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STUDY OF THE EFFECT OF COBALT PHYTATE IN TOXIC LIVER DAMAGE

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Abstract. According to WHO statistics, approximately 2 billion people worldwide currently suffer from liver disease. Therefore, the effectiveness of treatment for hepatobiliary diseases depends on the correct choice of medication, taking into account the mechanisms and etiologies of liver damage and the mechanisms of action of hepatoprotectors.

Key words: Cobalt phytate, silibor, carbon tetrachloride, ALT, AST, GGT, alkaline phosphatase.

Introduction. Over the past decade, there has been a worldwide increase in the incidence of adverse effects and complications from drug therapy, the majority of which are drug-induced liver injury (DILI). This is largely due to liberalized access to medications, as well as aggressive marketing by some pharmaceutical manufacturers. This has resulted in an increase in the incidence of DILI in a wide range of patient groups, including pregnant women.

It is well known that any medication, herbal preparation, or dietary supplement can lead to the development of DILI (5). However, hormonal contraceptives, anabolic steroids, antibacterial drugs, nonsteroidal anti-inflammatory drugs, systemic antifungal drugs, and antituberculosis drugs are the most common culprits (4). A significant proportion of cases of unspecified hepatitis and cirrhosis are also manifestations of DILI. The extraordinary diversity of mechanisms of DILI results in a wide variety of clinical manifestations. Drug therapy for toxic hepatitis should be administered cautiously, with careful monitoring of the patient's general condition and laboratory parameters. Unfortunately, randomized trials are currently lacking that would allow for the development of treatment algorithms for specific types of drug-induced liver injury and the accurate evaluation of the efficacy of hepatoprotectors. Therefore, a pathogenetic approach, adopted for liver injury (1,6), is traditionally used. This includes the use of hepatoprotectors, including essential phospholipids (prescribed only in the absence of cytolysis and cholestasis), UDCA preparations, amino acid derivatives (S-adenosyl L-methionine), and herbal preparations containing bioflavonoids (silibinin). Pathogenetic agents also include glucocorticoids and detoxification therapy agents (Ringer's solutions, dextrans, etc.). It is known that the search for and research into the development of new drugs and their implementation in medical practice are among the applied tasks of pharmacology. It should be noted that despite the multitude of medications used for liver diseases, the need for them remains undiminished. In this regard, the development of new hepatoprotectors, the study of their pharmacological properties, and the improvement of mechanisms for their implementation in practical healthcare are of particular importance. Therefore, the effectiveness of treatment for hepatobiliary diseases depends on the correct choice of medication, taking into account the mechanisms and etiological factors of liver damage and the mechanisms of action of hepatoprotectors (2, 3).

Study Objective. The aim of our study was to investigate the effect of cobalt phytate compared with the hepatoprotector silibor on liver enzymatic activity in experimental hepatitis.

Study Material and Methods. Hepatitis was induced by subcutaneous administration of carbon tetrachloride. Carbon tetrachloride is a known hepatotropic poison, causing toxic hepatitis in vivo, with its wide variety of clinical, biochemical, and morphological changes. Experiments were conducted on white rats weighing 200-250 grams. Hepatitis was induced by subcutaneous administration of a 50% carbon tetrachloride solution at a dose of 1 ml/kg for 4 days. The test drugs were administered orally for 10 days after hepatitis was induced. Cobalt phytate was administered at a dose of 100 mg/kg, and silibor at a dose of 100 mg/kg. The animals were examined daily, and their food intake was recorded. The experimental animals were divided into 4 groups: Group 1 – intact – animals in this group received distilled water orally; Group 2 – control – animals in this group were administered carbon tetrachloride in a 50% solution at a dose of 1 ml/kg; Group 3 – experimental – animals in this group were orally administered cobalt phytate at a dose of 100 mg/kg for 10 days after inducing acute toxic hepatitis; Group 4 – experimental – animals in this group received orally silibor at a dose of 100 mg/kg for 10 days after inducing toxic hepatitis.

To determine the efficacy and mechanism of action of the studied drugs in the carbon tetrachloride-induced toxic hepatitis model, the effects of the drugs were studied:

- on enzyme activities (ALT, AST, GGT, ALP) in the blood serum.

ALT, AST, gamma-glutamyl transferase, and alkaline phosphatase activity were determined using the GIPRESS DIAGNOSTICS test system (Belgium). The data were statistically analyzed using the Student's t-test with the probability of error (P) calculated. A significance level of P = 0.05 was considered statistically significant.

Research results. In liver pathology, the most informative enzymes are those localized in various liver cell structures. Cytoplasmic enzymes are relatively mobile and can be detected in the blood serum even with limited damage to cell membranes. Aminotransferases are organ-specific enzymes that characterize necrotic changes in both the cardiac muscle and liver cells. Changes in ALT and AST activity, markers of hepatocyte cytolysis syndrome under the influence of a hepatotropic poison, indicate profound disturbances in the mitochondria and nuclei of the liver cell and are a key link in the pathogenesis of liver damage. In liver damage, a significant factor is cholestasis, the severity of which is assessed by increased alkaline phosphatase activity, the most sensitive indicator of cholestasis. Based on the above, the effects of drugs on the activity of enzymes such as ALT, AST, GGT, and alkaline phosphatase were studied. The results of the studies showed that in the control series of experimental hepatitis experiments, enzyme activity increased. ALT activity increased by 1.9 times, AST activity by 1.3 times, lactate dehydrogenase activity by 121.1%, gamma-glutamyl transferase activity by 136%, and alkaline phosphatase by 102.1% compared to the intact series. The studied drugs contributed to a decrease in liver enzymatic activity during toxic liver injury.

Table. Effect of cobalt phytate and silibor on enzymatic activity in experimental hepatitis (P = 0.05).

Experimental conditions	ALT µkat/L	AST µkat/L	GGT µkat/L	ALP µkat/L
Intact	0,59+ 0,07	0,76+ 0,06	0,25+ 0,03	3,76+ 0,07
Control	1,14+ 0,14	1,35+ 0,08	0,59+ 0,16	7,6 + 0,19

Hepatitis + Phytate cobalt	0,88+ 0,06	0,83+ 0,04	0,27+ 0,08	4,09+ 0,07
Hepatitis + silibor	0,89+ 0,06	0,82+ 0,02	0,41+ 0,07	4,04+ 0,07

Thus, the results of the conducted studies showed that hepatitis caused by the administration of carbon tetrachloride increases the activity of ALT, AST, GGT, and alkaline phosphatase. Changes in the activity of the studied enzymes under the influence of the hepatotropic poison indicate profound damage to hepatocytes and are one of the important links in the pathogenesis of liver damage caused by this hepatotoxic poison. Cobalt phytate and silibor have a unidirectional effect in acute toxic liver damage, reducing the activity of the studied enzymes.

Discussion of the obtained results. The results of the study showed that in toxic hepatitis caused by the hepatotropic poison, along with a deterioration in the general condition of the experimental animals, liver function is also impaired. We set the objective of investigating enzymatic activity in toxic liver damage. In hepatitis of various etiologies, the activity of enzymes localized in various hepatocyte structures increases in the blood. This provides information on the depth of damage caused by hepatotropic poisons. The reduction in ALT, AST, GGT, and ALP levels in the blood of the study animals under the influence of the test drugs provides information on the membrane-stabilizing effects of cobalt phytate and silibor. All of these positive effects of cobalt phytate are apparently related to the stimulation of key cell membrane components. Inositol, contained in cobalt phytate, is likely involved in the synthesis of phosphatidylinositol, a key component of membrane lipid fractions.

Conclusions. The test drugs improved the general condition and behavior of the animals and prevented lethal outcomes in animals with experimental hepatitis. Cobalt phytate and silibor reduced the activity of ALT and AST transaminases, as well as GGT, LDH, and ALP, the activity of which significantly increases in experimental hepatitis.

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