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THE EFFECT OF WHITE MILK THISTLE (SILYBUM MARIANUM L. GAERTN.) SEED EXTRACT (IN COMPARISON WITH “METADOXIL” AND “TETURAM” DRUGS) ON CHANGES IN AMINOTRANSFERASE ACTIVITY IN RAT BLOOD SERUM UNDER CHRONIC ALCOHOL INTOXICATION

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Relevance of the topic. According to World Health Organization statistics, more than 3,000,000 people worldwide currently die directly or indirectly as a result of alcoholism each year on average, and the steady increase of this indicator is considered a serious medical and socio-economic problem; accordingly, developing new therapeutic and preventive approaches in this field and creating effective new-generation pharmacological drugs is of urgent importance [Mathurin et al., 2012; pp. 399-420].

In particular, interest in using substances isolated from medicinal plant species is growing in the treatment and prevention of various diseases, including liver diseases caused by alcohol, due to their economic advantages as well as the absence or low degree of additional adverse effects compared to synthetic drugs [Javed et al., 2018; pp. 1-9].

In particular, with the aim of restoring the structural-functional activity of the liver in alcohol intoxication, certain biologically active substances contained in the vegetative organs of the white milk thistle (*Silybum marianum* L. Gaertn.) plant have been identified [Evdokimov and Chekhlaty, 2015; p. 111].

The purpose of this study was to analyze the effect of local white milk thistle (*Silybum marianum* L. Gaertn.) seed extract (in comparison with “Metadoxil” and “Teturam” drugs) on changes in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) activity in rat blood serum under chronic alcohol intoxication.

Object and conditions of the study. The research was carried out in 2026 at the laboratory of the Republican Children’s Infectious Diseases Hospital, a specialized medical institution located in Nukus city (Republic of Karakalpakstan, Nukus city, K. Ayimbetov street, house 33, Guliston MFY area), under the Ministry of Higher Education, Science and Innovations of the Republic of Uzbekistan, Berdakh Karakalpak State University. The object of the study was substances with a broad spectrum of pharmacological activity isolated from the vegetative/generative organs of white milk thistle (*Silybum marianum* L. Gaertn.) — saponins, flavolignans, terpenoids, polyphenolic compounds, flavonoids, essential oils (0.1%), macro- and microelements, and vitamins (A, B, D, E, K), which have long been used



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in traditional Eastern and Chinese medicine to treat various diseases, including liver diseases [Demirci et al., 2014; pp. 453-457].

In the studies, white milk thistle (*Silybum marianum* L. Gaertn.) seeds ($m=200$ g) were incubated in a thermostat at $+60\pm0.5^{\circ}\text{C}$ for 48 hours, then mechanically ground. The ground powder material was extracted in a 250 ml glass flask with an ethanol solution (80%) for 48 hours, then evaporated at $+50\pm0.5^{\circ}\text{C}$ using a rotary evaporator RE100-Pro (Beijing Zetron Technology Co., Ltd., PRC), and the resulting extract was used in the studies [Adekunle et al., 2023; pp. 157-164].

For comparison purposes, “Metadoxil” (Metadoxine) (Doppel Farmaceutici SrL, Italy) (main component — metadoxine L-proline, 5-oxo-, 5-hydroxy-6-methylpyridine-3,4-dimethanol (1:1) $\text{C}_{13}\text{H}_{18}\text{N}_2\text{O}_6$ ($\text{Mr}=298.295 \text{ g}\times\text{mol}^{-1}$)), used in clinical practice for the treatment of alcoholism, and “Teturam” (Disulfiram) (Pharmstandard JSC, Russian Federation) (Tetraethylthiuram disulfide — $\text{C}_{10}\text{H}_{20}\text{N}_2\text{S}_4$ ($\text{Mr}=296.54 \text{ g}\times\text{mol}^{-1}$)) were used.

In the experiments, white, non-pedigree rats (*Rattus norvegicus*; ♀/♂, aged 5-25 days, $m=20-35$ g, and aged 60-80 days, $m=160-220$ g) were used, kept under standard conditions (room temperature $+20\pm5^{\circ}\text{C}$, relative humidity $75\pm10\%$, light regime 12:12 hours) with standard food (water) at the vivarium of the Karakalpakstan Republic Branch of the Republican Center for Plague Control (Nukus city, M. Jumanazarov street, house 65) and the Karakalpakstan Republic Laboratory for Animal Disease Diagnostics and Food Safety (Nukus city, Qala street, house 1).

International bioethical requirements were followed when working with experimental animals, in accordance with the rules developed by the Council for International Organizations of Medical Sciences (CIOMS, 1985) and the European Convention for the Protection of Vertebrate Animals used for Experimental and other Scientific Purposes (Strasbourg, 1986) [Motuziuk et al., 2024; pp. 1-15].

In the experiments, before the dislocation decapitation process, rats (*Rattus norvegicus*) were anesthetized by injecting a sodium thiopental solution (20 ml/ml) (“Sintez” JSC, Russian Federation) at a dose of 150 mg/kg via the tail vein [Costa et al., 2024; pp. 81-88].

The experimental model of chronic alcohol intoxication was induced in rats by orally administering “Qarataw” vodka (45% ethanol solution) at a dose of 2 ml/kg body weight, twice daily, for 7 days. In the control group, rats received distilled water in an amount equivalent to the ethanol solution used.

Analysis of certain biochemical parameters of blood (ALT, AST) in the experimental animals was carried out in 2026 at the laboratory of the Republican Children’s Infectious Diseases Hospital, a specialized medical institution located in Nukus city (Republic of Karakalpakstan, Nukus city, K. Ayimbetov street, house 33, Guliston MFY area), using a test kit (“Human Gesellschaft für Biochemica und Diagnostica” mbH, Germany) and a BA-88A semi-automatic biochemical analyzer device (“Mindray”, China) [Rostami et al., 2025; pp. 426-437].



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The De Ritis coefficient (AST/ALT) was analyzed to assess changes in aminotransferase activity in blood serum [Markiewicz-Gorka et al., 2011; pp. 1811-1827]. During decapitation, a peripheral blood sample (3 ml) was taken from the animal's tail vein using a medical syringe, placed into hermetically sealed special plastic vials containing heparin (2 ml) and Trilon-B solution (1.25%) (to prevent coagulation of the blood test sample), then centrifuged for 10 minutes at 3,500 rpm at $t=+24\pm0.5^{\circ}\text{C}$ using a DM0412 centrifuge (DLAB Scientific Co. Ltd, PRC), and the blood serum was separated and stored in a freezer at $t=-20\pm0.5^{\circ}\text{C}$ for subsequent analyses (ALT, AST).

Mathematical-statistical processing of the obtained experimental results was carried out using standard methods with the help of "Microsoft Excel 2007" (Microsoft, USA) and OriginPro v. 8.5 SR1 (EULA, USA) software packages. The results of experiments performed with $n=3-5$ repetitions are presented as $M\pm m$, where M represents the arithmetic mean value and m represents the standard error value. Additionally, the statistical reliability level of the differences between the experimental results and the control group was calculated based on Student's t -test, and values of $p<0.05$ and $p<0.01$ were considered statistically reliable. The reliability level of the difference between the values of the two experimental groups was calculated according to Student's criterion [Plokhinsky, 1970; pp. 20-367].

Results and their analysis. Thus, in the 5-25 day physiological age group, a significant increase in transaminase activity was observed in rat blood serum under the influence of chronic alcohol intoxication, including an increase in ALT activity by 63.78% (1.64-fold) and AST activity by 145.73% (2.46-fold) relative to control, with the De Ritis coefficient changing from 1.19 ± 0.02 to 1.79 ± 0.03 ; this condition is explained by the emergence of structural-functional disorders in hepatocytes under alcohol intoxication. Additionally, in the 60-80 day physiological age group, a significantly greater difference in changes in ALT and AST activity was observed under chronic alcohol intoxication compared to young rats (5-25 days); in particular, ALT activity increased by 79.46% (1.79-fold) and AST activity by 185.61% (2.87-fold) relative to control, with the De Ritis coefficient increasing from 1.27 ± 0.05 to 2.02 ± 0.04 . This condition indicates that dysfunctional changes in hepatocytes occur at a relatively higher level in older animals under alcohol intoxication. When the "Teturam" (Disulfiram) drug (250 mg/kg) was administered, the dynamics of changes in transaminase activity against the background of alcohol intoxication were even more pronounced in the negative direction, and it was found that the increase in AST activity in the 60-80 day physiological age group was more pronounced than in the 5-25 day physiological age group. Under the influence of "Metadoxil" (250 mg/kg), in 5-25 day rats with alcohol intoxication, ALT activity decreased by 21.81%, AST activity by 37.57%, and the De Ritis coefficient by 20.11%; in the 60-80 day group, these indicators decreased by 15.42%, 43.98%, and 33.66%, respectively, and the hepatoprotective effect of "Metadoxil" was noted to be more pronounced in older rats. Under the influence of white milk thistle (*Silybum marianum* L. Gaertn.) seed extract (250 mg/kg), in 5-25 day rats, ALT activity decreased by 32.09% (1.47-fold), AST activity by 53.04% (2.13-fold), and the De Ritis coefficient by 31.28% (1.46-fold) relative to alcohol intoxication; in the 60-80 day group,



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ALT activity decreased by 34.07% (1.52-fold), AST activity by 57.74% (2.37-fold), and the De Ritis coefficient by 36.14% (1.57-fold). The analysis of the obtained results confirmed that white milk thistle (*Silybum marianum* L. Gaertn.) seed extract possesses hepatoprotective activity in alcohol intoxication, optimizes aminotransferase activity, and shows a relatively more effective therapeutic effect in older animals.

CONCLUSION

The obtained results can be used as a scientific basis for developing effective hepatoprotective agents based on white milk thistle (*Silybum marianum* L. Gaertn.) seed extract for alcohol intoxication.

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