოების პათომორფოლოგიური კვლევის შედეგები ნივთიერება G10-ის კუჭში შეყვანის პირობებში ადასტურებს მის ჰეპატოპროტექტორულ მოქმედებას.

მიღებული შედეგები ხსნის ახალ პერსპექტივებს ნივთიერება G10-ის შემდგომი ფარმაკოლოგიური კვლევისათვის ფიტოთერაპიული საშუალების სახით პროფილაქტიკური და სამკურნალო დონისძიებების კომპლექსში მწვავე ტოქსიკური ჰეპატიტის დროს.

COUMARINS FROM *DAPHNE AXILLIFLORA* (KEISSL.) POBED. AND THE ANATOMICAL CHARACTERISTICS OF ITS LEAVES AND STEMS

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The genus Daphne L. belongs to the Thymelaeaceae family and is one of the most diverse genera of this family with over 90 described species [14]. This genus is found widely across Europe, Asia and Northern Africa, with eight species growing in Georgia: D. mezereum L., D. pontica L., D. albowiana Woronow ex Pobed. (D. pontica subsp. haematocarpa Woronow), D. glomerata Lam. (D. imerica C.Koch); D. caucasica Pall., D. axilliflora (Keissl.) Pobed. (D. caucasica Pall. var. axilliflora Keissl); D. transcaucasica Pobed. (D. oleoides auct.) and D. pseudosericea Pobed. D. axilliflora (Keissl.) Pobed. and D. pseudosericea Pobed. are endemic species of the Caucasus [1].

The genus Daphne is used in traditional medicine, especially in China and the Middle East. It is used for the treatment of gonorrhoea, skin disieases, aches, rheumatism, cancer, malaria and inflammations [7,15,16]. Biological and pharmacological research has shown that extracts and compounds isolated from different Daphne species possess significant antimicrobial, antioxidant, cytotoxic, antiviral and several other effects [5,11-13,15].

The chemical composition of the genus Daphne is quite diverse. The most important classes of compounds obtained are coumarins, flavonoids, lignans and terpenoids. Several alkaloids, steroids and phenylpropanoids have also been isolated from this genus. Daphne is known for the content of daphnane diterpenes, a wide range of mono-, di- and tricoumarins, and flavonoid glycosides [8,9,12,14,16].

D. axilliflora is an endemic species of the Caucasus [1]. The plant is widely spread in most parts of Georgia, commonly in forested areas. These are deciduous shrubs reaching heights of up to 2 m. The stems are thin, older ones with greyish bark, while young stems have a dark purple bark; stems are glabrous, except under the inflorescences of young stems that are slightly pubescent. Leaves on flower-bearing branches are small, 2-3 cm long and 0.5-0.75 cm wide, elongate-oval, cuneate at the base, obstuse at the tip; on non-flower baring branches they are larger, 5 -7 cm long and 1-1,5 cm wide, gradually cuneate at the base, acute at the tip; they are glabrous, adaxial part green, abaxial side pale green; Flowers bisexual, 4-merous, perianth tubular, white, fragrant; flowers are grouped together at the tips of branches in numbers of 7-12 positioned on shortened stems. Perianth tubular, thinly pubescent; four folded lobes of the perianth are wide-ovate, twice as short as the tube. Stamins 8, twice as many as perianth lobes, in two series, filaments short or absent, attached to the base of the perianth tube. The ovary is superior, glabrous, and almost sessile; the style is capitate. The fruit is a bright red drupe [1].