

Methods of Protection and Correction of Liver Cell Membranes in Xenobiotic Intoxication

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Abstract

This article presents the results of studies examining changes in toxic hepatitis and proposes methods for correcting this pathology. Methods for correcting these disorders using antioxidants, membrane stabilizers, immunomodulators, coenzymes, and other biologically active substances are proposed. The article also presents the results of using these substances in experimental studies.

Keywords: Toxic hepatitis, hepatotropic xenobiotics, heliotrine, biochemical changes, vitamin E, sodium selenite, liposomes.

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1. Introduction

One of the important problems of biological chemistry is the development of molecular mechanisms of pathological processes in the human body. One of the most common diseases in the territory of Uzbekistan is toxic hepatitis, as the widespread use of various chemicals in the food industry and agriculture leads to the growth of toxic forms of hepatitis. Changes in the functions of the liver, kidneys, heart, and lungs in this disease have been extensively studied by researchers at our institute. However, there is still not enough research dedicated to studying changes in the immune-competent organs in toxic hepatitis. There is currently limited data on the effects of various xenobiotics on membrane structure, the intensity of lipid peroxidation processes (LPO), and the mechanisms of damage to immune-competent organs. Information is insufficient on

the relationship between membrane components and the oxidant and antioxidant status of the organs under study. The question of correcting these disorders by the action of antioxidants, membrane stabilizers, immunomodulators, coenzymes, and other biologically active substances is also relevant.

During the biochemical correction of the structure and function of immune organ membranes in intoxication with hepatotropic xenobiotics, we paid attention to the following issues:

Regulation of lipid peroxidation (LPO) disturbances and associated changes in the activity of antioxidant enzymes and carbohydrate metabolism.

Changes associated with the state of phospholipids (FL) and glycolipids (GL) during intoxication with xenobiotics.

In intoxication with heliotrine and CCl₄ in rats, the liver's ability to detoxify toxic substances sharply decreases, LPO increases, the activity of antioxidant enzymes decreases, and the ability of cells to synthesize FL and GL is reduced. Cell membrane permeability is disrupted, leading to the release of cytoplasmic enzymes into the bloodstream. Therefore, correction of the above biochemical changes was carried out using membrane stabilizers, antioxidants, immunomodulators, coenzymes, and other biologically active substances. Liposomes, vitamin E, and sodium selenite were used by us to address these issues, as they possess membrane-stabilizing and antioxidant effects. Rats receiving heliotrine were used as an experimental model for testing therapeutic agents, as this model represents a marginal pathology and allows observation of the dynamics of poisoning and spontaneous restoration of organ structure and function.

The tested therapeutic agents were administered daily for 20 days starting from the 50th day of the experiment. Animal euthanasia was performed on the 70th and 90th days from the beginning of the experiment.

Experiments were conducted on male rats with an initial weight of 120-180 g, which were kept under standard vivarium conditions on a regular diet. The research was divided into 2 series. In the first series of experiments aimed at studying biochemical changes in membranes, two hepatotropic xenobiotics were used: CCl₄ and the alkaloid heliotrine. Rats were intoxicated with CCl₄ by inhalation at a dose of 0.3-0.4 ml per 100 g of body weight for 21 days. The second model was induced in rats by subcutaneous injection of heliotrine using N. Abdulayev's method. Rats receiving a physiological solution served as controls. Animals were euthanized on the 50th and 70th days of the experiment. The selection of these time periods was motivated by the investigation of certain mechanisms underlying the development of biochemical and immunological changes upon heliotrine intoxication (2,4).

In the second series of experiments on the model of heliotrine hepatitis (139 rats), we tested the efficacy of the drugs we used to correct the identified biochemical shifts.

The research on correcting pathochemical processes in the liver and immune system organs of experimental animals during xenobiotic intoxication was conducted in four directions:

- ✓ Study of the effect of vitamin E (100 mg/kg) on the parameters under investigation;

- ✓ Investigation of the effect of sodium selenite (40 µg/kg) on the parameters under investigation;
- ✓ Study of the effect of liposomes (250 µg/kg) on the parameters under investigation.

The influence on the investigated parameters of liposomes containing vitamin E and sodium selenite, which contained 250 µg of liposomes, 100 µg of vitamin E, and 40 µg of sodium selenite per 1 kg of animal body weight, was assessed. The tested drugs were administered daily for 20 days starting from the 50th day of the experiment. Animal euthanasia was conducted on the 70th and 90th days from the beginning of the experiment. Liver, spleen, and thymus were used for biochemical studies.

The table presents the results of the studies on the effect of the tested drugs on the general condition, mortality rate, and average lifespan of the experimental rats receiving heliotrine. As indicated by the data in the table, on the 50th day of the study (before treatment), the weight of the rats ranged from 114.8 to 139.5 g, indicating an increase in weight by 8-14 g, while in the control group II, the weight increased by 43 g. After the administration of the drugs on the 70th day of the study (20 days after the administration of the drugs), the weight of the animals increased by 28-38 g and ranged within 160.1-167.9 g. The weight of the animals in control group I decreased by 8 g on average and was 106.3 g.

The liver weight in rats euthanized on the 70th day in control group I was 5%, while in the experimental group, it was 3.0-4.0% of the body weight, respectively. Similar differences were observed in the spleen weight. On the 90th day of the study, the weight gain of rats in the experimental group averaged 65-76 g, while in control group I, it was 6 g. The liver weight in control group I at this time point of the study was 5.2%, and the spleen weight was 0.9%, while in the experimental group, it was 3.9-4.0% and 0.41-0.53% of the total body weight, respectively.

During the experiment, out of 37 rats in control group I receiving heliotrine and physiological saline, 12 animals died (39.8%) by the end of the experiment (90th day), with an average lifespan of 64.3 days. In the experimental group of 133 rats, 23 rats died during the experiment, with an average lifespan of 68-74.3 days. The mortality rate averaged 12-20%.

Thus, upon administration of the tested drugs to rats receiving heliotrine throughout the study period, an increase in body weight was observed. Along with this, there was a decrease in the mortality rate of animals and an increase in

the average lifespan of rats compared to control group I. The most pronounced changes were observed in animals receiving the entire complex of tested drugs.

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