

# The Effectiveness of Glyciram in Restoring the Functional State of the Liver After Acute Toxic Damage

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**Annotation:** The effect of glyceram and silibor on the secretion of bile and its ingredients was studied in white sexually mature rats with acute toxic hepatitis. It was established that glyceram has a more pronounced choleric effect than silibor. Recommend the use of glyceram as a pathogenetic treatment of liver disease.

**Key words:** toxic damage, glyceram, silibo, the monooxygenase system.

The liver is the central organ involved in ensuring the chemical homeostasis of the body. Harmful chemical environmental factors create a great burden on this organ. At the same time, neutralizing various xenobiotics, as well as endogenous toxic substances - products of impaired metabolism, it itself is damaged, which leads to inhibition of the functional state of hepatocytes and especially its monooxygenase system. [1,2].

In this regard, in ecologically unfavorable regions of the republic, it is necessary to carry out prevention of liver damage with the help of hepatoprotectors. The latter is supplied to the republic exclusively through imports. At the same time, our country has a huge supply of medicinal plants with anti-inflammatory effects, in particular preparations of licorice naked (lat. *Glycyrrhiza glabra*) - glyceram. However, its effectiveness in restoring the functional state of the liver has not been studied enough.

**Purpose of the study.** Study of the effect of glyceram on the exocrine function of the liver and the chemical composition of bile in rats with acute toxic hepatitis induced by carbon tetrachloride.

**Materials and research methods.** Experiments were carried out on 42 male white rats, mixed population with initial body weight of 160-180 g. Animals were kept under standard vivarium conditions with free access to food and water, natural change of light and darkness. The experiments were carried out in accordance with the "Rules for conducting work using experimental animals", as well as the rules adopted by the European Convention for the Protection of Vertebrate Animals used for experimental research or for other scientific purposes (ETS No. 123), Strasbourg, 03/18/1986. Research carried out at room temperature 20-22°C.

Acute toxic hepatitis was reproduced by daily injection of 50% oily carbon tetrachloride into the skin of animals at a dose of 0.5 ml/100 g of body weight for 4 days. 24 hours after reproduction of the hepatitis model, the animals were divided into 4 groups. Each experimental group included 6-8 individuals. Animals of the 1st group were experimentally treated with glyceram (50 mg/kg), and those of the 2nd group with silibor (50 mg/kg). Aqueous suspensions of drugs were administered orally using a metal probe with olive oil once a day. The duration of treatment measures was 6 days. The rats of the third group in this period received an aliquot of water (non-treated group). 24 hours after the final administration of drugs in animals of all groups, the intensity of bile secretion and the chemical composition of bile were studied [4].

At the same time, studies were carried out in 6 intact white male rats (Group 4), which did not

differ significantly in age and weight, body from animals of other groups. Bile was collected from rats for 4 hours under etaminal anesthesia (40 mg/kg, intraperitoneally) with a polyethylene tube inserted into the common bile duct. We took into account the rate of bile secretion and its total amount for each hour and in total for 4 hours of observation. The concentration (in mg%) of the total content of bilirubin, bile acids and cholesterol was determined in hourly portions of bile [4].

To eliminate differences in the data obtained due to different body mass of animals, all the results were recalculated per 100 g of body weight of rats and subjected to variation statistics using paired Student's t-test and one-way one-factor analysis of variance using the BIOSTAT software package. Differences were considered significant at  $p < 0.05$ ; in the case of  $0.05 < p < 0.10$ , differences were evaluated as a trend [5].

**Results and discussion** With parenteral administration of carbon tetrachloride, experimental animals develop acute hepatitis with cytolytic syndrome [5]. As shown by the results of this work in rats with acute hepatitis, there is a persistent and significant inhibition of the exocrine function of the liver and the chemistry of bile. So, after 6 days from the beginning of the reproduction of acute toxic hepatitis, bile excretion in experimental rats, compared with healthy ones, statistically significantly decreases by 39.0%. At the same time, distinct changes in the chemical composition of bile are revealed. From the data given in the table, it can be seen that in rats with hepatitis, the content of bile acids and cholesterol in bile decreases by 43.6 and 49%, respectively. Against this background, there is an inhibition of bilirubin excretion by 51.3% in the indicated period of the study. Consequently, in acute toxic hepatitis, accompanied by fatty degeneration, there is a significant violation of the excretory function of the liver, manifested in a decrease in the excretion of cholates, cholesterol and bilirubin in the bile. A distinct and stable decrease in the content of bile cholates in this pathology indicates a decrease in the intensity of their synthesis in hepatocytes, primarily, primary bile acids - cholic and deoxycholic, which should be considered as a result of a violation of those biochemical processes that carry out their synthesis. These data also indicate a significant inhibition of the functional state of hepatocytes, since all bile acids are synthesized only in hepatocytes from cholesterol [6, 7]. The decrease in cholesterol content in the bile of rats with hepatitis could be a consequence of both the suppression of the cholesterol-forming function of liver cells and the conversion of cholesterol into other compounds, since most of it is ultimately catabolized in this organ [7].

A decrease in the amount of bilirubin in bile in acute hepatitis indicates an inhibition of the conjugating function of the liver, because in hepatocytes, blood bilirubin under the influence of uridine diphosphate glucuronyl transferase is converted into bilirubin glucuronide, and only in this form enters bile [2,5].

Given this, it can be assumed that the activity of the enzyme in acute liver damage is significantly inhibited.

Table 1

**Influence of glyceram on biliary function of the liver with acute toxic hepatitis**

Groups	Bile, ml/100g.4g	Bile acids, mg/100g.4g	Cholesterol, mg/100g.4g	Bilirubin, mkg/100g.4g
Healthy	0,906 ± 0,048	5,71 ± 0,39	0,224 ± 0,028	87,23 ± 6,62

Hepatitis	0,555 ±0,071*	3,22 ±0,31*	0,114 ±0,007*	42,45 ± 4,77*
Hepatitis Glyceram	+0,899 ± 0,051a	4,31 ±0,17	0,179 ± 0,015a	81,94 ± 7,01a
Glyceram Silibor	+0,629±0,057*	3,51±0,41 *	0,154±0,019	48,33±3,79*

Note: \* - statistically significant results compared with healthy animals,  
 a - compared with the untreated group of animals.

The synthesis of bile acids, cholesterol and the conjugation of bilirubin with glucuronic acid is carried out with the direct involvement of the monooxygenase enzyme system (MOS) of hepatocytes [2,5,7]. On this basis, it can be argued that the marked violations of the excretory function of the liver and the chemical composition of bile in acute toxic hepatitis are the result of damage to the cytoplasmic reticulum of hepatocytes in which MOS is localized. This conclusion is consistent with the results of previous studies, which showed inhibition of the functional state of MOS, accompanied by a sharp slowdown in the processes of oxidative demethylation of xenobiotic hydroxylation as a result of a decrease in the content of cytochromes P-450 and B5 of the microsomal fraction in the liver in rats with acute induced carbon tetrachloride [4]. Experimental therapy with glyceram resulted in a distinct elimination of the above changes in the excretory function of the liver and the chemical composition of bile. Thus, in treated rats, compared with untreated rats, the amount of bile secreted during 4 hours of the experiment increases by 62%. It is noteworthy that the volume of bile excreted in experimental rats after 6 days of treatment reaches the level of healthy rats. Positive shifts after the treatment were also noted in the chemical composition of bile. From the data of the table it follows that the content of bile acids cholesterol and bilirubin increases by 34%, 57% and 93%, respectively, after the treatment.

Therefore, experimental therapy with glyceram leads to the elimination of violations of the functional state of the liver, caused by fatty hepatosis.

The results of this work show that the well-known and widely used in hepatology hepatoprotector - silibor has a distinct positive effect on the functional state of the liver during its acute toxic damage. So, after treatment under the influence of this drug, the amount of bile secreted by 4 hours of experience increases by 13.3%, and bile acids, cholesterol and bilirubin, respectively, by 9%, 35.1%) and 14%. However, the values of these indicators do not reach the level of healthy animals, which indicates a lower efficiency of silibor compared to glyceram in correcting violations of the functional state of the liver in its acute chemical damage.

In our opinion, the mechanism of the beneficial effect of glyceram on the functional state of the liver is probably associated with its stimulating effect on MOS, which is associated with the synthesis of bile acids and the processes of bilirubin conjugation.

Given the significant role in the development of toxic liver damage of free radicals [3,11,12,13], which have a cytotoxic effect, leading to tissue hypoxia, hepatocyte necrosis, and endogenous intoxication syndrome, it can be assumed that glyceram also has an antioxidant property. This assumption is consistent with the data

published literature showing high antiphlogogenic activity of derivatives of triterpenoid plants of the genus *Glycyrrhiza* L [9,10,14].

Based on the results of this work and literature data, glyceram can be recommended as a pathogenetic agent in the treatment of inflammatory-destructive liver diseases. The preventive use of this drug in environmentally unfavorable areas allows the prevention of pathologies of the hepatobiliary system.

## Conclusions.

1. Tetrachloromethane in experimental animals causes acute toxic damage to the liver, which

causes a significant inhibition of the functional state of the liver, manifested in a decrease in the excretion of bile and a decrease in bile acids, cholesterol and bilirubin in it.

2. Experimental pharmacotherapy of acute necrotic hepatitis with glyceram to a greater extent than silibor eliminates violations of the excretory function of the liver and the chemical composition of bile.

3. Glyceram can be recommended as an effective prophylactic for correcting violations of the functional state of the hepatobiliary system in its pathologies.

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