International Journal of Communication Networks and Information Security
2024, 16(4)
ISSN: 2073-607X,2076-0930
https://ijcnis.org/

Research Article

ROLE OF DOMESTIC AMINO ACID BLOOD SUBSTITUTE ON METABOLIC DISORDERS AND ENDOGENOUS INTOXICATION IN EXPERIMENTAL TOXIC HEPATITIS

Zukhra Sayfutdinova - Associate Professor, Department of Hematology, Transfusiology and Laboratory, Tashkent Medical Academy, Tashkent, Uzbekistan
Dilafruz Akhmedova - Associate Professor, Department of Normal and Pathological Physiology, Tashkent Medical Academy, Tashkent, Uzbekistan
Sevara Azimova - Professor, Department of Normal and Pathological Physiology, Tashkent Medical Academy, Tashkent, Uzbekistan
Zumrad Kurbonova - Associate Professor, Department of Hematology, Transfusiology and Laboratory, Tashkent Medical Academy, Tashkent, Uzbekistan
Sayyora Akhmedova - Associate Professor, Department of Human Anatomy, Operative Surgery and Topographic Anatomy, Tashkent Medical Academy, Tashkent, Uzbekistan

ARTICLE INFO
Received: 18 Aug 2024
Accepted: 30 sep 2024

ABSTRACT

The development of effective agents to correct metabolic balance in critical illness is critical for the successful treatment of serious diseases. Critical conditions such as trauma, poisoning, burns, sepsis and surgery, as well as diseases such as acute infections and cancer, can lead to increased breakdown of substances and increased catabolism. Poor nutrition can lead to weight loss, poor physical performance, and metabolic disorders. Amino acid mixtures are the best way to influence metabolic homeostasis, since protein synthesis occurs only from free amino acids. They are widely used in medical practice, including for parenteral nutrition. The RGNPMCG of the Ministry of Health of the Republic of Uzbekistan has developed a new blood substitute containing amino acids and an antioxidant complex, which has a wide spectrum of action and is able to influence protein synthesis by body cells, optimize the functioning of physiological systems, and accelerate recovery processes in severe diseases associated with impaired protein -energy metabolism. The purpose of this study is to study the impact and evaluate the effectiveness of a new domestic amino acid blood substitute on metabolic disorders and endogenous intoxication in toxic hepatitis.

Keywords*:* pathology, amino acid metabolism disorder, liver cirrhosis, fatty hepatosis, blood substitute, morphometry

Introduction

The problem of developing new, modern and effective means for correcting metabolic balance in critical conditions remains relevant. The success of treating serious diseases of various nature largely depends on solving this problem.

Modern ideas about the metabolic response in critical conditions and understanding of the mechanisms of metabolic disorders determine the need to use substances that can affect metabolic balance and the cellular energy-generating system [1; 2; 3].

Stressful situations, such as injuries, poisoning, burns, sepsis and surgical interventions, as well as some diseases, such as acute infections, cancer and others, lead to increased destruction of substances and increased catabolism. Malnutrition is a pathological condition caused by an imbalance in the supply and consumption of nutrients, which leads to loss of body weight, changes in body composition, deterioration in physical performance and metabolic disorders, as well as immune and endocrine

functions [4-6]. With a lack of nutrition, the body begins to use up fat reserves, then glycogen reserves in the liver and muscles, and then proteins in muscles and organs. This leads to a decrease in the content of total protein and albumin in the blood, atrophy of muscles and organs. Depending on the severity of the pathological process, 75-150 g of protein per day are destroyed in the body [7].

Even in the compensation stage, the destruction of proteins leads to a deficiency of essential amino acids and a negative nitrogen balance [8-10]. As a result of protein deficiency, dysfunction of organs and systems, delayed healing, disruption of reparative processes, a decrease in the body's defenses, and anemia often occur [4, 11]. Depletion of proteins up to 30-35% of the total protein pool in the patient's body can lead to death.

Various pathological changes in the body lead to changes at the molecular level and disrupt the processes of protein biosynthesis. This creates a need for correction of these important processes. One of the main directions of new, more advanced methods of regulating homeostasis is their ability to eliminate the pathology of metabolism (energy, plastic), water-electrolyte and acid-base balance, microcirculation disorders and other disorders of the homeostasis system. They are also capable of protecting cellular structures from oxidation by peroxide and free radicals, as well as supporting the functioning of vital organs and systems of the body during the treatment of various pathological conditions. To eliminate disturbances in the homeostasis system in severe diseases of various etiologies, the development of multicomponent correction agents as part of intensive care is promising [7, 12].

Mixtures of pure amino acids, formulated according to specific recipes, are the best means for influencing metabolic homeostasis, since protein synthesis occurs only from free amino acids. Nitrogenous preparations used for parenteral nutrition contain all necessary amino acids in sufficient quantities, including non-essential nitrogen such as glycine and others [13, 14].

The advantage of amino acid mixtures over protein hydrolysates clearly lies in their easy control over the composition of amino acids, the absence of humic substances, ammonia and other undesirable components. Many years of experience in the use of amino acid preparations as a basic method of intensive therapy to eliminate disturbances of water-electrolyte and protein metabolism, prevention and treatment of multiple organ failure, has confirmed their high effectiveness in the complex treatment of serious diseases of various etiologies. Total parenteral nutrition (TPN) is recommended for patients who cannot obtain the required amount of nutrients naturally or through the digestive system. This primarily applies to patients in critical condition and those for whom natural nutrition is contraindicated for some reason [15]. Modern advances in the field of PPP make it possible to widely use this method not only for the correction of nutritional deficiency in functional disorders of the gastrointestinal tract, cachexia, but also for long-term support of the nutritional state in patients with brain lesions (coma, hemorrhages), somatic, oncological, mental or infectious diseases , as well as in patients receiving aggressive treatment methods (chemo- and radiation therapy, etc.).

One of the criteria for the effectiveness of parenteral nutrition in critical conditions is maintaining protein metabolism at the proper level to reduce the hypercatabolic reaction of the body and ensure plastic processes. Currently, drugs containing a balanced ratio of essential and non-essential amino acids are widely used in medical practice, such as Infezol 40, Infezol 100 (Berlin-Chemie, Germany), Aminoplasmal E - 5%, 10% (B. Braun, Germany), Aminosol – 600, 800, KE (Hemofarm , Yugoslavia) [16, 17].

These preparations meet the basic requirements for modern amino acid solutions, although there are some differences in their compositions. At the moment, there are no data on the selection criteria and comparative clinical effectiveness of these drugs in intensive care of critical illnesses. Obviously, in clinical practice, preference should be given to amino acid solutions containing antioxidants that have the best pharmacological properties. Recently, much attention has been paid to bioenergetic antioxidant complexes, which can affect metabolism in cells and have a positive effect on the body as a whole [18] . The correct use of amino acid solutions and the development of an effective parenteral nutrition program are an important task for doctors. However, the high cost of foreign drugs limits their widespread use in medicine. In this regard, the development of domestic, more advanced means of correcting homeostasis in the field of metabolism is of significant importance. This will be a significant contribution to the development of domestic medicine [19-22].

In RSNPMCG Ministry of Health of the Republic of Uzbekistan a new blood substitute containing amino acids and an antioxidant complex was developed. This drug has a wide spectrum of action, which includes influencing protein synthesis by the body's cells, mobilizing energy and plastic resources, optimizing the functioning of physiological systems, as well as accelerating recovery processes in severe diseases of various etiologies associated with disorders of protein -energy metabolism.

Purpose of the research

The purpose of the studyis to study the influence and evaluate the effectiveness of a new domestic amino acid blood substitute on metabolic disorders and endogenous intoxication in toxic hepatitis.

Materials and Methods

The study was conducted at the Central Research Laboratory of the Tashkent Medical Academy. The study was conducted prospectivelyrandomized method. The experiments used 100 mature rats of both sexes weighing 220-250 g. The maintenance of animals, surgical intervention and withdrawal from the experiment were carried out in accordance with the ethical principles proclaimed by the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Purposes. The animals were kept in a vivarium, with free access to food and water and a spontaneous change of day and night. The experiments were carried out under conditions of spontaneous breathing and an ambient temperature of 24-25°C.

Anesthesia was provided by intraperitoneal injection of Nembutal 45 mg/kg. For invasive monitoring of hemodynamics, blood collection and transfusion, as well as administration of the study infusion , a tail catheter was installed at the beginning of the experiment.

Catheters were placed in the tail artery and vein. Catheterization was carried out as follows: The vascular bundles were divided and ligatures were applied above and below the planned catheter insertion site.

The experiment was divided into several phases:

1.initial condition. The animals were anesthetized, under local anesthesia with 2% - 1 ml of novocaine solution, catheters were installed in the vessels and blood was taken for testing.

2.single subcutaneous injection of heliotrine (25 mg/100 g) to obtain a model of toxic hepatitis.

3.withdrawal from the experiment 1 and 3 days after poisoning by intravenous administration of 150 mg/kg Nembutal , followed by blood sampling for laboratory analysis; On days 1 and 3, 30 animals each from the control and experimental groups were removed from the experiment and blood was taken for laboratory analysis. On days 1 and 3 after heliotrine intoxication , internal organs were taken from 12 animals from the control and experimental systems for morphological examination.

Acute intoxication with heliotrinewas reproduced by a single subcutaneous injection of a sublethal dose of heliotrine to rats , prepared at the rate of 40 mg per 100 g of body weight. The starting material was venous blood. The animals were divided into equal groups:

Group I - before reproducing heliotrine intoxication (intact)

Group II (control) - with heliotrine poisoning

Group III (control, comparison) - with heliotrine poisoning after administration of the comparison drug "Infezol40", for 5 days, 24 hours after the last injection;

Group IV (main, experimental) - animals with heliotrine poisoning after the introduction of a new amino acid blood substitute, within 24 hours, 5 days after the last administration.

Histological and morphological research methodswere carried out at the Pathological Center of the Republic of Uzbekistan.

Light optical microscopy was performed on histological liver samples fixed in a 10% solution of neutral formalin for 72 hours, followed by dehydration in concentrated alcohol and embedding in paraffin.

Sections 7 μm thick were prepared on a Leica SM 2000R microtome and stained with hematoxin .

To observe the sample and record images in 10 fields of view, a microvisor μVizo-103 (JSC LOMO, Russia) was used. The following parameters were examined in liver samples: diameter of the sinuses, diameter and cross-sectional area of the arteries, diameter and cross- sectional area of the venous vessels, diameter and cross-sectional area of the central vein.

Results and its Discussion

In our studies, we assessed the general manifestations of intoxication.

An experimental model of heliotrine liver damage recreates characteristic morphological and functional changes similar to infectious toxic hepatitis, ultimately leading to the development of cirrhosis. The choice of this model was determined by several factors. First, in the past, alkaloids from the heliotrine weed have caused similar liver damage in humans, often leading to cirrhosis. Secondly, numerous experiments using this model have shown that chronic exposure to heliotrine in rats reproduces all stages of the development of post-necrotic cirrhosis, resulting in a typical transformation of the liver structure. Some evidence suggests that even a single intraperitoneal injection of an alkaloid can, after some time, lead to the development of cirrhosis of varying severity.

In most cases, acute toxic liver failure was detected within 1-3 days after the start of exposure. After conducting a control liver biopsy in 30 animals, all of which were injected with heliotrine at various periods of time and its administration was stopped, 19 were found to have a progression of the process over a certain period of time. 5 days after stopping the administration of the alkaloid, the development of active mixed cirrhosis of the liver was clinically and histologically confirmed.

Thus, the model of heliotrine cirrhosis reflects one of the characteristic manifestations of such a disease in humans - the possibility of disease progression after the cessation of the etiological factor. Further study of the immunopathology of this condition confirmed the participation of autoimmune mechanisms in the development of heliotrine hepatitis and liver cirrhosis.

From studies conducted using heliotrine extract pubescent plant, it was found that in addition to heliotrine and lasiocarpine , which are the main alkaloids, it also contains saponins, heliotrine N-oxide , lasiocarpine N-oxide and other derivatives. It turns out that these substances cause significant changes in hemodynamics, which leads to disturbances in the functioning of the organ and the occurrence of pathology. A single administration of the alkaloid in animals was accompanied by high mortality (20-25%), especially on the second day.

When opening the abdominal cavity, a large amount of ascitic fluid of a dark purple color and a dense and dark brown liver were discovered. Morphological studies showed that under the influence of heliotrine , the liver decreased in size and had a nutmeg-shaped section with hemorrhagic areas. Under a microscope, destruction of the walls of the central veins and capillaries with their sharp thickening was discovered. In some cases, the walls of blood vessels in the central parts of the lobules were practically indistinguishable. There is also a gradual thinning of the trabecular structure towards the center of the lobules and the disappearance of Kupffer cells. The formation of obstacles to the blood flow of the portal vein in the center of the lobules (thrombosis is common) plays a decisive role in the development of this pathology.

Evaluation of histological parameters in heliotrine toxic hepatitis

Acute intoxication with heliotrine was carried out by a single administration of a sublethal dose of the alkaloid to rats for one day.

Acute hepatitis caused by heliotrine is characterized by the appearance of liquefaction necrosis, protein and fatty degeneration of hepatocytes , mainly localized in the central zone of the hepatic lobule, where the greatest activity of monooxygenases dependent on cytochrome P450 and damaging hepatotoxin metabolites is manifested . Macroscopically , the liver is enlarged in size, dense to the touch, and has a rounded edge.

Acute intoxication with heliotrine was carried out by a single administration of a sublethal dose of the alkaloid to rats for one day.

Evaluation of histological parameters in heliotrintoxic hepatitis

Acute heliotrine intoxication was caused by a single administration of a low dose of heliotrine to rats for 1 day. Acute toxic hepatitis (ATH), caused by heliotrine , was characterized by the development of liquefaction necrosis of protein and fatty hepatocytes , located mainly in the central zone of the hepatic lobule, where the activity and dominance of cytochrome P450-dependent monooxygenases is very high, producing harmful hepatotoxin metabolites . Macroscopically, the liver is enlarged, compact, the edge is rounded (Fig. 1, Fig. 2).

Acute heliotrine intoxication was caused by a single administration of a low dose of heliotrine to rats for 1 day.

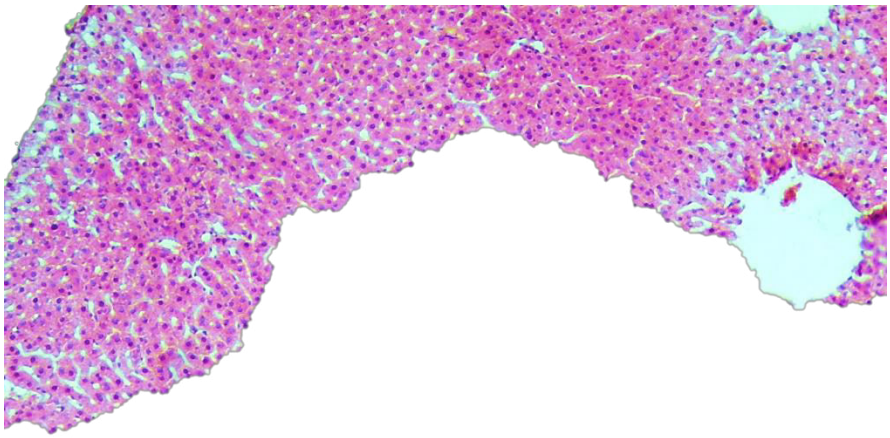

Figure 1. Morphology of the liver of rats fed a nutritious diet under normal conditions.

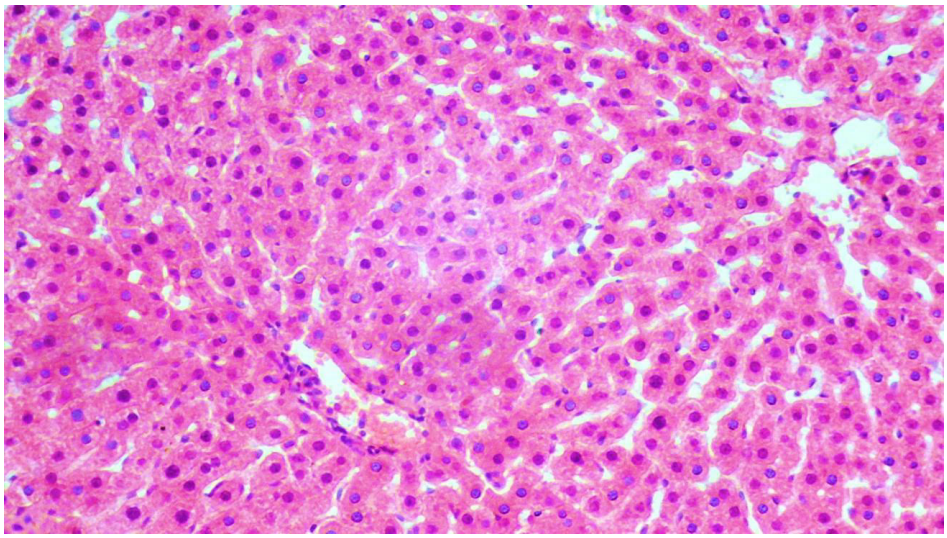

Figure 2. Liver tissue. Central artery. Hepatocytes are arranged in a columnar line, the cytoplasm is the same color. In hepatocytes, the nuclei are located in the center. Sinusoidal intervals of approximately equal width. Kupffer cells are detected . The distal cavities have the same width. Color: GE. 10x40.

With heliotrine hepatitis, a complex of several pathological processes occurs in the liver tissue. There is a slight morphological increase in the liver tissue, rounding of the edges, and liver consistency. Microscopically, the liver pieces are slightly enlarged. Sinusoidal cavities have different diameters, are enlarged near necrotic ones hepatocytes and are phagocytosed by macrophages (Fig. 3.). Some changes are also observed in the endothelial cells that form the wall of the sinusoids . There is increased transendothelial breakdown and accumulation of basophilic bodies around the wall. The contours of Kupffer cells are clearly enlarged, the distal spaces are expanded. It is found that at a size of 100x10, Ito cells are activated and form tumors facing the adjacent sinusoidal pores (if the test continues for 20 days, we see that the Ito cells have changed. Which leads to fibrogenesis and fibrosis of the liver). Foci of collicative necrosis are found in several hepatocytes with edematous degeneration. In the cytoplasm of hepatocytes, the development of acidophilic colored protein cells and hydropic dystrophies that form at different levels. In the cytoplasm of hepatocytes, the development of fat breakdown in the form of droplets of various levels is detected. The shape of the liver sections is not changed, many sinusoidal cavities are enlarged, necrosis and paranecrosis associated with the periphery are found in the hepatocytes around the central vein. In a field of view of 10x10 there are only 1-3 hepatocytes with 2 nuclei. Mitotic foci are found in 1-2 cells. Healthy hepatocytes surrounding necrotic hepatocyte ,increase in size. The cytoplasm of hepatocytes underwent plasmorexis , the nuclei - karyorrhexis and karyolysis .

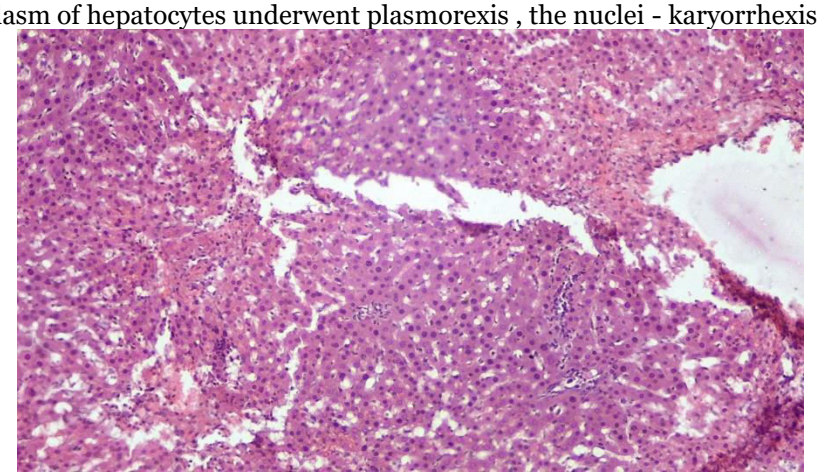

Figure 3. General view of liver tissue in acute heliotrine hepatitis. In general, most sinusoidal spaces are enlarged in various ways. The predominant structure of hepatocytes is disrupted . Outbreaks of fatty degeneration are detected in hepatocytes . Foci of leukocyte infiltration are detected in clusters and cavities of small basophilic bodies around the sinusoidal wall. Staining G-E. 4x10.

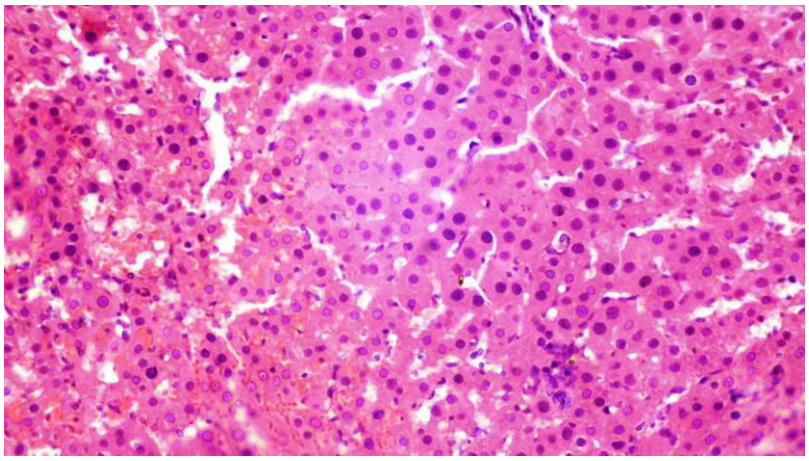

Figure 4. Liver tissue in acute heliotrine hepatitis. Destructive-destructive-necrotically altered hepatocytes . Enlarged sinusoidal spaces. Poorly developed neutrophil infiltration. Dye G-E. 20x10.

of hepatocytes were detected , especially pronounced in the central part of the lobule (Fig. 4). Cellular proliferation and infiltration reactions in the first destructive phase of the disease are weakly expressed. Lobular swelling associated with toxic damage to the capillary wall was also detected. In some places, the edema is moderate, leading to an expansion of the space between the trabeculae and capillaries (Disse's space), in some places it is more pronounced, manifested by a complication of hepatocytes : disruption of the connection and individual components that make up the trabeculae. Slit-like spaces are formed between the cellular elements, excluding the normal structure of the liver.

When heliotropin was administered for 2-3 days, the following conditions were detected in the liver tissue: fatty liver and centrilobular necrosis, centrilobular hemorrhage and cellular infiltration, histiocytic infiltration within necrotic foci, with proliferation of connective tissue, part of the lobular center was destroyed; liver cells regenerate, autolytic changes alternately occur, blockage of bile thrombi by small bile ducts and proliferation of small bile ducts. Mainly in the center of the lobules, necrosis of hepatocytes was detected with a pronounced fatty character and in places watery degeneration, the formation of progressive necrosis, signs of replacement of damaged hepatocytes with connective tissue, death of macrophages and histiocytes, and proliferation. The portal ducts are dilated and have a moderate lymphoid infiltrate with an admixture of macrophages, histiocytes and single neutrophils. Mitotic activity was increased and marked nuclear hyperplasia was observed, but the number of binucleate hepatocytes was reduced.

So, in most cases, acute toxic liver damage is detected within 1-3 days. In 30 animals after different periods of intoxication, in which control liver biopsies were performed and the administration of alkaloids was stopped, in 19 animals progression of this process was noted at different periods of time. Five days after stopping the administration of alkaloids, active mixed cirrhosis of the liver was clinically and histologically determined.

Acute toxic hepatitis (ATH), caused by heliotropin, is characterized by liquefaction necrosis, protein and fatty degeneration of hepatocytes , predominantly located in the central region of the liver lobules, where the activity of cytochrome P450-dependent monooxygenase is highest , which produces the highest monooxygenase activity. Damaging hepatotoxic metabolites predominate . To the naked eye, the liver is visible enlarged, dense, rounded at the edges.

Experimental study of new domestic drugs for the treatment of liver damage.

It is traditionally believed that lactic acid, pyruvate , glucose, derived indicators lactate / pyruvate , glucose / lactate and other indicators reflect the activity of anaerobic metabolism. However, the reason for a long-term increase in the values of these indicators can be any critical situation accompanied by adrenergic stress, in addition to damage to the respiratory chain. Therefore, the dynamics of the studied metabolic parameters is of great importance. Lactate is metabolized mainly in the liver and kidneys, so its metabolism plays an important role as lactate production increases in tissues damaged by ischemia- reperfusion , thereby restoring the balance between lactate production and clearance .

Heliotropin intoxication is a factor that actively influences the dynamics of multiple organ failure, including liver and kidney damage due to impaired tissue transport and oxygen extraction, catabolism of structural proteins, hypermetabolism in conditions of impaired nutrient delivery, and glycolysis. protein molecules and the development of water-electrolyte imbalance.

The research results show that when studying the antihypoxic effect on a model of heliotrope poisoning, the new domestic amino acid blood substitute increased the resistance of experimental animals to hypoxia: it significantly increased the life expectancy of animals by 25% ($p < 0.05$), IE. Mice

that were injected into the tail vein with a domestic amino acid blood substitute survived for 12.45 ± 0.67 minutes after the start of the experiment, while the rate for mice in the control group was 8.5 ± 0.32 minutes.

In a group of experimental rats that were injected with a new domestic amino acid blood substitute, no changes in behavior or functional state were observed during the day. They remained active, and the condition of the coat and skin remained normal without any changes. The rats did not refuse food and water, and there was no death. During the second day and in the subsequent observation period, no pathological changes were detected in the behavior and physiological parameters of the mice. Water and feed intake were normal, and there were no delays in growth and development. No mice died within 14 days.

In rats of the control group, which were administered the drug, short-term lethargy and inactivity were observed, which disappeared after 30-40 minutes. After 1 hour, the mice returned to their normal state, were active, and their physical indicators did not differ from normal. During the second day and the entire observation period of 5 days, no changes were observed in the behavior and other physical indicators of the rats.

Based on the data obtained, we can conclude that the new domestic amino acid blood substitute, when using the heliotrine intoxication model, helps to increase the survival rate of animals, which indicates its antihypoxic effect.

Dynamics of morphological changes in the liver in heliotrine toxic hepatitis during treatment.

Correction of experimental animals in the control group infected with heliotrine hepatitis was carried out with Infezol-40 solution. Morphology of the liver.

During the study, we studied metabolites that accumulate in the cytoplasm of hepatocytes during heliotrinosal hepatitis. To do this, we used watery dystrophy caused by toxic damage to hepatocytes as a model. In Figures 5-7, we examined a series of changes that occur in hepatocytes when an infezol-40 solution is introduced into the body of rats with this pathology.

In Figure 5, we restored the histioarchitecture of the liver in the case of heliotrinos hepatitis. We found that pairs of hepatocytes form a columnar structure, the width of the sinusoidal projections is stable, and there is a proliferation of hepatocytes with hyperchromic nuclei, of which 4-5 mitotic foci are noted (Figure 6). We also noticed that the cytoplasm of hepatocytes has reduced chromophobia , in contrast to acidophilic staining after infusion of infezol-40 solution. The accuracy of the hepatocyte boundaries was determined by the narrowing of the dissection cavities (expanded sinusoidal spaces in g). The relatively uniform size of most hepatocytes was demonstrated in Figures 7, 8.

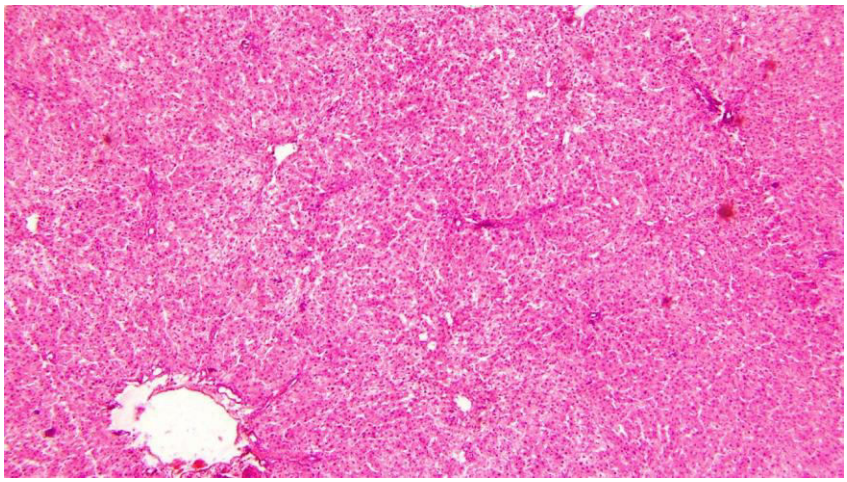

Figure 5. Liver of rats treated with Infezol-40 solution for heliotrine hepatitis. The columnar structure of hepatocytes is restored . The cytoplasm of hepatocytes against the general background looked the same with focal staining. The colors are almost the same. Fatty degeneration is detected in the form of poorly developed droplets. Sinusoidal spaces increase in different ways. GE coloring. 4x10.

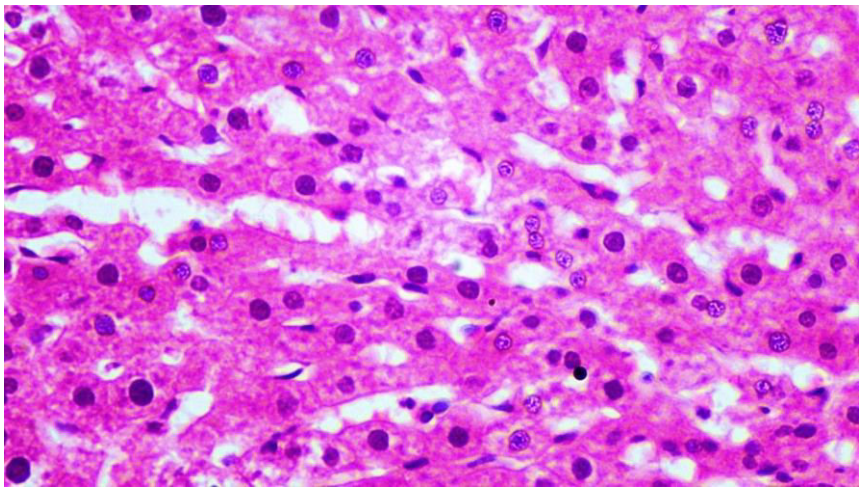

Figure 6. Majority hepatocytes look the same. Mitotic foci are detected around hepatocytes with single-cell necrosis. The cytoplasm of hepatocytes is relatively darker. Sinusoidal spaces are enlarged cylindrically. Kupffercells have an indeterminate outline. Disse space is mostly narrowed (4). GE coloring. 40x10.

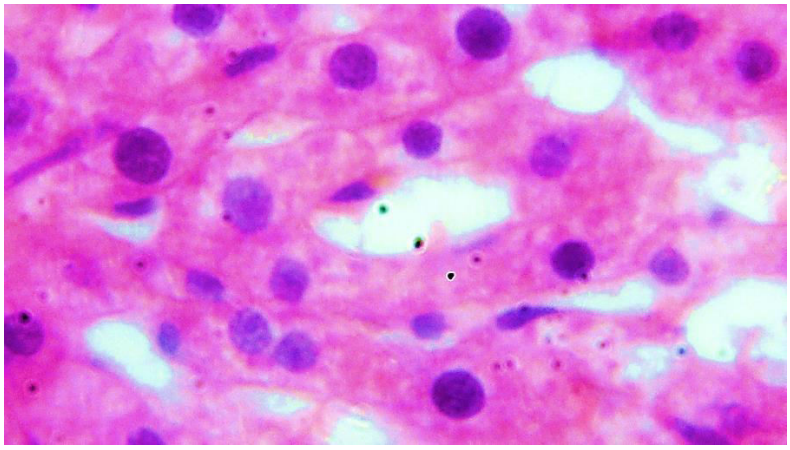

Figure 7. Stained bodies with acidophilic foci are found in the cytoplasm of hepatocytes . Kupffer cells are very close to hepatocytes , and the cavity of Disse is almost indistinguishable. The Ito cell, which is located perisinusoidally , is activated by accessing the adjacent sinusoidal space between hepatocytes through dilated areas. Hyperchromiain the nucleus of hepatocytes . Paint G-E. 100x10.

We found that Ito cells surrounding damaged hepatocytes were activated (Figures 9, 10) and functioned to repair damaged areas around necrotic hepatocytes . However, the relative return of endothelial cells into the wall of sinusoidal cavities around hepatocytes with paranecrotic necrosis around the centers of the fragment, as well as narrowing of transendothelial fissures, indicate a decrease in the vascular response.

We studied the morphology of the liver of rats that received a solution of an “amino acid blood substitute” for heliotrinos hepatitis. As a result of the administration of this solution, we observed restoration of the morphofunctional state of the liver. We especially note that sodium succinate , which is part of the “amino acid blood substitute,” stabilized the cell membrane, which was detected due to the clear and smooth boundaries of the hepatocyte membrane in Figures 11, 12. We also observed the formation of 15-25 hyperchromatically stained nuclear hepatocytes in a 10x10 field of view. The development of sinusoidal cavities of equal width and the stabilization of lost function are confirmed in Figure 8. Figure 9 demonstrates a homogeneous acidophilic staining of the cytoplasm of hepatocytes , indicating the regeneration and saturation of free protein structures (enzymes) in the cytoplasm. In comparison with hepatocytes observed during infusion of infezol-40 solution, the presence of sodium succinate (an antioxidant) and mannitol (a membrane stabilizer) in the “amino acid blood substitute” indicated a decrease in the number of sinusoidal cavities and interstitial tumors. Stabilization of the hepatocyte membrane occurs by recycling excess fluid in the sinusoidal cavities and disse cavities (Fig. 13).

Finally, we detected Ito cell activation between hepatocytes using large-scale 14-microscopy.

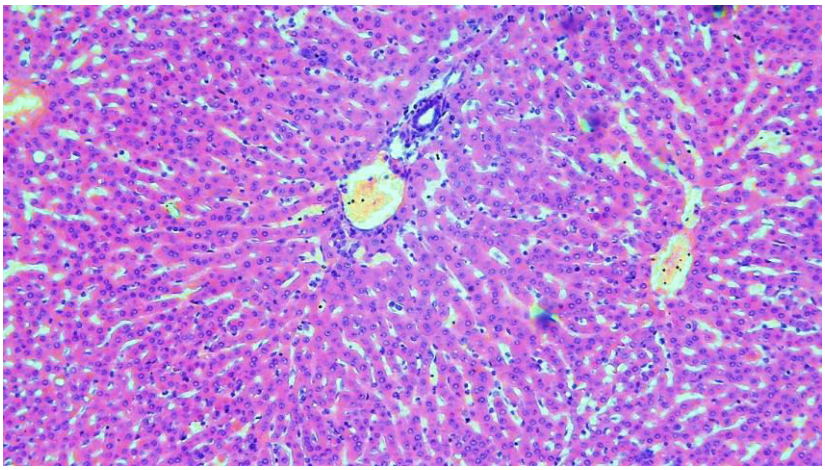

Figure 8. Rat liver with a solution of "amino acid blood substitute" for heliotrine hepatitis. The contours of poorly formed neutrophil infiltration around the triads are clear. The central veins are of medium fullness. The double columnar structure of hepatocytes is clear and smooth. Sinusoidal intervals have the same width. The nuclei of most hepatocytes have a hyperchromic appearance (contrasting shade). GE paint. 10x10.

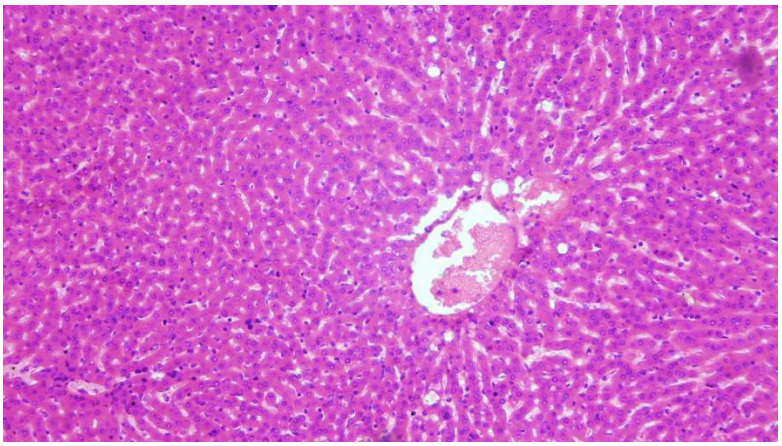

Figure 9. Rat liver with a solution of "amino acid blood substitute" for heliotrine hepatitis. Interestingly, the liver fragment looks almost identical to the normal state of histioarchitecture. Sinusoidal intervals have the same width. Paint G-E. 10x10.

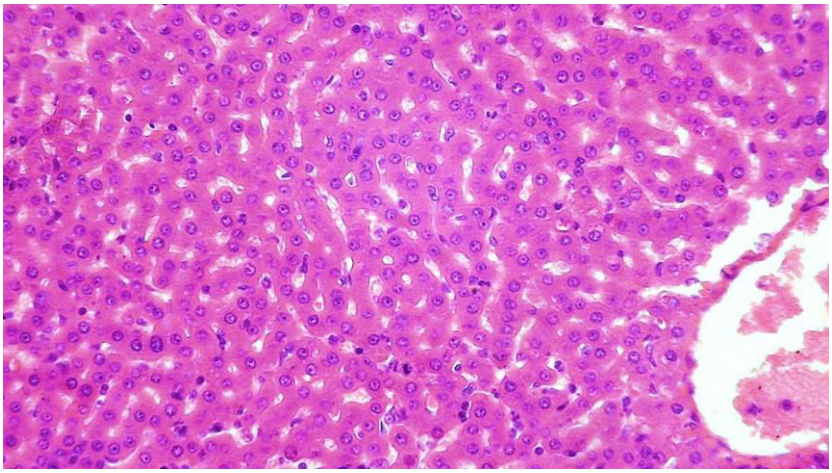

Figure 10. Rat liver with a solution of "amino acid blood substitute" for heliotrine hepatitis. The hepatocyte nucleus in most cases has a larger appearance and a contrasting hyperchromatic appearance. GE paint. 20x10.

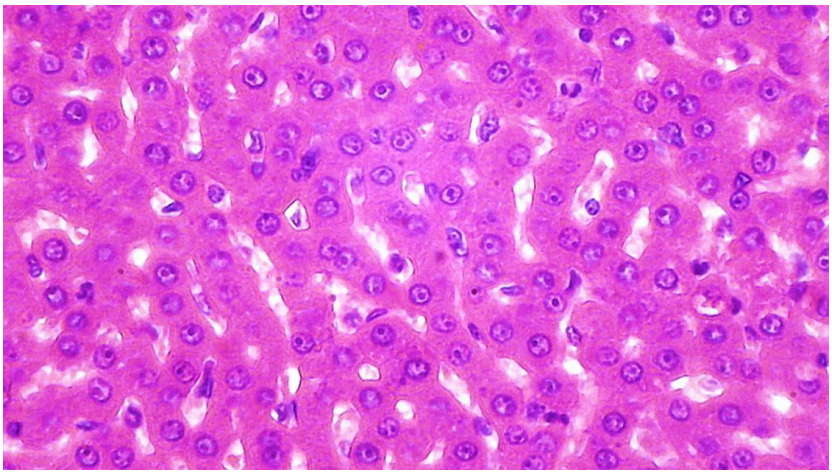

Figure 11. Rat liver with a solution of "amino acid blood substitute" for heliotrine hepatitis. The cytoplasm of hepatocytes is stained homogeneously acidophilic. The boundaries of the hepatocyte membrane are clear. The nuclei are stained dark basophil. The nuclei are also clearly visible. Sinusoidal segments of equal width. Hypertrophy of hepatocytes around foci of single-cell necrosis. Kupffer cells are enlarged. Staining G-E. 40x10.

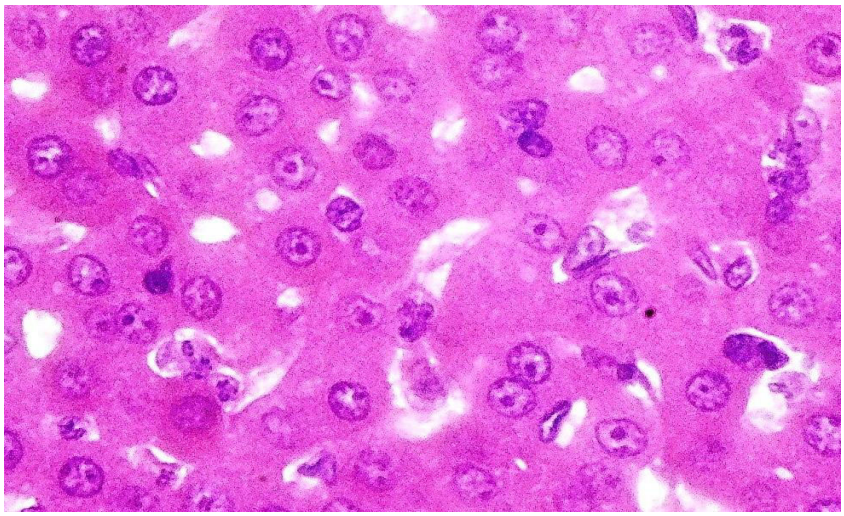

Figure 12. Rat liver with a solution of "amino acid blood substitute" for heliotrine hepatitis. The cytoplasm of hepatocytes has acidophilic homogeneity. Foam-like structures (neutral fats) in the cytoplasm of some hepatocytes. Kupffer cells are enlarged. Disse space of standard width. GE coloring. 80x10.

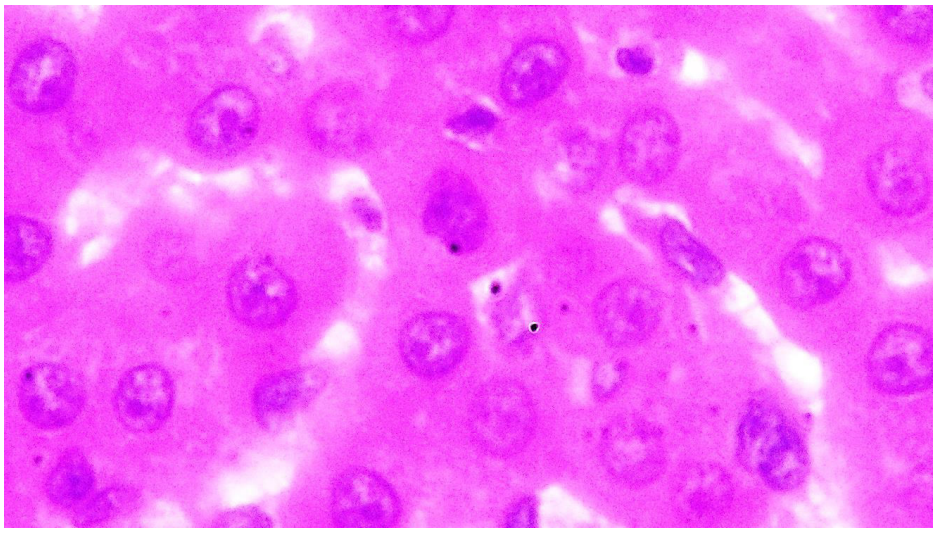

Figure 13. Rat liver with a solution of "amino acid blood substitute" for heliotrine hepatitis. Sinusoidal intervals have the same width. The dissected cavity is normally visible. On the left, acidophilus is uniformly stained around chromophobe foci in the cytoplasm of hepatocytes. Division of hepatocytes by mitosis around foci of monocellular necrosis. Tumor formation of Ito cells in the intercellular space (activated fibrosis). Painting GE 100x10.

Thus, a solution of Infezol-40 and "Amino acid blood substitute", used for heliotin hepatitis, is used every 24 hours for 5 days. With morphological changes in the liver of mice, regeneration of liver fragments was observed when a solution of an "amino acid blood substitute" was administered. Judging by the above micrographs, approximately 90-95% restoration of the histostructure of the liver is observed. Unlike the control group, edematous degeneration (uniform dark staining of the cytoplasm) in hepatocytes returns to normal, indicating the return of hepatocytes to a functional state. The fact that the dissection zone has the same width indicates restoration of hemodynamics in the liver and normalization of the vascular response. This means that the Amino Acid Blood Substitute solution has more advantages than the Infezol-40 solution, since it contains components necessary to ensure cellular metabolism (membrane stabilizing mannitol and sodium succinate). It has been established that the "Amino acid blood substitute" solution is an effective method for preventing damage to liver tissue in heliatrichepatitis and restoring lost morphology.

Conclusion

Acute toxic hepatitis (ATH), caused by the development of hepatitis necrosis, protein and fatty degeneration of hepatocytes , is localized mainly in the central zone of the hepatic lobule, where the dominance of cytochrome P450-dependent monooxygenases is high. Produces harmful hepatotoxin metabolites . Homemade amino acid blood substitutes containing sodium succinate and mannitol , the result after use depends on the stability of the cell membrane: clear and even boundaries of the hepatocyte membrane , the formation of 15-25 hyperchromatically colored nuclear hepatocytes , in a field of view of 10x10. Development of sinusoidal cavities of equal width, stability of the lost operating mode. Due to regeneration and saturation of the cytoplasm with free protein complexes (enzymes), a homogeneous acidophilic staining appears in the cytoplasm of hepatocytes . The action of sodium succinate (antioxidant) and mannitol (membrane stabilizer) in the composition of the "amino acid blood substitute" reduces the number of sinusoidal cavities and interstitial glands. The stability of the hepatic membrane is caused by excess fluid in the sinusoidal cavities and disc spaces.

References

1. Muller AWJ Cancer is an adaptation that selects in animals against energy dissipation //Medical Hypotheses. – 2017. – T. 104. – P. 104-115.
2. Illarioshkin S. N. Violations of cellular energy in diseases of the nervous system // Nervous diseases. – 2012. – No. 1. – pp. 34-38.
3. Fudin N. A., Klassina S. Ya., Pigareva S. N. Interrelation of indicators of the muscular and cardiovascular systems with increasing physical activity in persons involved in physical culture and sports // Human Physiology. – 2015. – T. 41. – No. 4. – pp. 82-82.
4. Skvortsova V. A. et al. Scientific substantiation of the scheme for introducing complementary foods set out in the "National Program for Optimizing Feeding of Children of the First Year of Life in the Russian Federation." Part I // Issues of modern pediatrics. – 2011. – T. 10. – No. 6. – pp. 128-136.

5. Komarova O. N., Khavkin A. I. Malnutrition in young children: pathogenesis, diagnosis, dietary correction // Attending physician. – 2014. – T. 9. – P. 24.
6. Khomyakov V. M. et al. Modern ideas about risk factors for the development of stomach cancer // Russian Journal of Gastroenterology, Hepatology , Coloproctology . – 2017. – T. 27. – No. 6. – pp. 78-86.
7. Lazebnik L. B. et al. Recommendations for the management of primary patients with symptoms of dyspepsia // Experimental and clinical gastroenterology. – 2018. – No. 5 (153). – P. 4-18.
8. Kostyukevich S.V. Innovation: the approach of modern Western authors in the context of Russian experience // Alma mater (Bulletin of Higher School). – 2011. – No. 4. – pp. 69-78.
9. Lysikov Yu. A. Amino acids in human nutrition // Experimental and clinical gastroenterology. – 2012. – No. 2. – pp. 88-105.
10. Grin A. A. et al. Algorithms for diagnosis and treatment of patients with combined spinal cord injury // Spinal surgery. – 2012. – No. 1. – pp. 8-18.
11. Kharchenko N. V. Optimization of treatment of diseases associated with Helicobacter pylori : what opportunities do we have today? – 2012.
12. Gelfand B. R. et al. Safety of parenteral nutrition in surgery and intensive care: questions and answers // Annals of Surgery. – 2012. – No. 4. – pp. 5-11.
13. Kaladze N. N. et al. Seasonal features of sanatorium-resort treatment for various diseases // Bulletin of physiotherapy and balneology. – 2019. – T. 25. – No. 1. – pp. 112-112.
14. Andreev D.N., Maev I.V., KucheryavyiYu.A. Resistance of Helicobacter pylori in the Russian Federation: meta-analysis of studies over the past 10 years // Therapeutic archive. – 2020. – T. 92. – No. 11. – pp. 24-30.
15. Minyaeva O. A. Amino acids as biological objects in aqueous solutions // Scientific review. Biological Sciences. – 2016. – No. 6. – pp. 43-47.
16. Chekman I. S. et al. Amino acids - nano-sized molecules: clinical and laboratory studies. – 2014.
17. 17 . Isaeva G. Sh., Valieva R. I. Biological properties and virulence of Helicobacter pylori //Clinical microbiology and antimicrobial chemotherapy. – 2018. – T. 20. – No. 1. – pp. 14-23.
18. Yakovlev A. Yu., Ulitin D. N. Reamberin : results of clinical studies in surgery and intensive care over the past five years // Medical alphabet. Emergency medicine. – 2012. – T. 3. – P. 54-58.
19. Saydalikhodjaeva, S., Boboyeva, Z., Akhmedova, D., Azimova, S. The anthropometric indicators' changes of patients after COVID-19. E3S Web of Conferences, 2023, 420, 05012
20. Akhmedova, D., Azimova, S. Comparative assessment of the spread of respiratory diseases of occupational etiology in regions with a highly developed mining industry. E3S Web of Conferences, 2023, 420, 05013
21. Talipova, N., Iriskulov, B., Azimova, S., Latipova, S. Genetic characteristics of the course of chronic hepatitis. E3S Web of Conferences, 2023, 381, 01098
22. Ermatov, N., Kassymova, G., Tajiyeva, K., Alimukhamedova, M., Azimova, S. Expression of tissue-specific genes in mice with hepatocarcinogenesis. International Journal of Pharmaceutical Research, 2020, 12(3), pp. 1776–1781