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Influence of milk phospholipids on microstructural changes in rat liver under tetracycline-induced hepatosis

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Abstract. The growing number of cases of adverse effects of medicines on the liver leads to hepatopathology and the development of complications such as cirrhosis, necrosis, liver failure, and liver carcinoma. Therefore, the purpose of this study was to determine the characteristic structural changes in the liver of rats with tetracycline damage and to find out the corrective effectiveness of milk phospholipids. The study performed histological examination of sections from different parts of the liver in experimental rats, which were stained with haematoxylin and eosin according to the conventional method. It was found that in case of artificial modelling of tetracycline-induced hepatosis in rats, the general architecture of the liver is preserved. At the same time, large-scale damage to hepatocytes and the development of fatty and granular dystrophy were recorded in the affected animals. Some of the damaged cells were destroyed, followed by lysis of fragments of the destroyed cells. The described microscopic changes were most pronounced in the areas of the liver under its capsule. As a result, there was partial or complete disorganisation of the liver lobes in all lobes of the organ. The use of milk phospholipids in the form of a biologically active additive "FLP-MD" as a corrective therapy in sick rats prevented the development of hepatocyte dyscomplexity, contributed to a substantial reduction in the count of destroyed cells in a state of dystrophy with isolated cases of disordered organisation of the liver laminae. This suggests a pronounced stimulatory effect of milk phospholipids on the processes of hepatocyte regeneration and repair in tetracycline-induced

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liver damage in rats. In case of separate administration of a milk phospholipid-based supplement to clinically healthy animals, the microscopic structure of liver samples did not differ from that of the control group. The findings of this study are of practical value for pathologists, clinicians, and therapists in case of development of drug-induced hepatopathology in animals, especially when using tetracycline antibiotics, and for determining the strategy in the treatment of such patients

Keywords: histological examination; corrective therapy; dystrophy; hepatopathology; complications; milk phospholipids

Introduction

The liver ensures the stability of the body's internal environment, supporting vital functions such as immunity, haematopoiesis, haemostasis, energy production, and detoxification of toxic substances. However, many pharmaceuticals can be hepatotoxic, leading to liver damage and even functional failure.

Tetracycline drugs are known for their ability to cause liver damage, which indicates the relevance of investigating their effects on this organ. According to P.B. Watkins *et al.* (2021), over 900 drugs provoke the development of hepatotoxic reactions, which often leads to the withdrawal of these drugs from therapeutic use. Damage to functional liver cells is usually accompanied by an increase in the activity of liver-specific enzymes in the blood, which reflects substantial structural and functional pathological changes in hepatocytes.

S. Thakur *et al.* (2024) found that individual differences, age, gender, xenobiotic intake, chronic or acute pathological processes, as well as environmental and genetic factors increased the risk of developing severe liver disease, such as cirrhosis, necrosis, liver failure, and cancer. M. Martin-Grau & D. Monleon (2023) analysed the results of metabolic studies of sex differences in the development and progression of pathological fat accumulation in the liver, the role of metabolic profiles in understanding the mechanisms and identifying sex-dependent biomarkers, and how this evidence may help in the future treatment of patients with fatty liver disease in its toxic damage. N.V. Bergasa (2022) found that 5% of all clinical complications and half of acute liver failure cases are the result of drug-induced hepatocyte damage.

H. Jaeschke & A. Ramachandran (2024) classified hepatotoxicity according to the severity and intensity of hepatocyte damage in the case of synthetic drugs, including antibiotics, against the background of simultaneous assessment of hepatic biomarkers. M. Sherman (2021) distinguished between distinct stages of liver damage, which are assessed as initial damage and severe disease. The stage of pathological changes in the liver parenchyma and their clinical manifestation depends on various specific and non-specific risk factors, the duration of their action on the organ and the aggressiveness of the lesion factor.

H. Jaeschke & A. Ramachandran (2024) argued that hepatotoxicity can also manifest itself in the form of mitochondrial dysfunction, decreased cellular respiration, or changes in the intensity of fatty acid oxidation. According to N.K. Björnsson & E.S. Björnsson (2022) and M. Machiels *et al.* (2022), hepatocellular, cholestatic, or mixed liver damage is distinguished. It was noted that, considering the significance of the full functioning of the liver for the body as a whole, damage to hepatocytes would inevitably affect the functional state of other organs and their systems. At the same time, V. Gryshchenko *et al.* (2019) reported on the general consequences of hepatopathology development due to the use of tetracycline hydrochloride, namely damage to the plasma membrane and intracellular membranes of hepatocytes. Another prominent target of possible therapeutic effects is opened for doctors – the restoration

and protection of cell membranes. This area of treatment is called membrane therapy. Since the lipid component of hepatocyte cell membranes is represented by essential phospholipids, the use of these biologically active substances in the treatment of patients with diffuse liver damage is of great interest to scientists and clinicians. D. Wupperfeld *et al.* (2022) found that essential phospholipids increased hepatocyte membrane fluidity, prevented apoptosis, and increased the intensity of hepatocellular export, which substantially improved the functional state of the liver.

A. Ortega-Alonso & R.J. Andrade (2018) investigated structural and functional changes in the liver upon liver disease, which helped to improve the diagnosis of hepatotoxicity of certain groups of xenobiotics and the effectiveness of corrective therapy. Assessing the unique signs of liver damage, F. Ezquer *et al.* (2022) argued that it is possible to quickly and accurately detect pathological changes in the liver and determine their severity. To counteract the pathological events that occur in drug-induced liver damage by means of cellular and molecular mechanisms associated with the therapeutic effects of membranotropic and hepatoprotective agents, it is important to reduce oxidative damage and the intensity of the inflammatory response, increase the regeneration of functional liver cells, restore energy balance, and maintain a suitable level of adenosine triphosphate (ATP) production in hepatocytes. Such a comprehensive effect on the recovery processes in damaged hepatocytes will help to ensure effective therapeutic support in case of drug-induced hepatopathology, which will reduce the risk of chronic liver damage and prevent the occurrence of complications that threaten animal health.

The relevance of the present study lies in the need for an in-depth investigation of the mechanisms of hepatotoxicity, especially using models that can reflect microstructural changes in the liver. This will enable a prompt and reliable assessment of the degree of damage to the organ and help to find innovative approaches to its protection and treatment.

The purpose of this study was to determine the nature of structural changes in the liver parenchyma during the experimental reproduction of tetracycline injury in rats and the corrective effectiveness of milk phospholipids.

Materials and Methods

The experimental studies were conducted at the laboratories of the Faculty of Veterinary Medicine of the National University of Life and Environmental Sciences of Ukraine during 2022-2023. To determine the corrective efficacy of milk-derived phospholipids in the form of a biologically active additive (BAA) "FLP-MD" on the microstructure of the liver parenchyma, laboratory rats (males) of the *Wistar* line with a body weight of 210 ± 40 g (n = 24), which M. Martin-Grau & D. Monleon (2023) explained as sex differences in the occurrence of hepatopathology and the specific features of the course in animals of different sexes.

The laboratory animals were kept in standard vivarium conditions at an indoor temperature of 22-24 °C and were fed a standardised complete food diet with free access to water. All necessary surgical interventions in the experiments were performed according to the ARRIVE guidelines, following the guidelines of Council Directive 2010/63/EU (2010) on the protection of animals used for scientific purposes.

According to the proposed scheme of V. Gryshchenko *et al.* (2019), tetracycline-induced hepatosis was reproduced in laboratory rats. For this, a 4% solution of tetracycline hydrochloride at the rate of 0.25 g/kg body weight was administered daily intragastrically to the animals for 7 days using an oral gavage tube. The "Self-Rehabilitation" group (n = 6) was formed from these animals. Animals that received a 1% solution of dietary supplement "FLP-MD" containing milk phospholipids intragastrically for seven days before intragastric administration of tetracycline hydrochloride and for the next two days after the antibiotic administration were classified as animals of the "Correction" group (n = 6). The daily dose of the supplement corresponded to 13.5 mg/kg body

weight (Litvinenko *et al.*, 2009). Animals were intragastrically injected with an equivalent volume of distilled water to the volume of antibiotic and supplement formed the "Control" group (n = 8). A separate group of healthy animals received only a phospholipid-containing dietary supplement, the main components of which (phospholipids) were produced from milk (the "Preparation" group, n = 6) in the dose specified above. At the end of the experiment, immediately after the animals were euthanised, liver samples were taken.

Notably, additional studies were aimed at investigating the dynamics of liver microstructure recovery in the "Correction" group and comparing the results with the "Self-Rehabilitation" group. This helped to assess not only the direct effect of phospholipids on the affected tissue, but also to determine their potential ability to accelerate regeneration processes. Furthermore, the study considered the possible side effects of the dietary supplement on other organs, which helped to draw more comprehensive conclusions regarding its safety and effectiveness.

At least 5 pieces of liver from different parts of the parenchyma – from its peripheral and central parts – were obtained from each animal. All pieces of the organ were to be fixed in formalin and then embedded in paraffin. Histological sections were prepared using a MS-2 sled microtome (Ukraine) and subsequently stained with Carazzi's haematoxylin and eosin (Goralskij *et al.*, 2015). The prepared histological specimens were examined and photographed using a microscope model MC 100 LED (Austria).

Results and Discussion

In laboratory rats of the control group, the microscopic structure of the liver corresponded to the typical microstructure of this organ in mammals. Specifically, the liver was constructed from individual lobules. In the centre of each lobule is a central vein surrounded by hepatocytes (Fig. 1a). The wall of central veins is represented by a single layer of endothelial cells (Fig. 1b). Rows of hepatocytes extend from the central veins to form the liver lobules. Intrahepatic blood capillaries passed between adjacent liver laminae. Their wall was also represented by a single layer of endothelial cells. Apart from the central vein, micrographs of liver samples showed the location of triads, including an artery, a vein, and a bile duct.

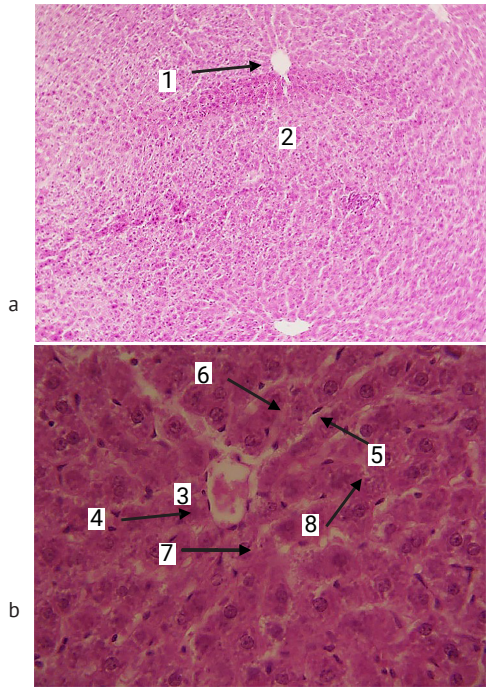

Figure 1. *Liver of a rat in the control group*
Note: a – 1 – central vein; 2 – hepatocytes. Carazzi's haematoxylin and eosin, x300; b – 3 – central vein; 4 – central vein endothelium; 5 – liver lamina; 6 – endothelium of intrahepatic blood capillary; 7 – hepatocyte; 8 – bile capillary. Carazzi's haematoxylin and eosin, x400
Source: authors' photo

Hepatocytes are polygonal cells characterised by a large, homogeneous cytoplasm and a large, rounded nucleus, which usually contains a single nucleolus. In functional liver cells in preparations obtained from clinically healthy experimental rats ("Control" group), the nuclei were located in the centre of the cell, and sporadic binucleated hepatocytes were observed. In the liver laminae, bile capillaries passed between adjacent hepatocytes (Fig. 1b).

As reported by S. Thakur *et al.* (2024), the liver is one of the crucial internal organs that protects the body from the negative effects of various toxins, acting as a universal metabolic barrier. Furthermore, in the liver, the enzymatic systems of hepatocytes fully or partially neutralise toxic substances, specifically, tetracycline antibiotics. The morphological and functional picture of the tissue microsection of the liver parenchyma contains common elements that are found in other structures of the mammalian body. These include lymphatic and blood microvessels, interstitium (loose connective tissue), and functional cells (hepatocytes), which reflect not only the functional tension of the organ itself, but also may indicate the body's overall response to a pathological factor.

There are thin, hardly visible strips of fibrous connective tissue between the lobes of the liver (Fig. 2). In some places, they form overgrowths, which housed the hepatic triads, including the hepatic triad artery, hepatic triad vein, and bile duct.

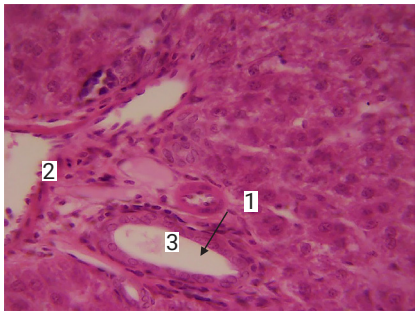

Figure 2. *Hepatic triad in a rat of the control group*

Notes: 1 – artery of the hepatic triad; 2 – vein of the hepatic triad; 3 – bile duct. Carazzi's haematoxylin and eosin, x400

Source: authors' photo

In clinically healthy rats, which were additionally intragastrically administered milk phospholipids in the form of the BAA "FLP-MD" ("Preparation" group), the microscopic structure of the liver did not differ from that of the control group. Analogously, lobules and hepatic triads of typical microscopic structure with all their structural elements were found in the organ (Fig. 3a; 3b). The above suggests the absence of toxic effects of the BAA "FLP-MD" on specialised liver cells in the experimental rats of the corresponding group.

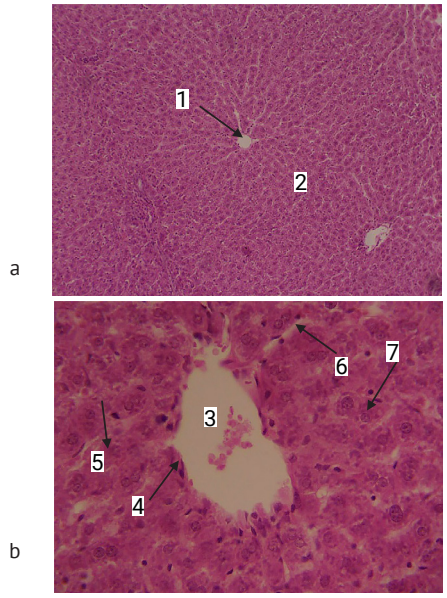

Figure 3. *Liver of a rat treated with milk phospholipids in the form of the BAA "FLP-MD" ("Preparation" group)*

Note: a – 1 – central vein; 2 – hepatocytes. Carazzi's haematoxylin and eosin, x300; b – 3 – central vein; 4 – central vein endothelium; 5 – liver lamina; 6 – endothelium of intrahepatic blood capillary; 7 – hepatocyte. Carazzi's haematoxylin and eosin, x400

Source: authors' photo

As reported by R. Ramachandran & S. Kakar (2009), the diagnosis of drug-induced liver injury is extremely challenging due to insufficient clinical information and difficulties in identifying the effects of non-prescription preparations and toxins.

In the modelling of hepatosis in experimental rats ("Self-Rehabilitation" group), it was found that the general architecture of the liver was preserved (Fig. 4a). Analogously to the control, lobules and hepatic triads of typical microscopic structure with all their structural elements were found in the liver. However, distinct microscopic changes were found in the liver lobules, which primarily involved damage to hepatocytes.

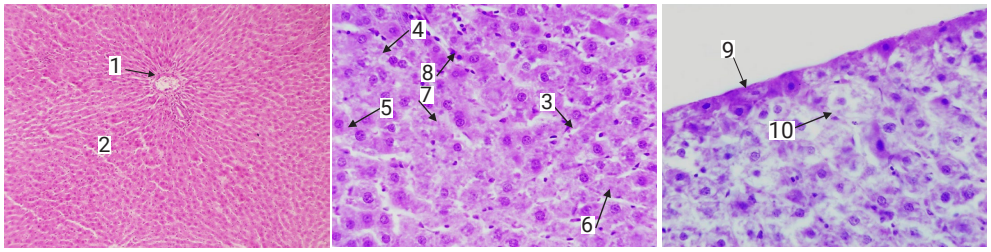

Figure 4. *Rat liver in the model of tetracycline-induced hepatosis ("Self-Rehabilitation" group)*
Note: a – 1 – central vein; 2 – hepatocytes. Carazzi's haematoxylin and eosin, x300; b – 3 – liver lamina; 4 – disorganisation of liver laminae; 5 – separation of hepatocytes from each other; 6 – granular dystrophy of hepatocytes; 7 – destruction of hepatocyte; 8 – hyperplasia of Kupffer cells. Carazzi's haematoxylin and eosin, x400; c – 9 – liver capsule; 10 – destruction and lysis of hepatocytes. Carazzi's haematoxylin and eosin, x400
Source: authors' photo

In case of tetracycline-induced hepatosis in laboratory rats, hepatocytes were separated from each other in many parts of the liver. A considerable share of liver cells were in a state of fatty and granular dystrophy. Some of the dystrophically altered hepatocytes were destroyed with subsequent lysis of fragments of destroyed cells. The destruction and lysis of hepatocytes was particularly pronounced in some areas of the liver under its capsule. All these changes led to partial or complete disorganisation of the liver laminae in all lobes of the organ (Fig. 4b; 4c). Comparable microscopic changes in the liver parenchyma were also observed by H.Y. Yong *et al.* (2020), specifically, the steatogenic effect of tetracycline hydrochloride, which was associated with a decrease in the intensity of mitochondrial β-oxidation of fatty acids by affecting the expression of genes related to lipid metabolism. Furthermore, according to these researchers, tetracycline reduces the expression of acylcarnitine transferase I, responsible for carnitine acylation in mitochondrial fatty acid transport, which leads to a decrease in β-oxidation of fatty acids. Subsequently, this leads to an increase in the intensity of triacylglycerol and cholesterol biosynthesis. The researchers suggest that the direction of fatty acids to the synthesis of triacylglycerols is the result of the inhibitory effect of the antibiotic as part of the mechanism of tetracycline-induced steatosis with a characteristic high content of lipid molecules in hepatocytes.

At the same time, D. Pessayre *et al.* (2012) noted that a frequent mechanism for the development of drug-induced hepatopathology is the development of reactive metabolites that exhibit direct toxicity or immune reactions. These pathological phenomena provoke damage to the mitochondrial membrane. Tetracycline has a direct cytotoxic effect, which is expressed in damage to the mitochondrial membrane or inhibition of the mitochondrial energy-producing function through various mechanisms. Such mechanisms may include blocking coenzyme A or inhibiting the activity of mitochondrial β-oxidation enzymes, electron transport in the respiratory chain, or ATP synthase. It is also possible to destroy mitochondrial DNA, inhibit its replication, or block the synthesis of mitochondrial protein. Tetracycline has many different effects on mitochondrial function. A severe impairment of oxidative phosphorylation reduces the hepatic ATP pool, which leads to functional disorders or cell necrosis. This drug is capable of secondary inhibition of ß-oxidation, provoking steatosis, and can also block the catabolism of pyruvate, which causes lactoacidosis. Like the previous researchers, they point to a substantial impairment in β-oxidation of fatty acids in this situation, which leads to liver fatty acidosis. At the same time, insufficient gluconeogenesis and increased use of glucose as an alternative to the inability to oxidise fatty acids, combined with mitochondrial toxicity of accumulated free fatty

acids and lipid peroxidation products, can drastically reduce energy production, which can lead to irreversible consequences. Therefore, scientists recommended that all new drugs be tested for mitochondrial side effects. The microscopic structural changes in the liver parenchyma, along with the cytotoxic side effects of tetracycline drugs already known from the literature, convince of the need to use corrective therapy with reparative properties in animals suffering from drug-induced hepatosis.

Furthermore, a distinct activation of fixed hepatic phagocytes (Kupffer cells) was recorded everywhere in the liver parenchyma, which was morphologically manifested by a considerable increase in their count, i.e., hyperplasia of these cells (Fig. 4b). We assume that this activation of hepatic phagocytes was caused by the need to eliminate fragments of destroyed hepatocytes from the organ. Histological examination of the liver samples of the "Self-Rehabilitation" group animals revealed no microscopic changes in the central veins, intrahepatic blood capillaries, as well as arteries, veins, and bile ducts of the hepatic triads. Therewith, no manifestations of any inflammatory reaction in the liver were recorded.

As noted in the previous study by V.A. Gryshchenko *et al*. (2018), most cellular functions are determined by the physicochemical properties of the lipid component of biological membranes, which is mainly represented by phospholipids. In this study, the development of a deficient level of phospholipids of both the total fraction and individual phospholipids (phosphatidylethanolamine, phosphatidylcholine, sphingomyelin, phosphatidylserine, phosphatidylinositol, and other representatives) was noted, which is important for elucidating the molecular basis of the pathogenesis of the pathological process in the drug-induced form of hepatopathology. Overall, this suggests the expediency of searching for biologically active substances that eliminate the negative effects of xenobiotics at the cellular level.

That is why a separate group of sick animals was administered milk phospholipids in the form of the BAA "FLP-MD" ("Correction" group). When these rats were administered corrective therapy in the form of a phospholipid-containing dietary supplement, the overall liver architecture was also preserved (Fig. 5a). In this parenchymal organ, as in the control group, lobules and hepatic triads of typical microscopic structure with all their structural elements were detected. Therewith, microscopic changes were found in some liver lobules, which consisted of damage to the microstructure of hepatocytes. However, in liver samples from animals of this group, in contrast to the microscopic picture in the modelling of hepatosis ("Self-Rehabilitation" group), no hepatocyte dyscomplexity was recorded in case of treatment with milk phospholipids. The count of liver cells in the state of fatty and granular dystrophy was noticeably lower (Fig. 5b).

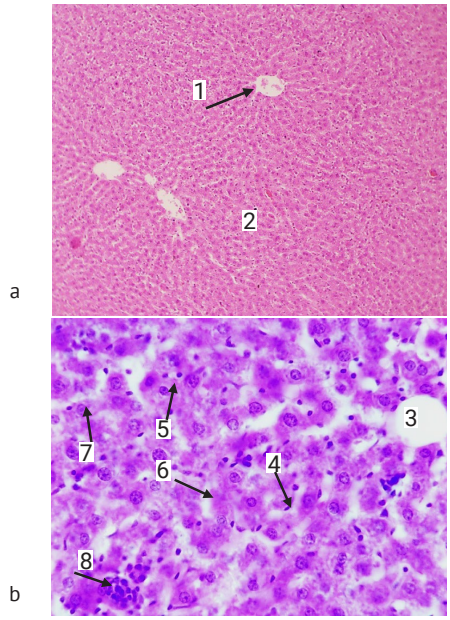

Figure 5. *Liver of a sick rat in the case of corrective therapy ("Correction" group)*

Note: a – 1 – central vein; 2 – hepatocytes. Carazzi's haematoxylin and eosin, x300; b – 3 – central vein; 4 – liver lamina; 5 – disorganisation of liver laminae; 6 – fatty and granular dystrophy of hepatocyte; 7 – destruction of hepatocyte; 8 – hyperplasia of Kupffer cells. Carazzi's haematoxylin and eosin, x400

Source: authors' photo

Notably, only single hepatocytes were destroyed, while the disruption of the orderly organisation of the liver laminae was substantially less pronounced than in the case of tetracycline-induced hepatosis in animals ("Self-Rehabilitation" group). This fact suggests a positive effect of phospholipids on the processes of hepatocyte regeneration and repair, which is consistent with the findings described in other studies.

Specifically, D.O. Melnychuk *et al.* (2014) reported the efficacious influence of milk phospholipids of the BAA "FLP-MD" in the restoration of quantitative indicators of pigment metabolism (unconjugated bilirubin, bilirubin glucuronide, bilirubin sulphate, stercobilin, and urobilin), which were studied in the liver, whole blood, contents of the caecum and faeces under conditions of exposure to ecopathogenic factors (cadmium and ionising radiation). Therewith, the components of the phospholipid-containing dietary supplement had a reparative effect on damaged membrane structures with simultaneous restoration of bile secretion and bile-forming functions of the liver.

At the same time, X. Zhang *et al.* (2018) provided evidence that the use of nanocarriers can exacerbate the side toxic effects of drugs, and therefore serious attention should be paid to the safe use of nanotechnology in drug delivery. M. Mitrovic *et al.* (2022) described potential mechanisms of the corrective effect of omega-3 phospholipids. Moreover, the results of preclinical studies showed that omega-3 phospholipids had a more pronounced antisteatotic effect on the liver compared to the use of omega-3 fatty acids administered as triacylglycerols alone. This antisteatotic effect is likely to involve numerous internal mechanisms that involve not only the liver, but also the intestines and adipose tissue. The need for further research on the possible impact of omega-3 phospholipids on progressive fatty liver disease was noted.

As stated in their studies by M. Yin *et al.* (2021) and D. Wupperfeld *et al.* (2022), the main functions of phospholipids are cell membrane repair, antioxidant action, protection of mitochondrial and microsomal enzymes from damage, as well as slowing down collagen synthesis, and increasing collagenase activity. The complex effect of phospholipids, according to D. Wupperfeld *et al.* (2022), was responsible for their physiological antifibrotic effect. In these animals, hyperplasia of Kupffer cells was also markedly pronounced (Fig. 5b). Microscopic changes in the central veins, intrahepatic blood capillaries, as well as arteries, veins, and bile ducts of the hepatic triads were not observed. There were no signs of any inflammatory reaction in the liver.

Thus, the use of milk phospholipids in the form of the BAA "FLP-MD" ("Correction" group) as a corrective therapy in rats with tetracycline-induced liver damage contributed to a noticeable reduction in dystrophic changes in the liver parenchyma, prevented the destruction of hepatocytes and disorganisation of hepatic beams in the liver lobules.

Conclusions

In the experimental studies, the corrective effectiveness of milk phospholipids in the form of the BAA "FLP-MD" was determined by analysing microstructural changes in liver samples from experimental rats. Specifically, the liver parenchyma of the control group was found to have a typical microscopic structure inherent in healthy animals. In clinically healthy rats, which were additionally intragastrically administered milk phospholipids in the form of the BAA "FLP-MD" ("Preparation" group), the microscopic structure of the liver did not differ from that of the control group. Analogously, lobules and hepatic triads of typical microscopic structure with all their structural elements were found in the organ. In the modeling of tetracycline-induced hepatosis in experimental rats ("Self-Rehabilitation" group), it was found that the general architecture of the liver was preserved. However, distinct microscopic changes were found in the liver lobules, which primarily involved damage to hepatocytes. Therewith, a considerable proportion of liver cells were in a state of fatty and granular dystrophy. Some of

the dystrophically altered hepatocytes were destroyed with subsequent lysis of fragments of destroyed cells. The destruction and lysis of hepatocytes was particularly pronounced in some areas of the liver under its capsule. All these changes resulted in partial or complete disorganisation of the liver lobes in all lobes of the organ. In the case of application of corrective therapy in the form of milk phospholipids of the BAA "FLP-MD" to sick rats ("Correction" group), no hepatocyte dyscomplexity was recorded, only sporadic hepatocytes were destroyed, a noticeably smaller count of liver cells were in a state of fatty and granular degeneration, while the disordered organisation of the liver laminae was substantially less pronounced than in the case of tetracycline-induced hepatosis modelling in animals ("Self-Rehabilitation" group). This fact suggests a positive effect of milk phospholipids on the processes of hepatocyte regeneration and repair in tetracycline-induced liver damage in rats.

In the future, it is planned to investigate the biochemical markers of the effectiveness of milk phospholipids on the structural and functional state of the liver in experimental hepatopathology.

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Conflict of Interest

None.

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Вплив фосфоліпідів молока на мікроструктурні зміни у печінці щурів за тетрацикліндукованого гепатозу

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Анотація. Зростання випадків негативного впливу лікарських препаратів на печінку призводить до гепатопатології і розвитку ускладнень, таких як цироз, некроз, печінкова недостатність і карцинома печінки. Тому метою цієї роботи було визначення характерних структурних змін у печінці щурів за тетрациклінового ураження та з'ясування коригувальної ефективності фосфоліпідів молока. Проведено гістологічне дослідження зрізів з різних ділянок печінки у піддослідних щурів, які фарбували гематоксиліном та еозином за загальноприйнятою методикою. Встановлено, що у разі штучного моделювання в щурів тетрацикліндукованого гепатозу загальна архітектоніка печінки зберігається. Водночас у хворих тварин зафіксовано масштабне пошкодження гепатоцитів та розвиток жирової і зернистої дистрофії. Частина пошкоджених клітин зазнавала руйнування з подальшим лізисом фрагментів зруйнованих клітин. Описані мікроскопічні зміни найбільше проявлялися на ділянках печінки під її капсулою. У результаті відмічалась часткова або повна дезорганізація печінкових пластинок в усіх часточках органу. Застосування хворим щурам фосфоліпідів молока у вигляді біологічно активної добавки «FLP-MD» в якості коригувальної терапії запобігало розвитку дискомплексації гепатоцитів, сприяло істотному зменшенні кількості зруйнованих клітин у стані дистрофії з поодинокими випадками порушення впорядкованої організації печінкових пластинок. Це свідчить про виражений стимулювальний вплив фосфоліпідів молока на процеси регенерації та відновлення гепатоцитів за тетрацикліндукованого ураження печінки в щурів. У випадку окремого застосування клінічно здоровим тваринам біодобавки на основі фосфоліпідів молока мікроскопічна будова зразків печінки не відрізнялася від такої у тварин контрольної групи. Результати дослідження мають практичну цінність для лікарів-патоморфологів, клініцистів і терапевтів за розвитку в тварин медикаментозної форми гепатопатології, особливо у разі застосування антибіотиків тетрациклінової групи, та для визначення стратегії у лікуванні таких хворих

Ключові слова: гістологічне дослідження; коригувальна терапія; дистрофія; гепатопатологія; ускладнення; фосфоліпіди молока