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Corrective efficacy of milk phospholipids in tetracycline-induced changes in the amino acid composition of blood in rats

Serhii Bryzhenko
Postgraduate Student
National University of Life and Environmental Sciences of Ukraine
03041, 15 Heroiv Oborony Str., Kyiv, Ukraine
https://orcid.org/0009-0001-5767-4634

Viktoriia Gryshchenko*
Doctor of Veterinary Sciences, Professor
National University of Life and Environmental Sciences of Ukraine
03041, 15 Heroiv Oborony Str., Kyiv, Ukraine
https://orcid.org/0000-0001-6601-1392

Abstract. The aim of the study was to establish the patterns of changes in the amino acid spectrum of whole blood in laboratory rats against the background of tetracycline-induced hepatopathy and the administration of milk phospholipids. To experimentally reproduce a model of acute hepatopathy, laboratory rats were intragastrically administered tetracycline hydrochloride at a dose of 250 mg/kg body weight for 7 days. Four groups were formed, including rats that were: clinically healthy; affected by tetracycline-induced hepatosis (without treatment); affected by tetracycline-induced hepatosis and administered milk phospholipids; clinically healthy and administered milk phospholipids. The amino acid profile of whole blood was determined using paper chromatography with ninhydrin detection. The development of an imbalance in the amino acid profile of whole blood in rats as a result of the cytotoxic effect of tetracycline hydrochloride on hepatocytes was experimentally established. In animals with experimental hepatopathy under conditions of spontaneous recovery, a significant increase in the level of the heterogeneous histidine/taurine/asparagine fraction (by 54%) was observed in whole blood, along with a tendency towards increased levels of the combined cystine/cysteine, glycine/serine, and ornithine cycle amino acid fractions. The concentration of individual amino acids remained relatively stable. Administration of the phospholipid dietary supplement to diseased animals was accompanied by a pronounced mobilisation of amino acids in the blood within the combined fractions of cysteine/cystine (by 161%), arginine/ornithine/lysine (by 69%), histidine/taurine/asparagine (by 196%), glycine/serine/

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Corresponding author (viktoriya_004@ukr.net)

glutamine/aspartic acid (by 92%), and valine/norvaline/tryptophan (by 86%), indicating stimulation of nitrogen metabolism and ureagenesis and reflecting activation of detoxification processes, antioxidant defence, and the hepatotropic effect of phospholipid correction. The obtained results may be used for the diagnosis of metabolic disturbances related to intermediate amino acid metabolism in drug-induced hepatopathies and as markers for evaluating the efficacy of newly developed medicinal products

Keywords: liver; hepatopathy; fatty hepatosis model; corrective therapy; paper chromatography; marker changes; drug-induced complications

Introduction

The problem of drug-induced liver injury (DILI) remains of considerable clinical and biomedical significance, since such lesions are accompanied by impaired functional status of the hepatobiliary system and, in some cases, may progress to acute liver failure. X. Yao *et al*. (2024) demonstrated that the commonly used antibiotics tetracycline and sulphadiazine exert a direct cytotoxic effect on liver cells: exposure in the Huh-7 cell model induced oxidative stress and membrane damage. Moreover, the toxicity of tetracycline proved to be significantly greater than that of sulphadiazine. These findings are consistent with the review by A. Borgne-Sanchez & B. Fromenty (2025), who emphasised that many drugs induce dysfunction of mitochondrial β-oxidation of fatty acids, leading to hepatic steatosis. In cases of marked inhibition of fatty acid β-oxidation, microvesicular steatosis developed with a risk of hypoglycaemia, whereas moderate inhibition resulted in macrovesicular steatosis, which over time progressed to steatohepatitis and cirrhosis. Within this pathogenesis, mitochondrial dysfunction and associated oxidative stress are key factors in the progression of hepatic lesions. Thus, excessive drug toxicity is capable of causing substantial disturbances in hepatic energy metabolism and provoking the accumulation of free radicals.

Oxidative stress necessitates activation of antioxidant defence mechanisms. L. Cesarini *et al*. (2024), in a systematic review, outlined the role of glutathione and other low-molecular-weight thiols in metabolic dysfunction-associated steatotic liver disease (MASLD). The researchers concluded that glutathione is critically important for maintaining redox balance in liver cells, and that disruption of glutathione homeostasis contributes to the development of steatosis. However, the authors noted that due to differences in measurement methodologies, it is currently impossible to define specific diagnostic threshold values for glutathione in MASLD. This indicates the need for standardised approaches to the investigation of hepatic redox status in future studies. Disturbances in oxidative metabolism are accompanied by alterations in the amino acid profile. L. Prechtl *et al*. (2024) identified a specific amino acid signature in coronary artery disease, characterised by decreased concentrations of ornithine cycle metabolites and antioxidant-related factors, namely histidine and lysine, which correlated with the severity of vascular lesions. The authors suggested that this signature reflected increased nitric oxide consumption and enhanced oxidative stress in affected patients.

Q. Tan *et al*. (2025) described another component of amino acid alterations, namely the tryptophan pathway. According to their review, metabolites of the kynurenine pathway (kynurenine and its derivatives) modulate immune response and hepatic fibrogenesis through activation of the aryl hydrocarbon receptor, suppression of T-cell activity, and inhibition of nuclear factor κB signalling pathways. Thus, alterations in this pathway may also influence the course of hepatopathology in both acute and chronic forms. Researchers Y. Yan *et al*. (2024) applied metabolomics and machine learning to a model

of post-hepatectomy liver regeneration. The authors identified a number of amino acid markers indicative of disturbances in relevant metabolic pathways during tissue recovery. These studies demonstrated that alterations in intermediate amino acid metabolism, both in cardiovascular pathology and during liver regeneration, are closely associated with oxidative status and general metabolic dysfunction.

Liver dysfunction significantly affects the metabolism of proteins and macronutrients. A study by S.K. Han *et al.* (2025) highlighted that appetite disorders and sarcopenia are extremely common in patients with chronic liver disease, and these conditions worsen the prognosis. The researchers described the complex interaction between the metabolism of carbohydrates, lipids and amino acids in liver cirrhosis. In this context, muscle tissue partially compensated for impaired liver function by detoxifying ammonia. Attention was also paid to the importance of branched-chain amino acids (BCAAs). Their deficiency contributed to muscle atrophy and encephalopathy, whilst the addition of BCAAs in many studies improved muscle mass and quality of life in patients. Although the results of these clinical trials remain inconclusive. Overall, an analysis of the scientific literature suggests that protein metabolism disorders and muscle mass loss are actual manifestations of metabolic imbalance in liver injury.

Thus, the available studies point to a specific chain of cause-and-effect relationships: drug toxicity causes mitochondrial dysfunction and oxidative stress in hepatocytes, leading to changes in the metabolism of amino acids and proteins. At the same time, none of the cited sources detailed the specific tetracycline-induced effects on the metabolism of nitrogen-containing compounds in the liver. Furthermore, there are no data in the literature regarding the possible corrective effect of milk phospholipids on these changes. All these factors point to an under-researched aspect of the problem and justify the relevance of a study dedicated to the effect of tetracycline-induced hepatopathy on amino acid metabolism and the role of the milk phospholipid fraction in restoring impaired metabolism.

The aim of the study was to identify the main patterns of disruption in the blood amino acid profile in rats with tetracycline-induced hepatopathy and to determine the corrective effect of the milk phospholipid fraction.

Literature Review

Current understanding of the pathogenesis of liver diseases highlights their close association with metabolic dysfunctions. Non-alcoholic fatty liver disease (NAFLD) affects approximately 30% of the world's population and is associated with obesity and metabolic syndrome. Drug-induced liver injury can be hepatocellular, cholestatic or mixed, and often involves immune/inflammatory responses. The main mechanisms of DILI include mitochondrial dysfunction, overproduction of reactive oxygen species (ROS), activation of apoptosis/necrosis, and immune-mediated damage to the bile ducts. The complex pathogenesis of DILI – a combination of metabolic and inflammatory factors – drives the search for new biomarkers and therapeutic approaches.

In this context, the amino acid profile of whole blood is considered a potential source of biomarkers for steatosis and fibrosis. Researchers A.I. Amanatidou *et al.* (2023) found that patients with NAFLD and obesity had elevated plasma concentrations of essential amino acids, particularly BCAAs (leucine, isoleucine, valine), and aromatic amino acids (e.g., tyrosine), compared with patients with a lower degree of steatosis. These amino acids correlated with the degree of hepatic steatosis as assessed by magnetic resonance imaging and with markers of fibrosis (MRI-cT1), indicating their diagnostic significance. Similarly, R. Allison *et al.* (2023) reported that DILI is associated with changes in amino acid metabolism, which are reflected in the ratios of hepatocellular to cholestatic lesions and immune responses. In patients with chronic hepatitis and hepatocellular carcinoma, S.E. Ghanem *et al.* (2022) observed a significant reduction in plasma BCAA levels

and an increase in aromatic amino acids (AAAs), which led to changes in the Fischer index (BCAA/tyrosine) – a potential non-invasive marker of liver disease severity. Together, these observations highlight the clinical value of assessing the blood amino acid profile as a marker of metabolic disturbances in hepatic steatosis.

Examining specific amino acid metabolic pathways is key to understanding the pathogenesis of steatosis and developing treatment strategies. The glutamate/serine/glycine (GSG) index was proposed by S. Leonetti *et al*. (2020) as a marker of NAFLD. The authors demonstrated that the GSG index was significantly higher in children with NAFLD and positively correlated with the percentage of fatty tissue in the liver and the level of aminotransferase activity. This suggests that metabolic imbalance in the glutamate and glycine cycles coincides with the progression of steatosis. Methionine and its metabolites also play an important role. In particular, Z. Li *et al*. (2020) noted in a review article that in chronic liver diseases, elevated concentrations of methionine and aromatic amino acids were observed, whilst BCAA levels decreased. At the same time, inhibition of the synthesis of S-adenosylmethionine (SAM), a key methyl group donor, was observed. SAM deficiency contributes to the progression of liver fibrosis and carcinogenesis.

The diagnostic relevance of the methionine cycle was confirmed by Y. Tang *et al*. (2022). The authors found higher levels of methionine metabolites, particularly S-adenosylhomocysteine (SAH) and homocysteine, in NAFLD, including a reduction in the SAM/SAH ratio. This suggested that disturbances in the metabolism of methionine, which accumulates during steatosis, may serve as a marker and a target for intervention. Taurine is another important factor which, according to a report by S. Baliou *et al*. (2021), acts as a potent antioxidant and cytoprotector – it supports mitochondrial function and glutathione stores, enhances antioxidant reactions, stabilises membranes and reduces the intensity of inflammation. This allows it to be considered a metabolic agent for mitigating oxidative stress in liver injury.

Tryptophan has also been found to have a protective effect on the liver. K. Gu *et al*. (2023) demonstrated that, in a model of lipopolysaccharide-induced liver failure, tryptophan helped to reduce the levels of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), H_2O_2 and malondialdehyde levels, and increased the activity of antioxidant enzymes, whilst simultaneously inhibiting the inflammatory pathways of pyroptosis and necroptosis. Thus, tryptophan improved parameters relating to both the development of oxidative stress and the onset of an inflammatory response resulting from liver injury. Y. Sun *et al*. (2023) obtained innovative results regarding the role of asparagine in acute toxic liver injury. In particular, increased expression of asparagine synthetase was observed in pericentral hepatocytes, and intravenous administration of asparagine was associated with a reduction in tissue necrosis. Mice with genetic inactivation of the asparagine synthetase gene exhibited more pronounced liver injury. However, with the additional administration of asparagine to the animals, this damage was almost completely reversed. These data highlight the importance of asparagine as a hepatoprotective agent during acute stress.

The link between amino acid metabolism and the manifestation of oxidative stress and inflammation is evident. Most of the amino acids listed are substrates for the synthesis of glutathione or other antioxidants. Z. Li *et al*. (2020) noted that methionine is one of the main target molecules for ROS, and disruption of its metabolism is associated with severe liver injury. Taurine has pronounced anti-inflammatory and antioxidant properties, whilst tryptophan is associated with increased activity of antioxidant enzymes and a reduction in oxidative stress. Against a background of amino acid imbalance, depletion of glutathione stores and excessive ROS formation exacerbate inflammation and promote the development of apoptosis and necrosis. Thus, disturbances in amino acid metabolism should be

considered a key link in the pathogenesis of DILI, and assessment of redox status is essential for a proper analysis of metabolic changes.

An experimental model of tetracycline-induced steatosis confirms the validity of metabolic correction. F. Aghaei *et al.* (2023) induced hepatic steatosis in rats via intraperitoneal administration of tetracycline (140 mg/kg). In these animals, significant lipid accumulation in hepatocytes and signs of oxidative stress were observed. In response, the application of physical exercise and the probiotic L. rhamnosus GG contributed to an increase in the activity of superoxide dismutase and high-density lipoproteins, and a reduction in the levels of triacylglycerols, ALT, AST and alkaline phosphatase (ALP). This indicates that combined therapeutic approaches are capable of mitigating tetracycline-induced liver injury. An analysis of existing studies suggests that a focus on metabolic and protective factors is promising, justifying the feasibility of evaluating the efficacy of the phospholipid fraction of milk as a potential therapeutic agent, which has already been partially demonstrated in studies of the amino acid profile of the liver and bile in experimental rats with tetracycline-induced hepatosis (Bryzhenko & Gryshchenko, 2026).

Despite the known changes in amino acid metabolism in NAFLD and DILI, there is a lack of direct data on the characteristics of the amino acid profile in tetracycline-induced steatosis. Studying these nitrogen metabolism metabolites in the blood of animals will enable the identification of specific markers of liver injury and the elucidation of its molecular mechanisms. This also highlights the need for new protective approaches, as amino acids that regulate redox and immune homeostasis may serve as criteria for determining the efficacy of therapeutic agents with hepatoprotective effects.

Materials and Methods

The experiment on laboratory rats was initiated on 15 January 2024 at the vivarium of the Educational and Scientific Institute of High Technologies of Taras Shevchenko National University of Kyiv (Kyiv, Ukraine), which is equipped with centralised water supply, sewage, ventilation, and air-conditioning systems. Chromatographic investigations of the amino acid profile of whole blood from experimental animals were conducted over the following two months (February-March 2024). Experimental procedures were carried out in accordance with the requirements of Directive 2010/63/EU (2010), Law of Ukraine No. 3447-IV (2006), and Order of the Ministry of Education and Science, Youth and Sports of Ukraine No. 249 (2012), and were additionally approved by the Bioethics Commission of the National University of Life and Environmental Sciences of Ukraine (NULES of Ukraine) (Protocol No. 10 dated 10 October 2023).

Clinically healthy male laboratory rats aged 3 months and weighing 180-220 g were used in the experiment. All experimental animals were assigned to groups and housed in separate cages under a standard vivarium diet with free access to feed and drinking water. Prior to the scientific experiment, the rats underwent a two-week quarantine period with clinical examination and regular monitoring of body weight and feed consumption. The duration of the experiment was 9 days.

According to the methodology of D. Korolova *et al.* (2023), fatty hepatosis was artificially modelled in laboratory rats. To reproduce hepatopathology, a soft silicone probe was used for daily intragastric administration of a 4% tetracycline hydrochloride solution at a dose of 250 mg/kg body weight for 7 days. Intragastric administration of high doses of tetracycline hydrochloride induced the development of fatty hepatosis in rats. Animals receiving intragastric tetracycline hydrochloride without subsequent therapy were assigned to the "Self-rehabilitation" group (n = 6). Rats in the "Tetracycline + Supplement" group (n = 6) received intragastric administration of a 1% solution of the dietary supplement "FLP-MD", based on the milk phospholipid fraction (experimental series, NULES of Ukraine), 1 hour prior to antibiotic administration. The dietary supplement was administered intragastrically for 9 days, one

hour before antibiotic administration, and additionally for two days after completion of the intoxication course. The daily dose of "FLP-MD" was 13.5 mg/kg body weight (Melnychuk *et al.*, 2009). The next experimental group, the "Supplement" group, consisted of clinically healthy animals additionally receiving milk phospholipids as part of the "FLP-MD" dietary supplement (n = 6). Rats administered distilled water in a volume equivalent to that of the antibiotic and dietary supplement were included in the "Control" group (n = 6). Throughout the experiment, daily monitoring of body weight was performed using ORION OS-0K22 electronic scales (ORION ELECTRONICS LTD, Europe), allowing dose adjustment of the administered substances. On day 10, blood samples were collected from rats of all groups for subsequent investigation of their amino acid profile. The spectrum of free amino acids was determined using partition paper chromatography with ninhydrin detection, modified on the basis of the classical methods of R. Consden *et al.* (1944) and S.M. Partridge (1948), taking into account the approaches of S. Moore & W.H. Stein (1948) and R.J. Block *et al.* (1955), which enabled qualitative and quantitative investigation of the amino acid composition of biological material, with the exception of proline and hydroxyproline, which produce a non-specific reaction with ninhydrin.

Sample preparation. Since certain amino acids possess similar Rf coefficient values and are incompletely separated under one-dimensional chromatography conditions, preliminary concentration of the samples was performed prior to analysis. For this purpose, each sample was applied three times in 20 µL aliquots onto a 3.5 × 3.5 cm square of ash-free filter paper, with each previous layer dried before application of the next. After saturation with the sample, the paper was fragmented into small pieces and placed into a test tube containing 2 mL of extraction mixture consisting of acetone : ethanol : water (7:2:1, by volume). This procedure ensured desorption of amino acids into solution and partial separation from macromolecules and salts capable of complicating further analysis. Following extraction, the solution was evaporated to dryness in an air stream at room temperature, and the dry residue was dissolved in 15 µL of distilled water. The obtained concentrate was applied onto the starting line of chromatographic paper in three successive 5 µL droplets at intervals of approximately 15 minutes for drying, resulting in the formation of a compact concentrated spot. The principle of repeated sample application to improve chromatographic analysis accuracy corresponds to the approach described by R.H. Hackman & M. Lazarus (1956). Preliminary elution of amino acids from saturated filter paper was used as an authorial modification of the method.

Chromatographic separation. Chromatographic paper Filtrak FN-1 (Germany) was used as the stationary phase for chromatographic separation. The mobile phase consisted of a six-component solvent mixture: isoamyl alcohol (Carlo Erba, France), n-butanol (Carlo Erba, France), glacial acetic acid (Merck, Germany), formic acid (BASF, Germany), distilled water, and butyl benzyl ether (Thermo Fisher Scientific, USA), mixed in a ratio of 21:8:10:1:10:1 (by volume) with the addition of 0.2% ninhydrin (Thermo Fisher Scientific, USA). Chromatography was performed by ascending paper chromatography in a sealed chamber, pre-saturated with vapours of this mobile phase (Consden *et al.*, 1944; Williams & Kirby, 1948). The sample application zones were positioned on a starting line approximately 2-3 cm from the lower edge of the paper. Development of the chromatogram lasted approximately 7 hours, during which the solvent travelled almost the entire length of the paper strip. If necessary, repeated solvent runs or extension of the development time to 12-20 hours may be employed to improve separation. However, in the present study, a single chromatographic run of approximately 7 hours was sufficient for separation of most fractions.

Development of the chromatogram. Following chromatographic separation, the paper strip was removed from the chamber and dried in a fume hood at room temperature for

approximately 1 hour until complete removal of residual solvent vapours. To visualise amino acids, the chromatogram was placed in a drying cabinet (Labexpert 3015, Ukraine) at 45°C for 120 minutes. During this period, ninhydrin (Thermo Fisher Scientific, USA), included in the mobile solvent, reacted directly with amino acids on the paper, forming coloured products. Consequently, additional application of the reagent was not required. The mild heating regime (45°C for 2 hours) ensured gradual development of amino acid spots. For comparison, standard methodologies involve brief immersion of the dried paper chromatogram in a ninhydrin solution, followed by repeated drying and heating for approximately 15 minutes at 60°C to produce purple spots (R.J. Block *et al.*, 1955). The approach applied in the present study, in which ninhydrin was incorporated directly into the eluent, simplified the visualisation procedure while providing an equivalent result.

Quantitative analysis. Following visualisation, amino acid spots were quantitatively evaluated using reflection densitometry. The intensity of spot coloration was measured in reflected light using a DO-1M densitometer (Ukraine). The use of spectral reflectometry for analysis of ninhydrin spots on chromatograms is a recognised approach for quantitative amino acid determination. Calibration curves were preliminarily constructed by applying known quantities of standard amino acids onto chromatographic paper, followed by the complete separation and visualisation procedure and measurement of the optical density of the resulting spots. Within the linear range of the ninhydrin reaction, optical density of coloration was proportional to the quantity of the corresponding amino acid. Optical density values obtained for experimental samples were compared with the calibration curve for the relevant amino acid, allowing determination of its concentration in the sample while taking into account dilution introduced during sample preparation. If individual amino acids were not separated because of similar Rf values and co-localised on the chromatogram, their quantities were recorded collectively, or additional separation approaches were applied, including solvent modification or two-dimensional chromatography.

Statistical analysis of the results. The obtained experimental data were processed using methods of variation statistics in Microsoft Excel 2016 software (Microsoft Corp., USA). For each parameter, the arithmetic mean (M), standard deviation (SD), and standard error of the mean (m) were determined. Statistical significance of differences between means was assessed using Student's t-test for independent samples with unequal variances (two-sample unequal variance t-test), with a significance level of $p < 0.05$.

Results and Discussion

The amino acid composition of blood was investigated as an informative marker of the systemic metabolic response of the organism to tetracycline-induced liver injury and to the corrective influence of the milk phospholipid fraction. Whole blood reflects integrated alterations in nitrogen-containing compound metabolism, providing grounds for considering its amino acid profile as a sensitive indicator of metabolic restructuring under conditions of toxic exposure in animals. The results present indicators of heterogeneous amino acid fractions in the whole blood of animals from different experimental groups in comparison with the control group. This approach made it possible to identify the most sensitive indicators of amino acid metabolism and to assess the direction of their alterations depending on the development of the hepatotoxic process and the application of the corrective factor. Collectively, this provides a basis for a more detailed interpretation of the role of individual amino acids in the mechanisms of liver injury and metabolic adaptation.

The heterogeneous cysteine/cystine fraction (Fig. 1) in the whole blood of rats with tetracycline-induced liver injury was considered one of the most sensitive indicators of redox homeostasis disturbance. In particular, rats with

tetracycline-induced hepatopathology ("Tetracycline + Supplement" group) receiving intragastric administration of the milk phospholipid fraction demonstrated an increase in the content of the heterogeneous cysteine/cystine fraction components by 161%, whereas in healthy animals receiving milk phospholipids ("Supplement" group), their concentration increased by only 65% compared with the control group (0.51 ± 0.07 mg%). In contrast, rats in the "Self-rehabilitation" group exhibited a tendency towards a 20% decrease in cysteine/cystine levels compared with the control.

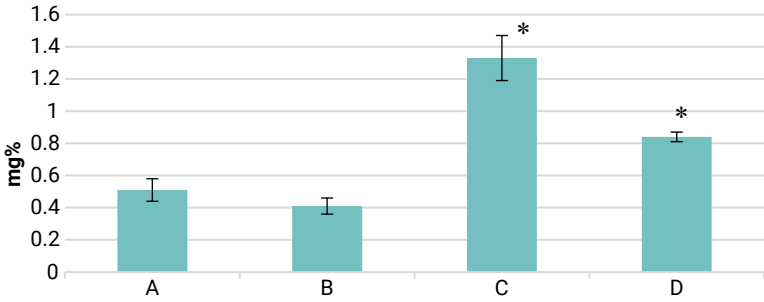

Figure 1. *Concentration of the cysteine/cystine fraction in the whole blood of rats with tetracycline-induced hepatosis following corrective therapy based on milk phospholipids (n = 6, M ± m)*

Note: * – $p < 0.05$, values significantly different compared with the control group of rats; A – clinically healthy animals, "Control" group; B – rats with tetracycline-induced hepatosis, "Self-rehabilitation" group; C – rats with tetracycline-induced hepatosis administered the milk phospholipid fraction, "Tetracycline + Supplement" group; D – clinically healthy rats administered the milk phospholipid fraction, "Supplement" group

Source: authors' own work

The peculiarities of the established changes may be associated with the fact that, under tetracycline-induced liver injury, a sharp increase in the content of cysteine/cystine amino acids may result from pronounced oxidative stress, activation of the methionine-homocysteine cycle, and "overloading" of the thiol reserve, when cysteine is massively mobilised for the resynthesis of glutathione and taurine, and is partly released into the bloodstream from damaged hepatocytes. In the group of animals receiving milk phospholipids, the marked increase in the concentration of amino acids of this fraction probably reflected moderate activation of their metabolism and enhanced synthesis and turnover of glutathione without pronounced liver injury. The established patterns are consistent with those described in the review by L. Cesarini *et al.* (2024), who emphasised that low-molecular-weight thiols, primarily cysteine and glutathione, are central components of redox homeostasis, and that their imbalance is closely associated with the severity of metabolic dysfunction-associated fatty liver disease. Y. Wang *et al.* (2018) additionally demonstrated that disruption of bile acid signalling alters cysteine catabolism and glutathione regeneration, thereby increasing liver susceptibility to oxidative injury, which corresponds to the findings of the present study showing a sharp increase in the total blood content of cysteine/cystine under tetracycline-induced hepatotoxic stress.

The experimentally established patterns indicate substantial activation of antioxidant defence mechanisms in the organism of rats with experimental hepatopathology, whereas further analysis of amino acids associated with the ornithine cycle allows a deeper assessment of alterations in the detoxification function of the liver (Fig. 2). In particular, the blood concentration of the arginine/ornithine/lysine amino acid fraction in rats of the "Self-rehabilitation" group remained within the control range, whereas in rats with tetracycline-induced fatty hepatosis treated with the milk phospholipid fraction, it increased by 69% relative to the control group (1.39 ± 0.19 mg%). In the group of healthy animals receiving the milk

phospholipid fraction (the "Supplement" experimental group), the total level of these amino acids exceeded the control values by 57%.

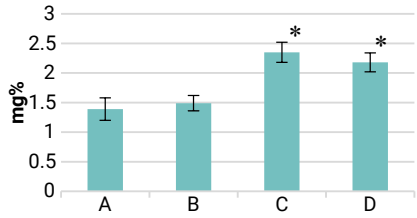

Figure 2. *Concentration of the arginine/ornithine/lysine fraction in the whole blood of rats with tetracycline-induced hepatosis following corrective therapy based on milk phospholipids (n = 6, M ± m)*

Note: * – $p < 0.05$, values significantly different compared with the control group of rats; A – clinically healthy animals, "Control" group; B – rats with tetracycline-induced hepatosis, "Self-rehabilitation" group; C – rats with tetracycline-induced hepatosis administered the milk phospholipid fraction, "Tetracycline + Supplement" group; D – clinically healthy rats administered the milk phospholipid fraction, "Supplement" group

Source: authors' own work

Thus, the most pronounced increase in the total blood content of arginine/ornithine/lysine in rats was observed specifically under tetracycline-induced injury ("Tetracycline + Supplement" group). In contrast, in the group of clinically healthy rats receiving the dietary supplement "FLP-MD" ("Supplement" group), this indicated moderate but persistent activation of nitrogen metabolism. From a biochemical perspective, arginine and ornithine are key metabolites of the ornithine cycle, which ensures ammonia detoxification, whereas lysine, as an essential amino acid, reflects the overall intensity of proteolysis and protein synthesis. The marked increase in the blood content of these amino acids in animals with tetracycline-induced fatty hepatosis treated with the dietary supplement "FLP-MD" ("Tetracycline + Supplement" group) may be interpreted as a consequence of their enhanced mobilisation in response to liver injury. In turn, the increase in blood arginine/ornithine/lysine levels in clinically healthy animals receiving the milk phospholipid fraction ("Supplement" group) was probably associated with stimulation of nitrogen metabolism and ureagenesis without pronounced cytolysis, which may reflect the anabolic and hepatotropic effects of phospholipid correction. Similar alterations in the arginine-ornithine pathway during liver injury have also been described by other authors. W. Saitoh *et al*. (2014), using models of acute liver injury in rats, demonstrated that the plasma arginine-to-ornithine ratio changes significantly, and that both amino acids may be regarded as specific biomarkers of liver injury. In a broader clinical context, L. Prechtl *et al*. (2024) showed that reduced concentrations of urea cycle amino acids (particularly arginine and ornithine) and lysine in circulating blood were associated with poorer outcomes in coronary heart disease, interpreting this as a sign of intensified ureagenesis and oxidative stress. Against this background, the multidirectional increase in the arginine/ornithine/lysine amino acid group in models of tetracycline-induced fatty hepatosis with and without phospholipid correction further highlights the sensitivity of urea cycle amino acids to the state of hepatic nitrogen metabolism and their potential use as biomarkers.

Alongside amino acids of the ornithine cycle, fractions associated with antioxidant defence are also of considerable importance. In this regard, quantitative changes in the total histidine/taurine/asparagine fraction were analysed in the whole blood of experimental rats (Fig. 3). In the whole blood of diseased rats from the "Self-rehabilitation" group, the content of the total histidine/taurine/asparagine fraction increased by 54% relative to the control group (0.94 ± 0.10 mg%), whereas in the group of animals with tetracycline-induced fatty hepatosis treated with the milk phospholipid fraction, its level increased by 196% compared with the control group. In healthy rats receiving milk phospholipids ("Supplement" group), this amino acid fraction showed only a tendency towards an increase of 18%.

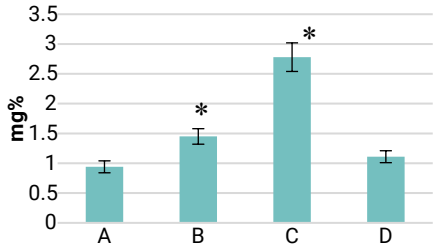

Figure 3. *Concentration of the histidine/taurine/asparagine fraction in the whole blood of rats with tetracycline-induced hepatosis following corrective therapy based on milk phospholipids (n = 6, M ± m)*

Note: * – $p < 0.05$, values significantly different compared with the control group of rats; A – clinically healthy animals, "Control" group; B – rats with tetracycline-induced hepatosis, "Self-rehabilitation" group; C – rats with tetracycline-induced hepatosis administered the milk phospholipid fraction, "Tetracycline + Supplement" group; D – clinically healthy rats administered the milk phospholipid fraction, "Supplement" group

Source: author's own work

The established patterns observed in animals of the "Self-rehabilitation" group may result from activation of protective mechanisms, since histidine exhibits buffering properties and participates in anti-inflammatory reactions (through carnosine and histamine), taurine is a key antioxidant and substrate for bile acid conjugation, and asparagine supports nitrogen and energy metabolism. In acute tetracycline-induced hepatocyte injury combined with the reparative effect of the milk phospholipid fraction, the sharp increase in the histidine/taurine/asparagine fraction compared with its content in animals of the "Self-rehabilitation" group probably reflected a combination of: enhanced synthesis of taurine and histidine-containing dipeptides and peptides in response to oxidative stress-induced inflammation; release of these amino acids into the bloodstream from damaged hepatocytes; and intensification of nitrogen metabolism, in which asparagine acts as an acceptor of amino groups. In healthy animals receiving phospholipids, only slight quantitative shifts in the amino acid parameters of this fraction were observed, indicating that phospholipid administration alone does not induce pronounced hyperaminoacidaemia of this amino acid group. A similar interpretation of these patterns was reported by S. Baliou *et al.* (2021), who described the marked hepatoprotective and antioxidant effects of taurine, contributing to the reduction of oxidative stress, steatosis, and mitochondrial dysfunction in various models of liver injury. This corresponds with the results described in the present study in response to tetracycline-induced hepatocyte damage. In turn, Y. Sun *et al.* (2023) indicated that activation of the asparagine synthetase pathway and increased asparagine availability protect pericentral hepatocytes during acute toxic liver injury, thereby reducing necrosis and improving cell survival. Against this background, the experimentally observed moderate increase in histidine/taurine/asparagine levels in the blood of rats from the "Self-rehabilitation" group and the sharp rise in their levels in animals of the "Tetracycline + Supplement" group may be interpreted as reflecting mobilisation of these amino acids in protective processes (antioxidant, anti-inflammatory, and detoxification), which is consistent with previously published experimental findings.

For further assessment of metabolic rearrangements in the organism of rats under the toxic effects of tetracycline on the liver, quantitative changes in the total glycine/serine/glutamine/aspartic acid fraction in whole blood were examined, as these amino acids are associated with nitrogen transport and detoxification processes (Fig. 4). Regarding the glycine/serine/glutamine/aspartic acid amino acid complex in whole blood, statistically significant changes were observed only in diseased rats of the "Tetracycline + Supplement" group, in which the concentration increased by 92% compared with the control group (1.75 ± 0.27 mg%). In animals of the "Self-rehabilitation" group and in clinically healthy rats receiving the milk phospholipid fraction ("Supplement" group), only a tendency towards increased values of this parameter was observed.

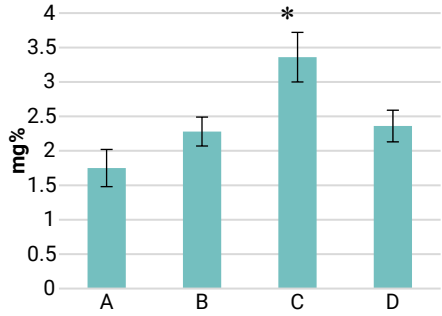

Figure 4. *Concentration of the combined glycine/serine/glutamine/aspartic acid fraction in the whole blood of rats with tetracycline-induced hepatosis following corrective therapy based on milk phospholipids (n = 6, M ± m)*

Note: * – $p < 0.05$, values significantly different compared with the control group of rats; A – clinically healthy animals, "Control" group; B – rats with tetracycline-induced hepatosis, "Self-rehabilitation" group; C – rats with tetracycline-induced hepatosis administered the milk phospholipid fraction, "Tetracycline + Supplement" group; D – clinically healthy rats administered the milk phospholipid fraction, "Supplement" group

Source: author's own work

The established patterns may indicate that, under tetracycline-induced liver injury, the sharp increase in the content of glycine/serine/glutamine/aspartic acid reflects activation of gluconeogenesis and alternative pathways of nitrogen detoxification. In particular, glutamine and asparagine serve as "reservoirs" for ammonia in cases of suppression of the urea cycle, whereas glycine and serine are mobilised as donors of one-carbon groups and substrates for glutathione synthesis. Against the background of tetracycline-induced mitochondrial dysfunction, the administration of milk phospholipids stimulates mobilisation of these amino acids in order to maintain adequate antioxidant, detoxification, and energy-dependent processes, which explains their accumulation in the blood. In clinically healthy animals receiving milk phospholipids ("Supplement" group), the absence of statistically significant differences in the levels of the studied amino acids compared with control values indicated a neutral effect of these phospholipids on nitrogen metabolism parameters and the implementation of antioxidant mechanisms. A similar role of glycine and serine in redox homeostasis during fatty hepatosis was described by S. Leonetti *et al.* (2020), who proposed the GSG index (glutamate/(serine + glycine)) as a non-invasive marker of paediatric NAFLD: decreased total serine and glycine levels and an increased GSG index were associated with greater hepatic fat content and elevated ALT activity. Thus, the substantial increase in the content of this heterogeneous fraction in the whole blood of rats under a model of acute tetracycline-induced hepatotoxic stress may be regarded as an early sign of strain in nitrogen metabolism and maintenance of antioxidant balance stability, which partly corresponds to changes described in the literature (primarily regarding quantitative changes in glutamine), but differs from the chronic metabolic context of NAFLD, where glycine and serine are often depleted.

At the next stage, quantitative parameters of the methionine/glutamic acid heterogeneous fraction, which characterises individual pathways of one-carbon and amino acid metabolism, were analysed (Fig. 5). In the case of the total methionine/glutamic acid amino acid fraction in the whole blood of rats, no statistically significant changes relative to the control group were recorded. In the "Self-rehabilitation" group, their level practically did not differ from the control value (1.86 ± 0.20 mg%), whereas in the group of animals with tetracycline-induced fatty hepatosis treated with the milk phospholipid fraction ("Tetracycline + Supplement"), only a tendency towards an increase in the parameter by 28% was observed, and in clinically healthy animals receiving the milk phospholipid fraction ("Supplement" group), the value exceeded the control level by 32%. Thus, the quantitative parameters of this amino acid fraction remained relatively stable even against the background of tetracycline-induced injury and administration of milk phospholipids.

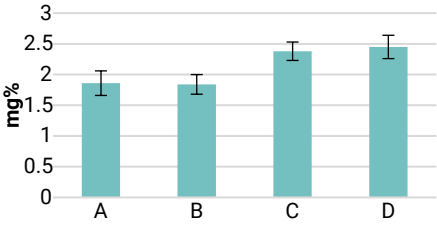

Figure 5. *Concentration of the combined methionine/glutamic acid fraction in the whole blood of rats with tetracycline-induced hepatosis following corrective therapy based on milk phospholipids (n = 6, M ± m)*

Note: * – p < 0.05, values significantly different compared with the control group of rats; A – clinically healthy animals, "Control" group; B – rats with tetracycline-induced hepatosis, "Self-rehabilitation" group; C – rats with tetracycline-induced hepatosis administered the milk phospholipid fraction, "Tetracycline + Supplement" group; D – clinically healthy rats administered the milk phospholipid fraction, "Supplement" group

Source: author's own work

The established findings may be interpreted as indicating the preservation of stability in one-carbon metabolism and transsulphuration pathways: methionine continued to be utilised for the synthesis of SAM, polyamines, and glutathione, whereas glutamic acid functioned as a key donor of amino groups in transamination reactions and as a substrate of the urea cycle. Clinical observations reported by Y. Tang *et al.* (2022) demonstrated that patients with NAFLD exhibited elevated levels of methionine metabolites, S-adenosylhomocysteine, and homocysteine, together with a reduced SAM/SAH ratio, confirming the presence of steatosis. Against this background, the absence of significant alterations in the present heterogeneous fraction in the conducted experiment indicates a relatively moderate degree of hepatocellular injury and partial preservation of methionine cycle regulation compared with the more severe or prolonged chronic processes described in clinical studies.

To assess possible alterations in gluconeogenesis and anabolic processes in the experimental rats, the quantitative parameters of the total alanine/tyrosine/threonine fraction were investigated (Fig. 6). In the heterogeneous fraction comprising this amino acid complex in the whole blood of rats, only tendencies towards quantitative changes relative to the control group (1.61 ± 0.28 mg%) were observed. In particular, in animals of the "Self-rehabilitation" group, the total concentration of these amino acids decreased by 43% compared with the control level, whereas in rats with tetracycline-induced hepatosis receiving the milk phospholipid fraction ("Tetracycline + Supplement" group), it increased by 49%. In clinically healthy animals receiving the milk phospholipid fraction ("Supplement" group), the concentration increased by 37% relative to the control group.

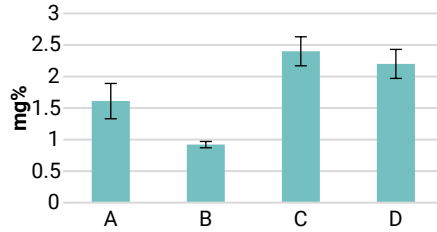

Figure 6. *Concentration of the combined alanine/tyrosine/threonine fraction in the whole blood of rats with tetracycline-induced hepatosis following corrective therapy based on milk phospholipids (n = 6, M ± m)*

Note: * – p < 0.05, values significantly different compared with the control group of rats; A – clinically healthy animals, "Control" group; B – rats with tetracycline-induced hepatosis, "Self-rehabilitation" group; C – rats with tetracycline-induced hepatosis administered the milk phospholipid fraction, "Tetracycline + Supplement" group; D – clinically healthy rats administered the milk phospholipid fraction, "Supplement" group

Source: author's own work

The identified tendencies in the quantitative changes of the investigated amino acid fraction indicated the relative stability of its parameters under conditions of acute liver injury in the experimental setting. The biological significance of this amino acid profile is consistent with the fact that alanine is a key gluconeogenic substrate and a marker of metabolic stress, whereas tyrosine belongs to the aromatic amino acids that are sensitive to impaired hepatic detoxification. In a clinical study by A.I. Amanatidou *et al.* (2023),

patients with obesity and NAFLD demonstrated significantly elevated plasma levels of L-alanine, L-threonine, and L-tyrosine, together with other amino acids, in groups with more pronounced hepatic steatosis and fibrosis. The findings obtained by these researchers confirmed that activation of gluconeogenesis and accumulation of aromatic amino acids in the blood are characteristic features of progressive chronic liver pathology. At the same time, the results reported by S.E. Ghanem *et al*. (2022) showed that in chronic hepatitis and hepatocellular carcinoma, it was specifically the increase in tyrosine and other aromatic amino acids against a background of decreased BCAA levels that altered the Fischer ratio and reflected hepatic insufficiency, whereas no such pronounced alterations were recorded in the present experiment.

Further analysis of the amino acid pool of whole blood in the experimental rats focused on determining the quantitative parameters of the total valine/norvaline/tryptophan fraction, the components of which reflect the specificity of alterations in BCAA and tryptophan metabolism (Fig. 7). In particular, a significant increase in the total concentration of the components of this fraction was observed in the whole blood of rats from the "Tetracycline + Supplement" and "Supplement" groups, by 86% and 50%, respectively, compared with the control group (1.61 ± 0.18 mg%). At the same time, diseased rats of the "Self-rehabilitation" group showed only a tendency towards an increased concentration of this heterogeneous amino acid fraction (by 64%) relative to the control group, indicating incomplete spontaneous restoration of their amino acid profile. The identified pattern may be interpreted as evidence of profound disturbances in the metabolism of BCAA (primarily valine) and the aromatic amino acid tryptophan under tetracycline-induced hepatotoxic stress. The sharp increase in the total concentration of valine/norvaline/tryptophan in whole blood reflected a combination of enhanced proteolysis in skeletal muscle and reduced utilisation of BCAA by the damaged liver, which typically occurred against a background of energy deficiency in hepatocytes. Administration of milk phospholipids to the experimental rats reduced the amplitude of these alterations, which may be associated with partial restoration of mitochondrial BCAA oxidation, membrane integrity, and transamination efficiency. However, they did not ensure complete normalisation of the amino acid profile. Likewise, elevated tryptophan levels may reflect a shift in its metabolism towards the kynurenine pathway, which is activated during inflammation and oxidative stress and provides substrates for the formation of immunomodulatory and antioxidant metabolites. The obtained results are consistent with contemporary metabolomic studies in MASLD/NAFLD. Regarding tryptophan, the review by Q. Tan *et al*. (2025) noted that metabolites of the kynurenine pathway play a dual role in liver diseases: on the one hand, they modulate the immune response and reduce oxidative stress, while on the other hand, under chronic activation, they may promote fibrosis and disease progression. Experimental work by K. Gu *et al*. (2023) in piglets demonstrated that dietary tryptophan supplementation attenuated lipopolysaccharide-induced liver injury, enhanced antioxidant activity, and reduced the expression of necroptosis and pyroptosis markers. Overall, this suggests that in the tetracycline-induced model of hepatopathology, the increase in the total level of valine/norvaline/tryptophan, as well as its partial restoration against the background of milk phospholipid administration, reflects a balance between catabolic processes (proteolysis, insulin resistance, activation of the inflammatory response) and adaptive mechanisms associated with BCAA- and tryptophan-dependent pathways. Thus, the pronounced quantitative alterations in the valine/norvaline/tryptophan fraction confirm substantial restructuring of energy and protein metabolism during experimental tetracycline-induced liver injury in laboratory rats.

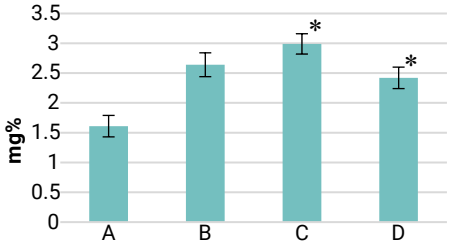

Figure 7. *Concentration of the combined valine/norvaline/tryptophan fraction in the whole blood of rats with tetracycline-induced hepatosis following corrective therapy based on milk phospholipids (n = 6, M ± m)*

Note: * – p < 0.05, values significantly different compared with the control group of rats; A – clinically healthy animals, "Control" group; B – rats with tetracycline-induced hepatosis, "Self-rehabilitation" group; C – rats with tetracycline-induced hepatosis administered the milk phospholipid fraction, "Tetracycline + Supplement" group; D – clinically healthy rats administered the milk phospholipid fraction, "Supplement" group

Source: authors' own work

The next stage of the analysis of the blood amino acid profile involved investigating the quantitative characteristics of the total leucine/norleucine/phenylalanine fraction in the whole blood of the experimental rats. The obtained results made it possible to assess the degree of stability of individual components of protein metabolism under conditions of medicinal toxic stress on the liver and the applied corrective intervention (Fig. 8). In particular, only moderate deviations relative to the control group (2.77±0.29 mg%) were recorded for the total concentration of leucine/norleucine/phenylalanine amino acids in the whole blood of animals from all groups. In rats of the "Self-rehabilitation" group, the total concentration of these amino acids showed a tendency to increase by 3%, in animals of the "Tetracycline + Supplement" group it changed by 5%, and in clinically healthy animals of the "Supplement" group by 9% compared with the control group. Thus, this amino acid complex may be regarded as relatively stable even under conditions of tetracycline-induced liver injury and the corrective influence of milk phospholipids. The obtained results differed from the pattern described by researchers in chronic liver diseases, where decreased BCAA levels (particularly leucine) and increased phenylalanine concentrations with a reduced Fischer ratio were considered typical. In the study by B. Kinny-Köster *et al.* (2016), alterations in plasma phenylalanine levels and the BCAA/AAA ratio were associated with mortality in patients with end-stage liver disease. In the work of M. Yamakado *et al.* (2017), the combination of BCAA with phenylalanine enabled differentiation between patients with fatty liver disease and individuals without steatosis, with amino acid alterations being considerably more pronounced than those observed in the present experiment. Against this background, the absence of significant quantitative changes in the leucine/norleucine/phenylalanine amino acid complex in the experimental rats rather indicates preservation of BCAA metabolism and the absence of pronounced decompensation in this metabolic direction, which is consistent with a model of acute rather than chronic toxic liver injury, as well as with the investigation of the amino acid pool in whole blood rather than plasma.

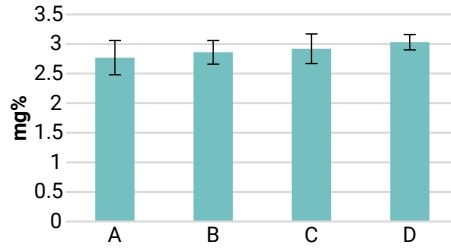

Figure 8. *Concentration of the combined leucine/norleucine/phenylalanine fraction in the whole blood of rats with tetracycline-induced hepatosis following corrective therapy based on milk phospholipids (n = 6, M ± m)*

Note: * – p < 0.05, values significantly different compared with the control group of rats; A – clinically healthy animals, "Control" group; B – rats with tetracycline-induced hepatosis, "Self-rehabilitation" group; C – rats with tetracycline-induced hepatosis administered the milk phospholipid fraction, "Tetracycline + Supplement" group; D – clinically healthy rats administered the milk phospholipid fraction, "Supplement" group

Source: authors' own work

Generalisation of the presented results demonstrated that the blood amino acid profile in tetracycline-induced hepatosis changed unevenly, with predominant involvement of those metabolic pools responsible for adaptation to oxidative stress, maintenance of nitrogen balance, and compensation for impaired liver function. The most pronounced response was observed in clusters associated with thiol metabolism, ureagenesis, antioxidant-related amino acids, and certain energetically important substrates, indicating the selective nature of metabolic restructuring during toxic liver injury of medicinal origin. Comparison of the results regarding alterations in the amino acid pool in animals from different experimental groups demonstrated that, against the background of administration of milk phospholipids in the form of the dietary supplement "FLP-MD", quantitative shifts in heterogeneous amino acid fractions acquired a different directionality compared with animals undergoing spontaneous self-rehabilitation, indicating modification of the systemic biochemical response of the organism under the influence of different factors. Thus, the identified alterations reflected not only the presence of hepatotoxic stress, but also the specific features of metabolic adaptation under conditions of corrective intervention.

Conclusions

The study demonstrated that tetracycline-induced hepatosis in rats is accompanied by pronounced alterations in the amino acid profile of whole blood, reflecting the systemic metabolic response of the organism to toxic liver injury. The amino acid fractions most sensitive to the effects of tetracycline were those associated with redox homeostasis, ammonia detoxification, nitrogen metabolism, and energy metabolism, namely cysteine/cystine, arginine/ornithine/lysine, histidine/taurine/asparagine, glycine/serine/glutamine/aspartic acid, and valine/norvaline/tryptophan fractions. Animals in the "Self-rehabilitation" group were characterised by signs of metabolic imbalance with accumulation of certain amino acid fractions involved in antioxidant defence and nitrogen metabolism, indicating delayed spontaneous recovery following tetracycline exposure. In particular, this group demonstrated a significant increase in the histidine/taurine/asparagine fraction by 54% compared with the control group, whereas changes in other amino acid fractions were predominantly trend-related in nature. The character of the detected alterations indicates that under conditions of tetracycline toxicity, metabolic stress develops alongside activation of nitrogen binding and excretion mechanisms, enhancement of antioxidant defence, and restructuring of amino acid supply to hepatocytes in response to cytotoxic injury.

The increased levels of certain amino acid fractions in whole blood reflected mobilisation of substrates required for maintenance of redox balance, detoxification reactions, and compensation for impaired hepatic functional status. At the same time, the absence of statistically significant changes in the heterogeneous methionine/glutamic acid, alanine/tyrosine/threonine, and leucine/norleucine/phenylalanine fractions indicated the selective nature of the metabolic response during acute tetracycline-induced injury. Administration of milk phospholipids as part of the dietary supplement "FLP-MD" was accompanied by pronounced restructuring of the blood amino acid profile. In particular, a significant increase was observed in the heterogeneous cysteine/cystine fraction by 161%, arginine/ornithine/lysine by 69%, histidine/taurine/asparagine by 196%, glycine/serine/glutamine/aspartic acid by 92%, and valine/norvaline/tryptophan by 86% compared with the control group, indicating a corrective and modulatory effect under conditions of drug-induced hepatosis. At the same time, administration of the milk phospholipid fraction to clinically healthy animals did not produce signs of severe metabolic distress, further confirming the adaptive rather than damaging nature of the observed alterations. In the group of healthy animals receiving milk phospholipids (the "Supplement" group), significant increases were detected in the

heterogeneous cysteine/cystine fraction by 65%, arginine/ornithine/lysine by 57%, and valine/norvaline/tryptophan by 50% relative to the control.

The obtained findings collectively demonstrate that the amino acid spectrum of whole blood sensitively reflects the severity of metabolic disturbances in tetracycline-induced hepatosis and may be used as an informative criterion for evaluating the systemic response of the organism to drug-induced toxic exposure. The practical significance of the study lies in substantiating the feasibility of further investigation of milk phospholipids as a promising means of metabolic correction in drug-induced hepatopathies in veterinary medicine, as well as in the use of amino acid fractions as potential markers for the preclinical assessment of the efficacy of corrective interventions. The obtained results expand current understanding of the metabolic mechanisms underlying tetracycline-induced liver injury and provide a foundation for further experimental validation of amino acid parameters as early biomarkers of toxic hepatopathy. Future studies are planned to determine the patterns of changes in the protein spectrum of the liver and whole blood in laboratory rats, taking into account the amino acid profile alterations described in the present study during the development of drug-induced fatty liver disease.

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None.

Conflict of Interest

None.

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Коригувальна ефективність фосфоліпідів молока за тетрациклініндукованих змін амінокислотного складу крові в щурів

Сергій Бриженко
Аспірант
Національний університет біоресурсів і природокористування України
03041, вул. Героїв Оборони, 15, м. Київ, Україна
https://orcid.org/0009-0001-5767-4634
Вікторія Грищенко
Доктор ветеринарних наук, професор
Національний університет біоресурсів і природокористування України
03041, вул. Героїв Оборони, 15, м. Київ, Україна
https://orcid.org/0000-0001-6601-1392

Анотація. Метою дослідження було встановити закономірності змін амінокислотного спектра нативної крові в лабораторних щурів на тлі розвитку тетрациклініндукованої гепатопатології та застосування фосфоліпідів молока. Для експериментального відтворення моделі гострої форми гепатопатії лабораторним щурам упродовж 7 діб внутрішньошлунково вводили тетрацикліну гідрохлорид у дозі 250 мг/кг маси тіла. Було сформовано чотири групи, які включали щурів: клінічно здорових; хворих на тетрациклініндукований гепатоз (без лікування); хворих на тетрациклініндукований гепатоз, яким вводили фосфоліпіди молока; клінічно здорових, яким застосовували фосфоліпіди молока. Амінокислотний профіль нативної крові визначали методом паперової хроматографії з нінгідриновим проявленням. Експериментально встановлено розвиток дисбалансу в амінокислотному профілі нативної крові щурів внаслідок цитотоксичного впливу тетрацикліну гідрохлориду на гепатоцити. У хворих на експериментальну гепатопатологію тварин за умов самореабілітації відзначалося достовірне підвищення в нативній крові рівня гетерогенної фракції гістидину/таурину/аспарагіну (на 54 %) та тенденцією до зростання вмісту сумарних фракцій цистину/цистеїну, гліцину/серину й амінокислот орнітинового циклу. Концентрація окремих амінокислот залишалася відносно стабільною. Введення хворим тваринам фосфоліпідної біодобавки супроводжувалось вираженою мобілізацією в крові амінокислот у складі сумарних фракцій цистеїну/цистину (на 161 %), аргініну/орнітину/лізину (на 69 %), гістидину/таурину/аспарагіну (на 196 %), гліцину/серину/глутаміну/аспарагінової кислоти (на 92 %) та валіну/норваліну/триптофану (на 86 %), що вказувало на стимуляцію азотного обміну й уреагенезу та відображало активацію процесів детоксикації, антиоксидантного захисту та гепатотропний ефект фосфоліпідної корекції. Отримані результати можуть бути використані для діагностики метаболічних порушень, які стосуються проміжного обміну амінокислот, за гепатопатології медикаментозного ґенезу та як маркери для оцінки ефективності новостворених препаратів

Ключові слова: печінка; гепатопатологія; модель жирового гепатозу; коригувальна терапія; паперова хроматографія; маркерні зміни; медикаментозні ускладнення