



Correction of the clinical and biochemical status of high-producing cows during the transition period

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Abstract. The relevance of this study is determined by the increasing number of diagnosed metabolic diseases in high-yielding cows during the transition period, particularly ketosis, fatty liver disease and their complications, including liver cirrhosis, reproductive dysfunctions and subsequent early culling of cows. Timely measures for preventing metabolic diseases during the transition period are important, as they involve the use of corrective therapy to normalise metabolism and increase productivity. Therefore, this study aimed to investigate the effect of a complex preparation on the clinical and biochemical status of high-producing cows during the transition period. Two groups were formed for the experiment: a control group and an experimental group, with 10 cows in each. During the experiment, general methods of clinical examination of cows were used, including inspection, palpation, percussion and thermometry, as well as biochemical analysis of blood serum parameters, including spectrophotometry and chromatography. These methods made it possible to identify biological markers for assessing changes in the clinical condition and individual metabolic pathways in cows under the influence of the complex preparation. The use of the complex preparation based on biologically active substances led to an increase in blood serum levels of glucose by 25.6%, the total lipoprotein fraction by 55.7%, vitamin A by 35.9% and vitamin E by 2.1 times in cows of

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the experimental group. It also reduced aspartate aminotransferase activity by 51.3%, the De Ritis ratio by 62.3%, the level of non-esterified fatty acids by 2.16 times and beta hydroxybutyrate by 42.7%. Early identification of the causes of metabolic disorders and pathological changes in the liver of high-producing cows during the transition period, together with the timely preventive use of a complex preparation based on biologically active components, made it possible to prevent the development of secondary diseases, particularly fatty hepatodystrophy, and to reduce economic losses caused by lower milk yield and the culling of cows under the conditions of a specific farm

Keywords: liver; hepatodystrophy; general clinical condition of the organism; biochemical analysis; spectrophotometry; high-performance liquid chromatography; biologically active substances

Introduction

Dairy farming is an important branch of animal husbandry; however, its efficiency is largely limited by the spread of metabolic disorders in high-producing cows, especially during the transition period. At this stage, animals experience the greatest physiological strain owing to the shift from the dry period to intensive lactation. This process is accompanied by a negative energy balance, mobilisation of fat reserves, impaired functional status of the liver and an increased risk of ketosis, fatty hepatodystrophy and other postpartum complications. These pathologies reduce milk productivity, impair reproductive function, increase treatment costs and may lead to the premature culling of animals, creating both a veterinary and an economic problem for dairy farms.

In this context, V. Kolosha (2022) noted that the economic efficiency of dairy farming should be considered in terms of animal reproduction, production intensification and optimisation of product volumes throughout the year. V.V. Vlizlo *et al.* (2021) reported that the high milk productivity of cows on farms largely depends on their health. The average productive lifespan of cows in countries with highly developed dairy farming is 3-4 years. This is considerably shorter than the natural lifespan of dairy cattle. The culling of cows on farms is associated with reduced milk productivity and impaired

reproductive function, which result from the development of various pathologies. The morbidity of high-producing cows on dairy farms is caused by disruptions in the technological processes of housing and feeding. Diseases in cows are especially common during the postpartum period. After calving, dairy cows are often diagnosed with metabolic disorders and lesions of the internal organs. Liver diseases in cows, in particular, are among the most common conditions and occur far more frequently than previously assumed, as these pathologies are either subclinical or present with general and non-specific symptoms.

D. Kibkalo *et al.* (2024) demonstrated that fatty degeneration is one of the leading liver pathologies in cows kept at dairy complexes. This pathology causes substantial economic losses, including the costs of treatment, lost income due to an irreversible reduction in milk productivity, acquired symptomatic diseases and infertility. C. Zhang *et al.* (2023) indicated that the liver is a key organ in the regulation of overall metabolism. Therefore, hormonal status, particularly in high-producing dairy cows, may be reflected in changes in the functional state of the liver, leading to the development of a range of local and systemic inflammatory and degenerative processes. Most often, this is fibrosis, a common pathology in cows with fatty

liver degeneration, which develops as a result of oxidative stress, inflammation and hepatocyte death. In particular, C.A. Risco & P. Melendez (2022) noted that, due to oxidative stress and hepatocyte inflammation, cows become more susceptible to secondary diseases, including ketosis, displaced abomasum, mastitis, retained placenta, metritis, reduced fertility and low milk production.

According to the findings of V.M. Olihevskiy & S.V. Huralaska (2025), metabolic disorders in first-lactation dairy cows impair the functional capacity of hepatocytes by altering their histological structure. In particular, diffuse vacuolisation of the hepatocyte cytoplasm, diffuse necrosis and lymphocytic-macrophage infiltration of the portal tracts were observed with the concurrent development of ketosis and endometritis. In cows with ketosis and hypocalcaemia, extensive hepatocyte vacuolisation, generalised tissue necrosis and mild lymphocytic-macrophage infiltration were recorded. In cases of ketosis and mastitis, marked diffuse vacuolisation of hepatocytes, indicating severe fatty degeneration, moderate diffuse necrosis and accumulation of inflammatory cells were observed, which pointed to focal chronic hepatitis. In cows in the second and third lactations, hepatocyte changes were even more pronounced, with the development of severe hepatitis combined with chronic inflammation and early fibrosis, reflecting a high level of metabolic stress. Thus, the authors indicated substantial morphofunctional changes in the liver under polymorbid pathology in cows, depending on the lactation period and the combination of metabolic diseases.

According to Ye. Mekuriaw (2023), feeding and housing practices, as well as breed differences, may lead to different degrees of negative energy balance in dairy cows. Holstein cows mobilise significantly more body energy at the beginning of lactation than Danish Red and

Jersey cows. Primiparous cows are more susceptible to metabolic stress during the transition period than multiparous cows. Therefore, the duration and severity of negative energy balance in dairy cows depend on their housing conditions. Although negative energy balance is common in highproducing dairy cows and may have consequences ranging from mild to severe, its extent can be minimised through proper feeding and the use of feed additives. Cows that were fed diets with a higher energy value had a better energy balance.

The transition period is extremely important in determining the future health of reproductive dairy cows and milk production. This period lasts from three weeks before calving to three weeks after calving, when the cow moves from the dry period to lactation. As noted by Ö. Kizil & M. Kizil (2023), the transition from pregnancy to a stage accompanied by intensive lactation is very often a critical factor. The welfare and productivity of cows can be substantially improved by identifying the factors that explain their high morbidity during the transition period. A key factor during this period is lipid metabolism in cows, as excessive lipid mobilisation from adipose tissue is associated with a higher incidence of health problems in these animals during the transition period.

This study aimed to determine the effect of an experimental complex preparation on the clinical status and selected aspects of carbohydrate, lipid, vitamin and mineral metabolism in highproducing cows during the transition period.

Literature Review

The most critical stage in dairy farming is the transition period. This is the time when the cow's requirements for nutrients needed for milk synthesis increase rapidly. M. Mezzetti *et al.* (2021) indicated that the rapid increase in milk yield during lactation leads to a mismatch

between nutrient requirements and the animals' adaptation to the negative energy and protein balance caused by the characteristics of late pregnancy and early lactation. For these reasons, numerous metabolic diseases often occur at the beginning of lactation, causing losses in dairy farming.

In their report, J.R. Roche *et al.* (2013) noted that reduced appetite in over-conditioned cows after calving causes a negative energy balance at the beginning of lactation, which leads to increased lipolysis of adipose tissue. This, in turn, results in even greater fat mobilisation and causes more pronounced fatty liver degeneration. Intensive lactogenesis directly contributes to substantial body weight loss in the animal. Therefore, cows are forced to mobilise body reserves, particularly from adipose and muscle tissue. During early lactation, a cow may lose approximately 20 kg of muscle tissue and 8 to 57 kg of body fat. E. Bombik *et al.* (2020) demonstrated that fatty liver degeneration is one of the most important metabolic diseases in high-producing cows during the early stages of lactation. The disease usually begins about 10 days after calving. Without appropriate treatment, fatty liver degeneration may lead to other metabolic disorders, infectious diseases or reproductive problems.

J. Habel & A. Sundrum (2020) indicated that an increased plasma level of non-esterified fatty acids (NEFAs) results from adipose tissue remodelling, which leads to their uptake by the liver in proportion to their plasma concentration. A concurrent deficiency of oxaloacetate, which is largely used for gluconeogenesis, together with elevated NEFA levels, leads to the accumulation of acetylCoA in the liver. Subsequently, instead of acetyl-CoA being utilised through the complete Krebs cycle, incomplete oxidation (ketogenesis) and re-esterification occur, followed by the storage of triacylglycerols (TAGs) in the liver. In addition to the

adverse effect of accumulated TAGs on overall liver function, elevated β -hydroxybutyrate levels impair the gluconeogenic capacity of hepatocytes. Thus, lipolysis becomes excessive, and glucose balance is substantially disrupted.

However, according to P. Melendez & P. Pinedo (2024), when hepatocytes take up large amounts of NEFAs, the process of β -oxidation may become overloaded, and their excess may again be used for TAG synthesis and for the generation of very low-density lipoproteins (VLDLs) for export into the bloodstream. The export of TAGs from the liver as VLDLs is a slow process in cattle and decreases during intense fatty acid oxidation and ketogenesis, leading to TAG accumulation in the liver. S. Oikawa *et al.* (2010) noted that TAGs in the liver are not broken down, oxidised or removed, and signs of fatty hepatodystrophy therefore develop rapidly.

Accordingly, D. Đuričić & M. Sablić (2025) demonstrated that treatment of affected animals should be aimed at restoring glucose and glycogen levels in the body, normalising acid-base balance and the functions of the liver, cardiovascular system and digestive system, and restoring mineral and vitamin metabolism. V.V. Vlizlo *et al.* (2021) indicated that a shortage of sugar, a low ratio between readily available carbohydrates and digestible protein, and other feeding-related factors cause metabolic disorders in cows. A dietary sugar deficiency intensifies gluconeogenesis, the mobilisation of lipids from depots and their accumulation in the liver. By contrast, P. Mandebvu *et al.* (2003) noted that preparations which reduce the mobilisation of fatty acids from adipose tissue or increase the export of lipoproteins from the liver may be used to prevent fatty liver degeneration and ketosis.

V. Horobets (2021) noted that the daily addition of protected vitamins, including choline, folic acid, riboflavin and vitamins A, D and E, to the diet during the transition period

increases dry matter intake in cows, improves their general health after calving and reproductive function, and normalises metabolism. As reported by J.M. Bollatti (2020), feeding protected choline to cows during the transition period increased milk yield and milk components, while also ensuring efficient feed utilisation during the first 105 days after calving, regardless of the animal's body condition. The author concluded that the use of protected choline reduces the nutrient requirements for maintenance in cows at the beginning of lactation or improves the uptake and transport of nutrients for the synthesis of milk components. Moreover, its effect on cow productivity is not necessarily mediated by improved markers of metabolic health or reduced TAG levels in the liver.

Studies conducted in the USA and the Netherlands have repeatedly shown that the addition of protected choline to the diet of cows promotes phospholipid synthesis and, according to M.A. Caudill (2010), substantially reduces fat accumulation in the liver. Ö. Kizil & M. Kizil (2023) indicated that magnesium deficiency in the blood plasma of cows with fatty liver degeneration, or hepatic lipidosis, during the early stages of lactation is not a direct cause of this condition, but only a contributing factor, as deficiency of this macroelement may aggravate inflammation and stress. At the same time, an adequate magnesium supply supports metabolism by helping to prevent excessive fat mobilisation, or lipolysis, which leads to fatty liver degeneration.

According to A. Pirestani & M. Aghakhani (2018), the addition of betaine to the diet of highproducing cows during the transition period has lipotropic, hepatoprotective and productivityenhancing effects. Betaine stimulates the export of TAGs from the liver by increasing the availability of methionine and S-adenosylmethionine (SAM) for the synthesis of phosphatidylcholine and apoproteins. It

also induces the expression of genes involved in fatty acid β -oxidation, has antioxidant and anti-inflammatory effects, and improves cellular resistance to heat stress.

The studies cited above confirm the substantial effect of chemically diverse substances on metabolism in high-producing cows during the period of increasing milk yield. However, the development and testing of a complex preparation for the treatment and prevention of metabolic diseases in cows during the transition period remains relevant, as does the study of its effect on the functional state of the liver, particularly the activity of cellular enzymes and selected metabolites of carbohydrate and lipid metabolism.

Materials and Methods

The studies were conducted during 2025 under the conditions of an industrial farm in eastern Ukraine, using Holstein cattle. The farm was free from infectious and invasive diseases. The cows were kept in standard tied-housing facilities. The lighting level in the building where the cows were housed was 200 lux. The floor in the cow area was covered with rubber mats. Feeding took place at a feed table positioned at the level of the sole of the cow's forelimbs. The animals were supplied with tap water through automatic drinkers.

Cows on days 50-70 of their first lactation were selected for the experiment, corresponding to the period of intensive increase in milk productivity. Two groups were formed: a control group and an experimental group, with 10 animals in each. The cows' diet consisted of the following feeds: hay, straw, maize silage, haylage, cornage, molasses and compound feed containing sunflower and soybean meal, as well as wheat, maize, chalk, salt, a premix for dairy cows and a buffer. All feed ingredients were mixed into a single total mixed ration in the proportions specified in the prescribed diet.

The dietary components were calculated and included in the diet in the amounts required for the corresponding physiological period of the cows and their needs during this period.

The cows in the control group received feed according to the standard diet. The cows in the experimental group received the same diet and the experimental complex preparation *Metanorm*, hereinafter referred to as the complex preparation. The preparation contains essential minerals, including magnesium, zinc, cobalt, copper, manganese, iron and molybdenum, as well as silymarin, methionine, choline chloride, L-carnitine, betaine, niacin and vitamin E, which have a positive effect on metabolism in animals. The preparation was administered at a dose of 40.7 g per animal once daily for 20 days. The clinical status of cows in both groups was assessed using generally accepted methods. During the study, the animals' habitus, the condition of the visible mucous membranes, hair coat, skin, superficial lymph nodes, and individual organs and systems were evaluated.

For the laboratory study, blood samples were collected from the cows before administration of the preparation, 10 and 20 days afterwards. For the analysis of biochemical blood parameters, samples were collected from five cows in each group into sterile disposable vacuum tubes containing silicon dioxide as a clot activator. During transport, the blood samples were stored in an insulated bag with cold packs and separated by a layer of cotton wool to slow biochemical processes in whole blood cells and, consequently, prevent changes in blood parameters.

The necessary methods, reagents and instruments were selected for laboratory studies to determine metabolic parameters in cows. Blood serum analysis included determination of lipoprotein content (total fraction), NEFAs, beta-hydroxybutyrate, vitamins A and E, glucose, total calcium and inorganic phosphorus, as well as the activity of aspartate

aminotransferase (AST), alanine aminotransferase (ALT) and alkaline phosphatase (ALP). Biochemical parameters were determined using an automatic biochemical analyser, *Biochem-200*, HTI (USA), with biochemical reagents produced by HTI (High Technology Inc., USA). Vitamin levels were determined using a high-performance liquid chromatograph, *LC 300*, PerkinElmer (USA), with a reversed-phase C18 column. Laboratory studies were carried out at the Biosafety Centre, the Research Centre for Biosafety and Environmental Control of Agro-Industrial Resources, Dnipro State Agrarian and Economic University, Dnipro.

Statistical processing of the study results was performed using Microsoft Excel 2016. The significance of the obtained results was determined using Student's t-test. A difference between values was considered statistically significant when the coefficient (P) did not exceed 0.05, which is a generally accepted approach in scientific research.

During the experiment involving the use of the newly developed preparation to normalise metabolism in cows after the end of the transition period on a dairy farm, all bioethical requirements concerning animals were observed in accordance with Law of Ukraine No. 249 (2012) and the European Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes (1986).

Results and Discussion

The choice of the complex preparation as a means of preventing metabolic pathologies in highproducing cows was associated with its composition, which includes a complex of essential macro- and microelements, as well as substances of different chemical nature: silymarin, protected methionine, choline chloride, L-carnitine, betaine and vitamin E. These components have a positive effect on metabolic processes in animals. The action of the

preparation is primarily aimed at preventing the most common metabolic pathologies of the transition period, namely ketosis and hepatic lipodosis, by optimising metabolism and thereby normalising biochemical blood parameters. A major advantage is the integrated approach to preventing the development of irreversible changes in cows during negative energy balance in the period of intensive lactation.

Before the complex preparation was administered, the clinical signs of metabolic disorders in cows were not pronounced. Among the existing symptoms, mild depression, reduced mobility and a pale pink conjunctival colour were observed, while the pulse rate was at the upper limit of the physiological range or slightly increased. The cows' appetite was variable and reduced; pica and weak rumen contractions were also recorded. Body temperature in these animals remained within the physiological range. In some cows, the area of hepatic dullness extended beyond the last rib. The

superficial lymph nodes accessible for clinical examination showed no visible changes. After 20 days of complex preparation and administration, cows in the experimental group consumed feed more actively; the animals rose readily and approached the feeder at each feed distribution. Signs of pica disappeared.

Determination of aspartate aminotransferase (AST) activity in blood serum is important for early diagnosis and for monitoring treatment in cows. Before administration of the complex preparation, serum AST activity in cows of both the control and experimental groups exceeded the upper limit of the physiological range (Table 1). This indicated liver cell damage caused by fatty infiltration, as V.I. Levchenko *et al.* (2002) noted that, with the development of fatty hepatosis in cows, AST activity rises above the upper limit of the physiological range already at the stage of ultramicroscopic organ changes, when the activity of other enzymes still changes only slightly.

Table 1. Blood serum enzymes in the experimental cows during the transition period, $M \pm m$, $n = 5$

Parameter	At the beginning of the experiment/before administration of the preparation		10 days after administration of the preparation		20 days after administration of the preparation		Reference range
	Control group	Experimental group	Control group	Experimental group	Control group	Experimental group	
Aspartate aminotransferase, U/L	128.33 ± 12.76	101.33 ± 4.36	134.33 ± 15.26	92.67 ± 4.01*	153.0 ± 6.27	49.33 ± 6.39 ^Δ	10-50
Alanine aminotransferase, U/L	29.33 ± 1.52	26.67 ± 0.76	33.67 ± 1.87	30.0 ± 1.59	34.67 ± 1.84	34.0 ± 0.37*	10-40
De Ritis ratio (AST/ALT), units	4.43 ± 0.54	3.82 ± 0.22	4.09 ± 0.65	3.13 ± 0.24	4.46 ± 0.27	1.44 ± 0.17 ^Δ	1.03.4
Alkaline phosphatase, U/L	128.0 ± 8.4	98.67 ± 3.27 ^Δ	169.0 ± 25.96	109.0 ± 4.15 ^Δ	138.13 ± 16.17	125.33 ± 60.79*	20150

Note: * – $P < 0.05$, significant compared with the value before administration of the preparation; $\Delta P < 0.05$, significant compared with the control group

Source: authors' development

Observation of cows in the control group and determination of serum AST activity over the 20-day experiment showed a tendency towards an increase of 19.2% compared with the

value recorded before administration of the preparation. This indicates a gradual increase in damage to the cell membranes of the liver. By contrast, administration of the complex

preparation to cows in the experimental group reduced serum AST activity by 8.5% as early as day 10 and by 2.05 times on day 20 compared with the value at the beginning of the experiment. On day 20 of complex preparation administration, serum AST activity in cows of the experimental group was significantly lower than that in cows of the control group, by more than 3 times. This indicates that the ingredients of the administered preparation contributed to the restoration of cell membranes and the liver parenchyma as a whole, and also led to normalisation of the functional state of the liver.

For cattle, the assessment of AST activity in blood serum is more informative, whereas ALT has relatively low activity in the cells of large animals. During the study, ALT activity remained within the physiological range. Following administration of the complex preparation, serum ALT activity in cows of the experimental group increased significantly by 27.4% compared with the value recorded before treatment. An increase in ALT activity within the physiological range may indicate greater intensity of metabolic processes in cows under the influence of the ingredients of the complex preparation. Consistent changes were also observed in the De Ritis ratio, which is determined as the ratio of serum AST activity to ALT activity. On day 20 of complex preparation administration, the De Ritis ratio in the blood serum of cows in the experimental group decreased significantly by 2.6 times compared with its value before administration of the preparation and by 3 times compared with its level in animals of the control group on day 20 of the experiment.

Throughout the study period, serum ALP activity in cows showed minor fluctuations both over time within each group and between the groups. However, its values remained within physiological limits. Before administration of the complex preparation, serum ALP activity

in cows of the experimental group was significantly lower, by 22.9%, than that in cows of the control group. After 10 days of the experimental period, the significant difference remained, and ALP activity in the blood serum of animals in the experimental group was 35.5% lower. However, after 20 days of the experiment, the activity of this enzyme in cows of the experimental group was remaining 9.3% lower, although no significant difference between these values was recorded. The increase in serum ALP activity in cows of the experimental group within the physiological range may indicate more intensive metabolism in the mammary gland, caused by increased milk yield. After 20 days of complex preparation and administration, cows in the experimental group, unlike animals in the control group, showed a significant increase in milk yield of 3.4 L per animal compared with the beginning of the experiment.

During the analysis of biochemical blood parameters before administration of the complex preparation, a low serum glucose concentration was found in cows of both the control and experimental groups (Table 2). This value was below the minimum physiological reference level. This may indicate a carbohydrate deficiency in the feed components of the diet during intensive lactation and confirms that the animals were in a state of negative energy balance. According to data published by the National Academies of Sciences (2021), plasma glucose concentration decreases after calving. Under physiological conditions, glycogen reserves in the liver of cows begin to be replenished and increase by day 14 after calving. This probably reflects activation of the gluconeogenic metabolic pathway of glucose formation in hepatocytes, which is important for maintaining an adequate level of lactation. If this process is impaired, the cow may develop ketosis, lipomobilisation syndrome and hepatic lipidosis.

Table 2. Biochemical parameters in the blood serum of the experimental cows during the transition period, $M \pm m$, $n = 5$

Parameter	At the beginning of the experiment/before administration of the preparation		10 days after administration of the preparation		20 days after administration of the preparation		Reference range
	Control group	Experimental group	Control group	Experimental group	Control group	Experimental group	
Glucose, mmol/L	2.23 ± 0.04	2.07 ± 0.02	2.57 ± 0.04	2.60 ± 0.04*	2.37 ± 0.06	2.60 ± 0.13*	2.54-1.6
Vitamin E, µg/mL	5.46 ± 0.48	3.83 ± 0.54	6.47 ± 0.63	4.9 ± 0.61	6.39 ± 0.54	8.02 ± 0.70*	3.014.0
Vitamin A, µg/100 mL	23.52 ± 0.85	22.26 ± 0.65	30.68 ± 0.21*	25.89 ± 2.06	26.54 ± 1.35	30.24 ± 2.82*	12.550.0
Non-esterified fatty acids, mmol/L	0.52 ± 0.03	0.54 ± 0.04	0.48 ± 0.04	0.32 ± 0.04*Δ	0.49 ± 0.04	0.25 ± 0.04*Δ	up to 0.25
Beta-hydroxybutyrate, mmol/L	1.14 ± 0.04	1.17 ± 0.04	1.07 ± 0.05	0.89 ± 0.04*Δ	1.09 ± 0.05	0.67 ± 0.05 *Δ	0.6-0.8
Lipoproteins, mg%	442.0 ± 37.59	438.67 ± 38.87	436.33 ± 39.79	655.20 ± 53.17*Δ	594.0 ± 36.72	683.0 ± 41.91*	400800
Total calcium, mmol/L	2.57 ± 0.02	2.43 ± 0.02Δ	2.5 ± 0.04	2.5 ± 0.04	2.4 ± 0.04	2.53 ± 0.06	2.43.12
Inorganic phosphorus, mmol/L	2.03 ± 0.07	1.87 ± 0.11	1.77 ± 0.18	1.6 ± 0.04	2.27 ± 0.06	2.03 ± 0.15	1.5-2.2
Ca/P, units	1.27 ± 0.03	1.33 ± 0.08	1.53 ± 0.15	1.57 ± 0.02	1.07 ± 0.04	1.27 ± 0.11	1.2-1.6

Note: * – $P < 0.05$, significant compared with the value before administration of the preparation; Δ $P < 0.05$, significant compared with the control group

Source: authors' development

As a result of administering the complex preparation, a significant increase in serum glucose concentration was recorded in cows of the experimental group on both day 10 and day 20, by 25.6% compared with the value at the beginning of the experiment. During this period, a tendency towards an increase in serum glucose content was also observed in animals of the control group. However, after 20 days, its content remained below the lower limit of the physiological range and was 9.7% lower than that in the blood serum of cows in the experimental group. The increase in serum glucose content in cows of the experimental group compared with the control group after 20 days of complex preparation administration may be due to the presence of cobalt in its composition. Cobalt chloride enhances the breakdown of fibre by rumen microorganisms and, according to O.O. Skyba (2005), glucose synthesis in animals

decreases under hypocobaltosis. The increase in serum glucose content in cows of the experimental group under the effect of the complex preparation contributed to the normalisation of glucose levels and prevented metabolic disorders associated with glucose deficiency. In addition, M. Ardalán *et al.* (2010) reported the effect of another ingredient of the complex preparation, protected choline. In particular, the authors assessed the effect of choline on the incidence and severity of ketosis in cows fed protected choline during the periparturient or transition period. This was accompanied by a significant increase in blood glucose content and a decrease in the levels of fatty acids and β-hydroxybutyrate. The effect of the complex preparation on selected indicators of lipid metabolism and fat-soluble vitamins in the blood serum of cows during the period of increasing lactation was studied. Before administration

of the preparation, the content of vitamin E in the blood serum of cows in the experimental group was at the lower limit of the physiological range, whereas in the blood serum of cows in the control group, this indicator was 42.6% higher, although no significant difference was recorded (Table 2).

The low content of vitamin E in the blood serum of cows in the experimental group may be a sign of fatty liver degeneration. I. Politis (2012) noted that low vitamin E content is associated with reduced hepatocyte function, for example, lower intensity of gluconeogenesis and ureagenesis, increased oxidative stress indicators, such as a lower plasma α -tocopherol concentration, and intensified inflammation. At the same time, L.M. Sordillo (2013) also reported a decrease in plasma α -tocopherol concentration during the transition period, which, in the author's view, may affect immune function. Therefore, a deficient level of vitamin E may contribute to the activation of oxidative stress, thereby provoking the development of immunosuppression.

Administration of the complex preparation to cows led to a significant increase in vitamin E content in the blood serum of cows in the experimental group after 20 days, by almost 2.1 times compared with its level in these animals before the preparation was used. In the blood serum of cows in the control group, only a tendency towards an increase in vitamin E content was found: by 18.5% on day 10 and by 17.0% on day 20 compared with this indicator at the beginning of the experiment. On day 20 of preparation administration, vitamin E content in the blood serum of cows in the experimental group was 25.5% higher than that in cows of the control group. The increase in serum vitamin E content in cows of the experimental group may indicate restoration of the antioxidant status of the experimental animals under the effect of the complex preparation, as vitamin E acts

in the body as a stabiliser of unsaturated fatty acid metabolism. This prevents the formation of peroxide and hydroperoxide compounds, provides antioxidant protection and thereby maintains the integrity of cell membranes.

The vitamin A content in the serum of cows in both groups remained within the physiological range throughout the experiment. At the same time, certain fluctuations and differences were recorded in the serum vitamin A content of cows in the control and experimental groups. In the blood serum of cows in the control group, vitamin A content increased significantly by 30.4% after 10 days of the experimental period compared with the value at the beginning. In the blood serum of cows in the experimental group, vitamin A content also increased significantly, by 35.8%, after 20 days of the experimental period, compared with the value recorded before administration of the complex preparation. Administration of the complex preparation contributed to a tendency towards a 13.9% increase in vitamin A content in the blood serum of cows in the experimental group on day 20 compared with that in cows of the control group. The increase in vitamin A content in the blood serum of cows in the experimental group may contribute to the stabilisation of the structural state of cell membranes and to a reduction in the activity of indicator enzymes. K. Schulz *et al.* (2025) noted that vitamin A plays an important role in the interaction of proteins and lipids in cell membranes, supports their function and regulates permeability, while its deficiency increases the elimination of cellular enzymes. In addition, vitamin A plays a significant role in maintaining the functional state of the liver and prevents the development of hepatic lipodosis in dairy cows, while its deficiency may intensify metabolic stress. Ensuring an adequate level of vitamin A in the blood supports liver and immune cell function, reducing the

incidence of fatty liver degeneration and related metabolic disorders.

R. Jorritsma *et al.* (2001) demonstrated that plasma NEFA levels in cows increase when animals are in a state of negative energy balance. This may occur when dry matter intake decreases during the prepartum period and almost always occurs during the first few weeks of lactation, since feed intake is low while energy requirements are high, leading to mobilisation of body reserves. Before administration of the complex preparation, serum NEFA levels in cows were high compared with reference values. Since serum NEFA levels are elevated in most cows during the perinatal period, a certain degree of fat accumulation in the liver is observed in early lactation. As shown by H. Abu Damir *et al.* (1994), low glucagon content leads to low blood glucose concentration, low insulin levels and high fatty acid mobilisation, causing lipomobilisation and fatty degeneration of the liver.

Administration of the complex preparation to cows in the experimental group led to a significant decrease in serum NEFA content: by 40.7% as early as day 10 and by 2.16 times on day 20 compared with the value at the beginning of the experiment. In the blood serum of cows in the control group, this indicator decreased by only 5.8% after 20 days of the experimental period compared with the value at the beginning of the experiment. On day 20 of complex preparation administration, the NEFA content in the blood serum of cows in the experimental group decreased by 1.96 times compared with that in cows of the control group. The reduction in NEFA content (Table 2) in the blood serum of cows in the experimental group under the effect of the complex preparation indicated positive metabolic changes in the body and a reduction in lipomobilisation syndrome. By contrast, signs of lipomobilisation syndrome remained in cows of the control group. These changes may be due to inclusion of magnesium

in the complex preparation. N.C. Ünal *et al.* (2025) found that magnesium has a moderate negative correlation with NEFAs and a moderate positive correlation with glucose. The obtained results indicated that NEFA levels increase due to negative energy balance and against the background of hypomagnesaemia. Magnesium deficiency may indirectly increase the incidence of transition-period diseases in dairy cows and weaken their metabolic adaptation. Ö. Kizil & M. Kizil (2023) noted that magnesium deficiency in the blood plasma of cows with fatty liver degeneration, or hepatic lipodosis, during the early stages of lactation is not a direct cause of this condition, but only a contributing factor, as magnesium deficiency may aggravate inflammation and stress. At the same time, an adequate magnesium supply supports metabolism by helping to prevent excessive fat mobilisation, or lipolysis, which leads to fatty liver degeneration. Magnesium is involved in numerous enzymatic reactions in the liver related to carbohydrate metabolism and protein synthesis. It also supports antioxidant defence mechanisms, protecting liver cells from peroxide damage.

The most characteristic signs of lipomobilization syndrome and fatty hepatodystrophy include weight loss, reduced milk productivity, a depressed general condition and other clinical manifestations. The 4.2 L decrease in milk yield in cows of the control group after 20 days of the experimental period, compared with the baseline value, may confirm this. I. Pishchan (2017) indicated that the mobilisation of reserve body lipids in animals inhibits feed intake, suppresses the fat-synthesising function of the udder parenchyma and may lead to ketosis. As a result, the energy efficiency of milk synthesis decreases, in contrast to the use of energy obtained directly from feed.

Excessive formation of NEFAs as a result of lipolysis in fat depots activates the production

of ketone bodies. Therefore, the beta-hydroxybutyrate content in the blood serum of cows at the beginning of the experiment was above the upper limit of the physiological range (Table 2). This indicated strain on metabolic processes associated with insufficient dietary energy and, consequently, lipomobilisation syndrome in lactating cows. Administration of the complex preparation to lactating cows led to a significant reduction in beta-hydroxybutyrate content: by 23.9% on day 10 and by 42.7% on day 20 compared with the value recorded before its use. The beta-hydroxybutyrate content in the blood serum of cows in the experimental group decreased significantly on days 10 and 20 of the experimental period, by 16.8% and 61.5%, respectively, compared with the value recorded in cows of the control group. The decrease in NEFA and beta-hydroxybutyrate content in the blood serum of cows in the experimental group may be due to the presence of cobalt, niacin and L-carnitine in the complex preparation. As demonstrated by U. Nuber *et al.* (2016), parenteral administration of a commercial mixture of butaphosphan, an organic phosphorus compound, and vitamin B₁₂ before calving or at the beginning of lactation reduced the plasma concentration of NEFAs and β -hydroxybutyrate in cows. Niacin, which is included in the complex preparation, also contributed to the reduction in these indicators. According to Y. Lin *et al.* (2025), the use of a protected form of niacin for the prevention and treatment of hepatic lipodosis in dairy cows during the transition period suppressed lipolysis, reduced the release of NEFAs from adipose tissue and decreased the level of ketone bodies. U.M. Vus *et al.* (2025) noted that the use of L-carnitine in dry-period cows has positive effects on energy metabolism, reduces the concentration of ketone bodies in the blood, improves milk productivity and reproductive function, and lowers the risk of fatty hepatosis by stimulating fatty acid oxidation

and reducing their accumulation in hepatocytes as TAGs. The main function of carnitine is to transport long-chain fatty acids (C16-C22) across the inner mitochondrial membrane for β -oxidation. Activated fatty acids in the form of acyl-CoA cannot cross the inner mitochondrial membrane independently because it is impermeable to CoA derivatives. Carnitine plays a critical role in energy metabolism by providing a substrate for β -oxidation and ATP formation. In high-producing cows during the transition period, which are in a state of negative energy balance with intensive fatty acid mobilisation, the need for carnitine increases to ensure adequate mitochondrial oxidation of these fatty acids.

The content of total lipoproteins in the blood serum of cows in the control and experimental groups remained within the physiological range throughout the study period. No difference in the content of total lipoproteins in the blood serum of cows in the control and experimental groups was observed before the beginning of the experiment. In the blood serum of cows in the control group, after 20 days of the experimental period, a tendency towards a 34.4% increase in total lipoprotein content was found compared with this indicator in cows at the beginning of the experiment. In the blood serum of cows in the experimental group, the level of total lipoproteins increased significantly by 49.4% after only 10 days of complex preparation administration and by 55.7% on day 20 compared with the value recorded before administration of the preparation. The content of the total lipoprotein fraction in the blood serum of cows in the experimental group increased significantly after 10 and 20 days of complex preparation administration, by 50.2% and 15.0%, respectively, compared with this indicator in cows of the control group. The increase in the content of the total lipoprotein fraction in the blood serum of cows in the experimental group was due to the inclusion of

lipotropic substances in the complex preparation. In this context, J.K. Drackley (2026) noted that lipotropic substances include a group of nutrients capable of preventing excessive lipid accumulation in the liver by stimulating their mobilisation and export in lipoproteins. V.V. Sakhniuk *et al.* (2017) found that lipotropic substances, including methionine, choline, betaine, L-carnitine, vitamin B₁₂ and others, exert a preventive effect against fatty hepatosis in cows by increasing synthesis and supplying methyl groups for phosphatidylcholine synthesis, the transport of long-chain fatty acids and other processes. This is important for the formation and secretion of VLDLs by stimulating the synthesis of apolipoprotein B100, the protein component of VLDLs. This process occurs through maintenance of the glutathione pool, via cysteine, a key antioxidant that protects hepatocytes from oxidative damage. According to U. Arshad *et al.* (2023), the requirement for choline in high-producing cows during the transition period increased markedly because of its secretion in milk, as part of phosphatidylcholine and sphingomyelin, and its use in the synthesis of VLDL phospholipids, the export of which from the liver intensifies under conditions of fat reserve mobilisation.

Throughout the study period, no significant fluctuations in total calcium content were found in the blood serum of cows in the control and experimental groups. Similar results were also obtained for inorganic phosphorus content, except for a slight increase of 0.07 mmol/L above the upper limit of the physiological range in the blood serum of cows in the control group on day 20 of the experiment. The calcium-to-phosphorus ratio in the blood of the experimental cows remained within the physiological range throughout the experiment. On the one hand, this indicated stabilisation of calcium/phosphorus metabolism in cows after calving and, on the other hand, showed that the

administered preparation did not affect these parameters.

Based on the study results, the complex preparation with hepatoprotective action was found to have a corrective effect on the clinical status of the body and on the metabolism of carbohydrates, lipids, vitamins and minerals, as well as on the enzymatic activity of cow blood serum during the transition period. In particular, its ability to prevent excessive fat mobilisation, or lipolysis, from fat depots and the accumulation of NEFAs and β -hydroxybutyrate in the blood plasma of cows was experimentally confirmed. These processes cause the development of fatty liver degeneration and other secondary complications. The use of this preparation is especially important during the transition period, which is the most critical stage for lactating cows and is characterised by negative energy balance.

Conclusions

Examination of cows before administration of the complex experimental preparation showed the presence of mild clinical signs of metabolic disorders, characterised by depression, reduced mobility, pale conjunctiva, variable and reduced appetite, pica, weak rumen contractions and, in some cows, areas of hepatic dullness extending beyond the last rib. Minor changes were also observed in the biochemical parameters of cow blood serum before administration of the complex preparation, in particular: low glucose content, NEFA and beta-hydroxybutyrate levels above the upper limit of the physiological range, high AST activity and an increased De Ritis ratio. Administration of the complex preparation, based on essential mineral elements, silymarin, methionine, choline chloride, L-carnitine, betaine and vitamin E, which have a positive effect on metabolic processes in cows, contributed to a reduction in clinical signs, restoration of appetite and an increase in productivity by

4.0 L per cow per day. After administration of the complex preparation to the experimental cows for 20 days, a significant increase in serum glucose concentration by 25.6% and a decrease in NEFA and beta-hydroxybutyrate levels by 2.16 times and 42.7%, respectively, were recorded. This indicated the restoration of energy metabolism and the recovery of cows in the experimental group from negative energy balance. At the same time, after 20 days of complex preparation administration, serum AST activity in cows decreased by 51.3% compared with the value at the beginning of the experiment and by more than three times compared with its activity in the blood serum of cows in the control group. Vitamin E content increased by 2.1 times compared with the value at the beginning of the experiment and by 25.5% compared with cows in the control group. This indicated

restoration of the antioxidant status in cows of the experimental group and stabilisation of the structural state of hepatocyte cell membranes. No substantial effect on calcium-phosphorus metabolism in cows was recorded after administration of the complex preparation.

A promising area for further research is to determine the effect of the complex preparation on immune status indicators and protein metabolism in cows during the transition period.

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Conflict of Interest

None.

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Корекція клініко-біохімічного статусу організму високопродуктивних корів транзитного періоду

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Анотація. Актуальність дослідження зумовлена зростанням випадків діагностування метаболічних хвороб у високоудійних корів під час транзитного періоду, зокрема кетозу, жирового гепатозу та їх ускладнень у вигляді цирозу печінки, репродуктивних дисфункцій з наступною ранньою вибраковкою корів. Важливу роль відіграють своєчасні заходи з профілактики метаболічних хвороб транзитного періоду, що передбачають застосування засобів коригувальної терапії для нормалізації обміну речовин й підвищення продуктивності. Тому, метою цієї роботи було дослідити вплив комплексного препарату на показники клініко-біохімічного статусу організму високопродуктивних корів під час транзитного періоду. Для проведення досліджу було сформовано дві групи: контрольну і дослідну, по 10 корів у кожній. Під час відтворення досліджу використовували загальні методи клінічного обстеження корів (огляд, пальпацію, перкусію і термометрію) та біохімічного дослідження показників сироватки крові (спектрофотометрію та хроматографію), що спрямо встановленню біологічних маркерів з оцінки змін клінічного стану та окремих ланок метаболізму в організмі корів під дією комплексного препарату. Застосування комплексного препарату на основі біологічно активних речовин призводило до підвищення в сироватці крові корів дослідної групи вмісту глюкози (на 25,6 %), сумарної фракції ліпопротеїдів (на 55,7 %), вітамінів А (на 35,9 %) та Е (в 2,1 рази) та зниження активності аспаратамінотрансферази (на 51,3 %), величини коефіцієнта де Рітиса (на 62,3 %), рівня неестерифікованих жирних кислот (у 2,16 рази) і бета-гідроксибутирату (на 42,7 %). Раннє визначення причин порушення обміну речовин та патологічних змін у печінці високопродуктивних корів у транзитний період та вчасне застосування з профілактичною метою комплексного препарату на основі біологічно активних компонентів дало можливість запобігти розвитку вторинних захворювань, зокрема жирової гепатодистрофії, зменшити економічні втрати від недоотримання молока і вибракування корів в умовах конкретного господарства

Ключові слова: печінка; гепатодистрофія; загальний клінічний стан організму; біохімічний аналіз; спектрофотометрія; високоефективна рідинна хроматографія; біологічно активні речовини