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# Assessment of the Chronic Process in the Liver under Study Conditions Using Conventional and in-Depth Laboratory Studies

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***Abstract:*** ***The presented article describes the work carried out on white rats in an experiment on the occurrence of severe liver pathologies, as in humans. When assessing the pathological process in the liver, in-depth laboratory studies were mainly carried out in combination with traditional examination methods. Thus, in the conducted studies, a substance with hepatotoxic properties of heliotrin, when administered according to a subtoxic dose scheme, caused severe functional and morphological changes in the liver. It was found that the change in normal and deep laboratory blood parameters characterizing inflammatory processes in the liver corresponds to morphological data.***

***Keywords:*** ***Fibrogenesis, Hepatoprotectors, Heliotrin, Liver Fibrosis and Cirrhosis, Chronic Toxic Hepatitis.***

## 1. INTRODUCTION

The problem of treating hepatitis of various etiologies is an extremely urgent task of modern medicine. Currently, despite the large arsenal of hepatoprotectors, clinicians do not always manage to stabilize the course of hepatitis, increase regenerative activity and prevent the development of fibrosis and cirrhosis of the liver. Because the effect of many drugs positioned as hepatoprotectors in acute and chronic liver pathology is in many cases insufficient and is not confirmed by independent comparative studies [1, 2, 3]. In this regard, the search continues for new medicinal agents, including those of plant origin, with a wide range of pharmacological activity and economic availability. In addition, on the model of different etiological toxic hepatitis, it was shown that the introduction of different biological substances to animals contributes to the normalization of blood biochemical parameters [4, 5, 6]. Thus, studies of the hepatoprotective effect of drugs based on antioxidant properties remain an urgent direction in toxicology. Therefore, in order to further expand the

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pharmacological spectrum of action of this agent, studies of its effect on the processes of fibrogenesis and the formation of liver cirrhosis in a long-term experiment were conducted. To compare the hepatoprotective effect of drugs on structural changes in the liver, the carbon tetrachloride model, isoniazid and heliotrin are often chosen. In studies of hepatoprotective properties, functional changes are often considered together with structural changes, although some researchers have found discrepancies in the levels of enzymemia with morphological manifestations in chronic heliotrin intoxication of rats. Heliotrin, as carbon tetrachloride, damages the liver, initiating the formation of various radicals and reactive oxygen species, leading to inflammation and depletion of antioxidant protection for the second time [7-12]. Thus, the increasing medical and social significance of chronic liver diseases requires new efforts in the development of issues of etiology, pathogenesis, immunology, diagnosis, treatment and prevention of these diseases. Currently, the radical surgical method of treating cirrhosis of the liver is orthotopic liver allotransplantation. However, its technical complexity, the shortage of donor organs, and the high cost of treatment limit the widespread introduction of this operation into clinical practice and stimulate the search for new available methods of treatment [13]. Therefore, reproduction in animal experiments of models of hepatitis and cirrhosis of the liver, close to clinical conditions, is still necessary [14]. Experimental models make it possible to give a comprehensive assessment and develop methods for adequate correction of liver failure, which is not always possible in clinical trials. For this reason, we used a method that is widely used in the context of the study of chronic toxic hepatitis.

**The purpose of the work:** Investigation of the effect of a toxic substance on the parameters of tumor necrosis Alpha factor-FNOAA, CD68, CD34 and CD95 in the blood of laboratory white rats under conditions of chronic heliotrine hepatitis.

## 2. MATERIAL AND METHODS OF RESEARCH

The experiment was performed on white female laboratory rats weighing 100 ± 10 g, obtained from a vivarium of used animals kept under standard conditions on a normal food and water diet. Manipulations with animals were carried out according to the manual [15]. Toxic liver damage was modeled by intragastric administration of heliotrin in low doses according to the scheme: 10 mg/100 g per kg of body weight, 7 mg/ 100 g per kg of body weight, 5 mg/ 100 g per kg of body weight, 3 mg/100 g per kg of body weight. All animals were divided into 6 groups of 10 individuals each. From the experiment, rats were removed by decapitation after 1, 3 and 5 weeks. The activity of ALT, AST, alkaline phosphatase, LDH, the level of total protein, direct bilirubin and glucose were determined in the blood serum. Chronic toxic liver damage or chronic intoxication was confirmed hematologically, biochemically and morphologically on the 35th day of the experiment [7, 16]. Alpha - factor of tumor necrosis in the blood-testing for FNOa and cd68+, CD34+ and CD95+. In diseases accompanied by inflammation, in particular, among the mechanisms leading to the pathogenesis of hepatitis, tissue damage is noted due to energy imbalance, excessive peroxidation and the development of secondary immunodeficiency. The following indicators were determined in the blood serum by the IFT method: the level of the main factors causing inflammation (Alpha - factor of tumor necrosis-fnoa), CD68+, CD34+[17,18,19]. Based on

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the conducted studies, the obtained results were compared with the control group of mukhakamasi, and statistical processing of the results was carried out using the methods of R.B. Strelkov presented in [20].

## 3. RESULTS AND THEIR DISCUSSION

1. Hematological and biochemical analysis of rat blood during the development of chronic heliotrine hepatitis. Toxic damage to the liver in rats as a result of the introduction of heliotrin led to a violation of the functional state of liver cells. As a result of these functional disorders, the activity of transaminases (AST and ALT) in the blood serum of rats with chronic gh was 238.6% and 281%, respectively, compared with the levels of these indicators in the control group. It was found that the total amount of protein decreased to 46% compared to the control group, while the total amount of bilirubin increased to 138.1%. There was also an increase in the amount of alkaline phosphatase and HHD to 10.3 and 145%, respectively, compared with the control group.

Table 1. Changes in the functional state of liver enzymes in chronic heliotrine hepatitis.

| Experimental groups | Intackt group | Control group |
|---|---|---|
| Doses mg/kg | Dist. water | Heliotrin |
| ALT u /l | 95,6±2,4 | 268,9±9,6 |
| AST u /l | 156,6±4,8 | 373,6±11,21 |
| Total protein (g/l) | 85,6±4,8 | 58,7±2,9 |
| Albumin g/l | 48,5±2,9 | 33,3±3,6 |
| Total Bilirubin mkmol/l | 2,15±0,96 | 5,12±0,96 |
| Koeffitsient of de Rits (AST/ALT) | 1,63±0,22 | 1,35±0,11 |
| ALPh, u /l | 394±4,48 | 434,4±6,52 |
| LDH, u /l | 625,5±11,6 | 1532,5±22,4 |
| HHD u /l | 1,15±0,11 | 1,46±0,11 |
| Amilase (u /l) | 495,7±11,22 | 442,6±6,48 |

Note: * - differences compared to the data of the control group-P<0.005

Thus, as the degree of liver damage worsened, as can be seen from the table, significant changes in biochemical parameters were also observed. in subsequent studies, the amount of cytokines was mainly tracked dynamically, and it was analyzed whether these changes were proportional to biochemical changes in the blood.

2. Investigation of the effect of a toxic substance that damages the liver on CD68, CD34 indicators in conditions of chronic heliotrine hepatitis. In animals with chronic heliotrine intoxication, the relative number of CD68-positive lymphocytes increased inside liver fragments during 5 weeks of the experiment. The number of intrahepatic CD34-positive lymphocytes in experimental rats also increased significantly compared to the control group (Table 2).

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Table 2. Changes in CD68, CD34, in conditions of chronic heliotrin hepatitis.

| Experimental groups | Doses in mg/kg | $CD_{68}$, % on the square | $CD_{34}$, % on the square |
|---|---|---|---|
| Intackt group | Dist. water | 3,89±0,21 | 4,75±0,48 |
| Control group | Dist. water | 5,49±0,9* | 27,68±1,15 |

Note: * - differences compared to the data of the control group-P<0.005

Thus, in conditions of chronic heliotrine hepatitis, the hepatotoxic substance negatively affected the relative number of CD68 and CD34-positive lymphocytes in liver tissue.

3. Investigation of the effect of a toxic substance that damages the liver on CD68, CD95, as well as anti-inflammatory cytokine - fno - na in conditions of chronic heliotrine hepatitis. In chronic experimental hepatitis, there was a significant increase in proinflammatory cytokine - FHO - α in blood serum to 96.64 ±10.2 pg/ml compared with the norm (P<0.001). This is also relative to the control value (p<0.025), confirmed by a direct correlation between the value of fno-O and the severity of fibrosis. (Table 3).

Table 3. Dynamics of changes in immunity indicators in blood serum. blood in the process of developing chronic heliotrine hepatitis.

| Experimental groups | $CD_{68}$, % on the square | $CD_{95}$, % on the square | ΦНО-α (ркg/ml) |
|---|---|---|---|
| Control group | 3,89±0,21 | 4,75±0,48 | 38,72± 2,54 |
| Group 1 | 4,97±0,39 | 12,54±0,9 | 68,22±5,07 |
| Group 2 | 5,08±0,45 | 16,44±1,25 | 75,9±6,22 |
| Group 3 | 5,46±0,41 | 20,21±1,62 | 84,24±6,55 |
| Group 4 | 5,81±0,61 | 22,65±1,49 | 86,61±5,62 |
| Group 5 | 6,24±0,48 | 27,54±0,97 | 91,72±6,45 |
| Group 6 | 5,49±5,9* | 27,68±1,15 | 96,64 ±10,2 |

Note: * - differences compared to the data of the control group-P<0.001

As shown in the table above, chronic administration of a hepatotoxic substance led to an aggravation of the degree of liver damage and even to the appearance of fibrosis-specific assays.

## 4. CONCLUSIONS

Thus, in the conducted studies, a substance with hepatotoxic properties of heliotrin, when administered according to a subtoxic dose scheme, caused severe functional and morphological changes in the liver. It was found that the change in blood parameters characterizing inflammatory processes in the liver corresponds to morphological data.

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## 5. REFERENCES

1. Байгильдин С.С., Репина Э.Ф., Хуснутдинова Н.Ю., Смолянкин Д.А., Каримов Д.О., Кудояров Э.Р. Морфология печени крыс через 24 часа после интоксикации тетрахлорметаном и последующей коррекции. Медицина труда и экология человека. 2020; 3:74-79
2. Семенова Е. В. Гепатопротекторная активность некоторых производных 3-гидроксипиридина при токсических повреждениях печени *диссертация+. Саранск: Мордовский государственный ун-т им. Н.П. Огарева; 2009.
3. Оковитый С.В. Клиническая фармакология гепатопротекторов // Фарминдекс Практик. Гепатология. – 2002. – Вып. 3. – С. 34–42.
4. Tolstikova T.G., Sorokina I.V., Tolstikov G.A., Tolstikov A.G., Flekhter O.B. Bioorganicheskaya khimiya. 2006. no 1. pp. 42–55. 11.
5. Tolstikova T.G., Sorokina I.V., Tolstikov G.A., Tolstikov A.G., Flekhter O.B. Bioorganicheskaya khimiya. 2006. no. 3. pp. 291–307.
6. Толстикова Т.Г., Жукова Н.А., Семенов Д.Е., Бессергенева Е.П., Сорокина И.В., Баев Д.С., Глухов Б.М. Биохимические показатели крови и количество гепатоцитов в печени крыс с токсическим гепатитом при действии аланинамида бетулоновой кислоты // Фундаментальные исследования. – 2012. – № 5-1. – С. 120-123;
URL: https://fundamental-research.ru/ru/article/view?id=29858
7. Aripov A.N, Akhunjanova L.L, Khamroev T.T, Aripov Abdumalik Nigmatovich, Akhunjanova Lola Lazizovna, & Khamroev Tolmas Tolibovich. (2022). Differential Analysis of Chronic Toxic Hepatitis Caused by The Introduction of Heliotrin Solution in Various Ways. Texas Journal of Medical Science, 4, 58–62. Retrieved from https://zienjournals.com/index.php/tjms/article/view/670
8. Чаиркина Н.В., Инчина В.И., Семенова Е.В., Семенов А.В., Исаак И.Н. Возможности коррекции гибридными антиоксидантами морфофункциональных изменений при токсическом повреждении печени. Морфологические ведомости. 2007;1(1-2):232-6.
9. Shah M. D., D'souza U. J., Iqbal M. The potential protective effect of Commelina nudiflora L. against carbon tetrachloride (CCl4)-induced hepatotoxicity in rats, mediated by suppression of oxidative stress and inflammation. Environ Health Prev Med. 2017; 22(1):66.
10. Yang C., Li L., Ma Z., Zhong Y., Pang W., Xiong M., et al. Hepatoprotective effect of methyl ferulic acid against carbon tetrachloride-induced acute liver injury in rats. Exp Ther Med. 2018; 15(3):2228-38.
11. Zhou C., Yin S., Yu Z., Feng Y., Wei K., Ma W., et al. Preliminary characterization, antioxidant and hepatoprotective activities of polysaccharides from Taishan Pinus massoniana pollen. Molecules. 2018; 23(2):281.
12. Репина Э.Ф., Хуснутдинова Н.Ю., Тимашева Г.В., Байгильдин С.С., Каримов Д.О., Мусина Л.А. и соавт. Морфологические особенности гепатопротекторного действия антигипоксантов при остром поражении печени тетрахлорметаном в эксперименте. Токсикологический вестник. 2019;154(1):43-8.

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13. Долгих, М. С. Перспективы терапии печеночной недостаточности с помощью стволовых клеток / М. С. Долгих // Биомедицинская химия. — 2008. — Т. 54, Вып. 4. — С. 376–391. 4.
14. Руководство по экспериментальному (доклиническому) изучению новых фармакологических веществ / Под общ. ред. член-корр. РАМН проф. Р. У. Хабриева. — 2-е изд., перераб. и доп. — М.: Медицина, 2005. — 832 с.
15. National Research Council. 2011. Guide for the Care and Use of Laboratory Animals: Eighth Edition. Washington, DC: The National Academies Press. https://doi.org/10.17226/12910.
16. Aripov A.N., Aripov O.A., Akhunjanova L.L., Nabiev A.O., Nabieva D.A., & Khamroev T.T. (2022). Study the antifibrous efficacy of plant proanthocyanidin in rats with chronic heliotrine liver damage. Frontline Medical Sciences and Pharmaceutical Journal, 2(05), 16–25. https://doi.org/10.37547/medical-fmspj-02-05-03.
17. Leytin V. Blood Rev. 2012; Mar; 26(2): 51-63. doi: 10.1016/j.blre.2011.10.002.
18. L. Fontana, E. Moreira, MI. Torres, MI. Fernández, A. Ríos, Sánchez de Medina F, A. Gil, Serum amino acid changes in rats with thioacetamide-induced liver cirrhosis. Toxicology. 1996 Jan 8;106(1-3):197-206. doi: 10.1016/0300-483x(95)03177-h.
19. Mokrenko E.V., Vяzmin A.Я., Shabanov P.D., Suslikova M.I., Mokrenko M.E., Gubina M.I. Цitokinovыy profil krovi krыs pri эksperimentalnom parodontite i deystvii immunomodulяtorov // Sovremennыe problemы nauki i obrazovanия. – 2020. – № 6. ; URL: https://science-education.ru/ru/article/view?id=30432
20. Стрелков Р.Б. Статистические таблице для ускоренной количественной оценки фармакологического эффекта. Фармакология и токсикология 1986. №4 с.100-104.