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THE STUDY OF THE HEPATOPROTECTIVE EFFECT OF ANACARDIC ACID IN A CARBON TETRACHLORIDE-INDUCED HEPATITIS MODEL

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Abstract. This study explores the hepatoprotective effects of anacardic acid, a polyphenolic compound, in a rat model of acute liver injury induced by carbon tetrachloride (CCl_4). Given the increasing exposure to hepatotoxic xenobiotics from household, industrial, and agricultural chemicals, the development of effective and multi-targeted hepatoprotective agents is critical. The experiment was conducted in compliance with international animal ethics guidelines using Wistar rats. The research assessed various doses of anacardic acid administered both orally and intraperitoneally. Biochemical markers such as ALT, total protein, diene conjugates, and malondialdehyde (MDA) levels were measured to evaluate liver function and oxidative stress. The findings demonstrated that anacardic acid, particularly at a dose of 5 mg/kg administered intraperitoneally, significantly mitigated liver damage, restored biochemical parameters, and showed comparable efficacy to the standard hepatoprotective agent Karsil. These results suggest that anacardic acid possesses promising hepatoprotective properties and warrants further investigation as a potential therapeutic agent for hepatobiliary pathologies.

Keywords: Anacardic acid, hepatotoxicity, carbon tetrachloride (CCl_4), hepatoprotection, oxidative stress, liver enzymes, polyphenols, ALT, MDA, rats, acute liver injury.

Introduction. Toxic liver damage is one of the most common etiological factors of hepatobiliary pathology. It is associated with a significant increase in exposure to hepatotoxic xenobiotics, including household, industrial, and agricultural chemicals. These exogenous factors not only have specific mechanisms of action but also initiate a universal and potent endogenous mechanism of hepatocyte damage in the form of oxidative stress [6]. The byproducts of this process—aggressive and numerous reactive oxygen species (ROS)—lead to metabolic disorders, membranopathies, functional impairments, mutations, accelerated apoptosis, and other forms of cellular pathology.

Moreover, the multifactorial nature of toxic liver injury requires hepatoprotective agents to provide multi-level protection, which is currently exhibited by only a limited number of

hepatoprotectors (e.g., Legalon, Silybor, Hepaton) [5]. A characteristic feature of modern hepatoprotective agents is their origin from plant-based raw materials and their content of polyphenolic compounds with antioxidant activity, such as flavonoids, flavolignans, cinnamic acids, and others [2].

Materials and Methods. The study was conducted on 240 mature male and female Wistar rats weighing between 170–280 grams, in accordance with the international recommendations of the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes [1]. Acute liver injury was induced by administering a 50% solution of carbon tetrachloride (CCl_4) orally using a metal atraumatic probe [7].

In the experiments, the polyphenol *anacardine* under investigation was administered using oral and intraperitoneal routes. The polyphenol was given orally at doses of 100, 300, and 500 mg/kg twice daily for 12 days via gastric intubation. Additionally, it was administered intraperitoneally at doses of 5, 15, and 25 mg/kg twice daily for 12 days.

It should be noted that the tested polyphenol was administered for 5 days prior to the introduction of carbon tetrachloride, and then concurrently with it for 7 days—specifically, 1 hour before each administration of CCl_4 [3,7].

The acute toxicity of the studied drug was assessed in accordance with methodological guidelines for evaluating the general toxic effects of pharmacological agents. The experiment was conducted based on the method of V.V. Gatsura. After 14 days of administering the investigated preparation to animals with carbon tetrachloride-induced liver damage, sodium etaminal was injected intraperitoneally at a dose of 40 mg/kg. The duration of sleep (in lateral position) was recorded in minutes. Statistical results were processed and expressed as the arithmetic mean (M) and its standard error (m).

Sodium etaminal and the studied polyphenolic compound *anacardin* were administered orally in different doses (100, 300, and 500 mg/kg), as well as intraperitoneally in doses of 5, 15, and 125 mg/kg. The assessment was performed under acute toxic liver injury conditions induced by carbon tetrachloride, and sodium etaminal was administered intraperitoneally at a dose of 40 mg/kg on the 14th day of compound administration [6]. Control animals received the same volume of purified water.

According to the obtained results, compared to the control group, administration of anacardin led to a significant and reliable reduction in sleep duration — particularly by 55.7% at a dose of 100 mg/kg.

Results. The observed reduction in sodium etaminal-induced sleep duration during administration of the test compounds is likely due to the hepatoprotective effect, which preserves the activity of the hepatic microsomal system responsible for catalyzing biotransformation reactions of xenobiotics, mediated by endoplasmic reticulum enzymes of the cytochrome P450 system.

Our study focused on determining the optimal therapeutic dose of the investigated compound that would normalize altered biochemical parameters in hepatocytes under conditions of carbon tetrachloride-induced liver damage. To achieve this goal, the contribution of the compound was evaluated based on its ability to normalize reduced total protein levels and elevated ALT enzyme activity, both of which are typical markers observed during hepatocellular cytolysis.

In our experiments, we first determined the levels of diene conjugates. The concentration of diene conjugates was expressed in μmol/L. Carbon tetrachloride (CCl_4) poisoning disrupted all liver

functions: protein-synthetic activity (total protein content decreased by 27.2%), and severe hepatocyte damage was observed through increases in serum diene conjugates and malondialdehyde (MDA), a thiobarbituric acid-reactive substance (TBARS), by 41.2% and 175.1%, respectively, compared to the intact animal group.

When anacardine was administered orally at a dose of 100 mg/kg, levels of primary LPO products (diene conjugates), final LPO products (TBARS, including MDA), and total protein in serum remained significantly elevated compared to the intact control — 109.9%, 145.2%, and 88.5%, respectively.

At a dose of 300 mg/kg, compared to 100 mg/kg, administration of anacardine resulted in a significant reduction in serum diene conjugates and TBARS, with levels decreasing by 10.2% and increasing by 20.6%, respectively, compared to control.

These results clearly show that CCl_4 intoxication disrupted all hepatic functions: protein synthesis (with total protein decreasing by 26.2%), and caused severe hepatocellular damage, indicated by increases in serum diene conjugates and MDA by 41.2% and 175.1%, respectively, compared to the intact animal group.

General indicators, including survival rate, detailed biochemical analyses of blood serum and liver, and data calculated based on the hepatoprotection coefficient, suggest that an intraperitoneal dose of 5 mg/kg of anacardine may be recommended as an effective therapeutic dose.

Conclusion. In carbon tetrachloride-induced hepatitis models, comparison of anacardine's hepatoprotective effect with Karsil showed a reduction in serum diene conjugates (by 49%) and TBARS levels in serum (by 36.4%) and liver (by 41.7%) compared to the control group. Increased activity of ALT and decreased total protein levels, which are indicative of cytolysis, were also normalized under the influence of the administered preparation.

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