



Hematological and biochemical indicators of lambs' blood after the use of chemotherapeutic agents for spontaneous eimeriosis

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Eimeria infection is one of the protozoal diseases of animals caused by various species of *Eimeria* and causes reduced productivity and raised mortality in ruminants, especially in young ones. To study the effect of anti-eimeriosis drugs on the morphological and biochemical parameters of lambs' blood infected with *Eimeria*, 3 groups of Romanov breed animals, two months old, affected by the *Eimeria* pathogen were formed. The first group of animals was treated with a drug containing the active ingredient decoquinat; the second group of animals with a drug containing the active ingredient toltrazuril; the third group of lambs were given a combined drug containing 80 mg of norsulfazole, 70 mg of sulgin, 30 mg of trimethoprim, 45 mg of oxytetracycline hydrochloride and 25 mg of tylosin tartrate per 1 g; the fourth group of lambs was the control group, the animals were free from the *Eimeria* pathogen and were kept separately. The blood of the animals was analysed on days 7 and 14 of treatment. In the blood of the experimental lambs, an increase in the number of red blood cells, neutrophils, lymphocytes, and monocytes was noted. There was also a decrease in the total number of leukocytes, eosinophils, young and segmented neutrophils. According to the results of the treatment, there was an increase in the content of total, albumin, hemoglobin and glucose, as well as the activity of gamma-glutamyl transferase. At the same time, there was a decrease in the content of globulins and the activity of aspartate aminotransferase and alanine aminotransferase compared to the biochemical parameters of healthy lamb blood serum of the control group. According to treatment results, the restoration of sick lambs' blood parameters to those of healthy animals was noted; however, the most stable effect was using the combined drug.

Keywords: eimeriosis; treatment; anti-eimeriosis drugs; morphological indicators of blood; biochemical indicators of blood; lambs.

Introduction

Sheep are regarded as being one type of potential livestock that are widely raised in various regions around the world for both purposes of producing meat and wool (Gondipon & Malaka, 2021). Parasitic diseases of sheep are prevalent worldwide and cause significant economic losses, consisting of reduced productivity, deterioration in the quality of livestock products, and animal mortality. At the same time, the most common cause of digestive tract disease in lambs is protozoan parasites of the genus *Eimeria* (Ernst & Benz, 1986; Silva et al., 2014; Mohamaden et al., 2018; Gutj et al., 2019; Bangoura & Bardsley, 2020; Boyko et al., 2021). This type of parasite localizes and develops in the small and large intestines of infected animals. *Eimeria* are characterized by a strict species affiliation to the hosts they parasitize. Animals become infected by ingestion of food or water contaminated with sporulated oocysts. In the sheep's body, sporozoites leave the oocysts and enter the cells of the intestinal mucosa – enterocytes – and undergo numerous binary divisions. The exogenous stage of development takes place in the external environment and requires proper conditions: temperature, humidity, and oxygen (Kareem & Yücel, 2015; Sujani et al. 2023). There are also researchers who say that the optimum temperature for sporulation is 20–25 °C. The time required to sporulate to the infective stage is a special trait of each coccidia species, so this trait is used in identification. Under conditions of oxygen and appropriate humidity and optimum temperature, oocysts can sporulate (Felici et al., 2021).

This parasitosis is characterized by pronounced clinical symptoms: oppression of the animal, lack of appetite, abdominal pain, and diarrhea. The genus *Eimeria* causes the death of a large number of host intestinal cells and enterocytes leading to reduced absorbance of the critical electrolytes and nutrients (Jacobson et al., 2020; Ahmadi et al., 2021). Feces

acquire a watery consistency with blood impurities and a significant amount of mucus. Subsequently, anemia, emaciation, dehydration, and death are observed in such animals (Andrade et al., 2012; Roeber et al., 2013; Keeton & Navarre, 2018). The highest mortality rate in young animals is recorded for diarrhea with a significant amount of blood (Kareem & Yücel, 2015). *Eimeria* can occur in clinical and hidden forms (Lagares, 2008).

Eimeria most often affect young animals under the age of 4 months. Clinical signs can also occur in adult animals. However, adult animals are more likely to act as parasite carriers. In the case of coccidiosis, a parasitic infestation of the intestines, wet weather is known to promote incidences in livestock (Lopes et al., 2013). The analysis of risk factors showed that intensive rearing, no rotation of pasture, dirt, and slatted floors, and age up to 12 months were associated with infection (Cameiro et al., 2022).

Eimeria are associated with significant economic costs of animal treatment, loss of body weight gain, and death of lambs, especially at the age of less than three months (Reeg et al., 2005; Elmadawy & Elkhaiaf, 2014; Ramadan et al., 2018).

Traditionally, the fight against *Eimeria* in sheep is achieved through careful observance of zoohygienic requirements, as well as the introduction of coccidiostatic drugs into the feed or vaccination with live or weakened parasites (Mohamed et al., 2022). Necropsied sheep showed mild mesenteric lymphadenomegaly, diffuse proliferative enteritis in the small and large intestines, and mucosal thickening. Histopathological studies exhibited diffuse proliferative enteritis and presence of structures compatible with intracellular coccidia at different stages of development (Olmos et al., 2020).

At the same time, when pronounced clinical signs of ovine *Eimeria* are registered, treatment is mostly ineffective, but the severity of the dise-

ase can be reduced by early use of some coccidiostats, in particular, toltrazuril, diclazuril, and sulfaquinoxaline (Kareem & Yücel, 2015). However, in recent years, there has been a rapid increase and spread of resistance of parasitic pathogens to chemotherapeutic drugs worldwide (Vlasenko & Stybel, 2012). Also, the recent emergence of ovine *Eimeria* spp. resistance to toltrazuril highlights the urgent need for the development of alternative control strategies (Odden et al., 2018).

That is why this work aimed to determine changes in the morphological and biochemical parameters of the peripheral blood of lambs with *Eimeria* after the use of the studied chemotherapeutic drugs with an eimeriostatic effect.

Material and methods

The research was carried out on two-month-old Romanov sheep kept on farms in Cherkasy region, Ukraine. The animals were selected according to the principle of analogy: they had approximately the same weight, sex (male lambs), severity of clinical manifestations, and keeping and feeding conditions.

According to our previous studies, we found that lambs in these farms were infected with four taxa of *Eimeria*: *E. arloingi* Marotel, (1905) (prevalence – 41%), *E. crandallis* Schneider, (1985) (prevalence – 29%), *E. intricate* Spiegel, (1925) (prevalence – 15%), and *E. faurei* Moussu and Marotel, (1902) (prevalence – 15%). The level of damage caused by the *Eimeria* pathogen among experimental lambs of one month of age was 95%, with an amplitude of infection intensity of 587–10,000 oocysts (Soroka & Filipenko, 2022).

To study the effect of eimeriostatics on the morphological and biochemical parameters of lambs' blood, four groups (three experimental and control) of animals were formed, each consisting of 10 Romanov sheep. The animals were given drugs *per os*, individually, daily for two four-day treatment courses with a break of three days. The first group of lambs was administered “Quinosan” (containing the active ingredient decoquinate) at a dose of 0.33 g of the drug per 10 kg of body weight per day. The second group of animals was administered “Baycox 5%” (containing the active ingredient toltrazuril) at a dose of 3 mL of suspension per 10 kg of body weight. The third group of lambs was administered “Brovaseptol” (a combined preparation containing 80 mg of norsulfazole, 70 mg of sulgin, 30 mg of trimethoprim, 45 mg of oxytetracycline hydrochloride and 25 mg of tylosin tartrate per 1 g) at a dose of 2 g per 10 kg of animal body weight. The fourth group of lambs was the control group, the animals were free from the *Eimeria* pathogen and were kept separately.

For the study, blood was collected from lambs by puncture of the jugular vein in the morning before feeding, in two tubes: one tube with an anticoagulant (heparin) for morphological studies and the second tube without a stabilizer for biochemical studies. Blood samples were taken on days 7 and 14 from the start of treatment. Separately, blood was taken from sick lambs at the beginning of treatment for further study and comparison.

Determination of hematological parameters of blood (number of red blood cells and leukocytes) was carried out by counting blood cells in the Goryaev chamber. The leukocyte formula was determined by counting leukocytes in a Romanowsky-Gimza stained smear. Hemoglobin content was determined using the hemoglobin cyanide method (Vlizlo et al., 2012). Serum biochemical parameters were determined using an automatic biochemical analyzer DS-261 (Sinnowa, China, 2021) of closed type with a flow cuvette and a photoelectrocolorimeter Apel AP-120 (Japan, 2021). The total protein content was determined by the biuret reaction, and the ratio was determined by polyacrylamide gel electrophoresis.

All studies were conducted in accordance with the Council of Europe Convention for the Protection of Vertebrate Animals Used for Experimental and Other Scientific Purposes of March 18, 1986, Directive 2010/63/EU of the European Parliament and of the Council of September 22, 2010, on the protection of animals used for scientific purposes and the Law of Ukraine of February 21, 2006, No. 3447-IV (as amended on June 22, 2017, No. 2120-VIII) “On the Protection of Animals from Cruelty”.

The development of this protocol was approved by the Bioethics Committee of the National University of Life and Environmental Scien-

ces of Ukraine (conclusion of the Bioethics Committee No. 21/22 of September 18, 2022).

Descriptive statistics were calculated and presented as mean \pm standard error of mean ($x \pm SE$). All sample distributions were assessed for normality using the Shapiro-Wilk test. (REF) For normally distributed variables, the comparison between control and infected groups was performed using one way ANOVA. For the three treatment groups, the comparison between infected pre-treatment groups and treatment on days 7 and 14 was made using repeated-measures ANOVA followed by post hoc pairwise comparison with Bonferroni correction. We used an alpha level of 0.05 for all statistical tests. The statistical processing of the data was performed using SAS version 9.X for Mass (SAS Institute Inc., USA).

Results

Morphological studies of blood make it possible to describe qualitative and quantitative characteristics of blood cells, which can help evaluate the course of the main disease and predict its outcome. Hematological studies also provide invaluable information regarding the pathogenesis of the disease and help in understanding the mechanisms of participation of individual organs and systems in this process.

According to the results of the determination of morphological indicators of blood in lambs that were sick with eimeriosis, a significant decrease in the number of erythrocytes by 29.6% was established compared to animals that were free of *Eimeria* oocysts and had no clinical signs according to laboratory studies. Erythropenia indicates blood loss associated with damage to the intestinal wall by single-celled parasites and the development of hemorrhagic enteritis. At the same time, sick animals had a significant leukocytosis: the total number of leukocytes increased by 47.1% compared to healthy lambs.

General leukocytosis obviously indicates a syndrome of the general inflammatory reaction of the body to the penetration of parasites into the internal environment and massive damage to the lamb's digestive tract. Eosinophilia against the background of eimeriosis of lambs is also noteworthy: the number of eosinophils increased by 55.4% compared to healthy animals, which may indicate significant sensitization for this parasitosis. The increase in the number of young neutrophils in peripheral blood by 75% indicates a violation of neutrophilopoiesis. A slight decrease in rod neutrophils (by 8.7%) and an increase in segmented (by 29.5%) neutrophils may indicate degenerative displacement of the nucleus to the right. Such a reaction is a response of the body as an element of the physiological compensatory mechanism to the stimulation of exchange products that are formed as a result of *Eimeria* parasitism.

The appearance of young neutrophils in the hematological profile may indicate a violation of neutrophilopoiesis, which led to the appearance of young cell forms in the bloodstream. The number of lymphocytes in the blood of sick lambs also changes, in particular, a sharp decrease in lymphocytes by 31.6% and monocytes by 12.4% compared to animals that were not sick with eimeriosis. Such changes may indicate an acute course of the disease (Table 1).

Table 1
Morphological parameters of the blood of lambs with and without *Eimeria* ($x \pm SE$, $n = 40$)

Hematological parameters	Lambs free from <i>Eimeria</i> oocysts – control ($n = 10$)	Lambs with <i>Eimeria</i> , before treatment ($n = 30$)
Erythrocytes, $10^{12}/L$	11.83 \pm 0.19	8.32 \pm 0.32**
Leukocytes, $10^9/L$	9.21 \pm 0.27	17.41 \pm 0.98**
Basophils, %	0	0
Eosinophils, %	2.54 \pm 0.36	5.73 \pm 1.59**
Neutrophils, %		
young	0.24 \pm 0.07	0.81 \pm 0.14*
stick-nucleated	4.65 \pm 0.21	4.25 \pm 0.48
segmented nuclear	34.68 \pm 2.17	49.29 \pm 2.78**
Lymphocytes, %	55.48 \pm 1.88	37.94 \pm 3.43**
Monocytes, %	2.53 \pm 0.21	2.23 \pm 0.54

Notes: * – $P < 0.05$; ** – $P < 0.01$ – relative to the control group of lambs; two groups were compared using one way ANOVA.

In determining the effectiveness of anti-eimeriosis agents, the effect of chemotherapy drugs on the morphological indicators of lambs sick with eimeriosis was also studied, in particular, the rate of restoration of the hematological profile to the indicators of healthy animals after their use.

It was established that on the 7th day of the use of decoquinat (1 experimental group) in sick lambs, the indicators of peripheral blood improved, in particular, a slight increase in the number of erythrocytes by 19.3%, a decrease in the total number of leukocytes by 24.4%, and eosinophils by 8.7%, an increase in the number of rod-shaped and a decrease

in the number of segmented neutrophils by 10.6% and 35.1%, respectively. It is worth noting the appearance of basophils, which were not observed with the use of other chemotherapy agents. At the same time, the use of toltrazuril (experimental group 2) for the treatment of experimental lambs increased the number of red blood cells by 22.7%, rod neutrophils, lymphocytes and monocytes by 4.5%, 28.3% and 19.7%, respectively. There was also a decrease in the total number of leukocytes by 38.5%, eosinophils by more than two times – by 52.1%, young and segmented neutrophils by 37.5% and 27.7%, respectively (Table 2).

Table 2

Morphological parameters of the blood of lambs with *Eimeria* before and after treatment with three chemotherapy drugs on days 7 and 14 ($\bar{x} \pm SE$, $n = 30$)

Hematological parameters	Treatment 1 (n = 10)			Treatment 2 (n = 10)			Treatment 3 (n = 10)		
	day 0	day 7	day 14	day 0	day 7	day 14	day 0	day 7	day 14
Erythrocytes, $10^{12}/L$	8.33 ± 0.32**	9.16 ± 0.61	10.83 ± 0.29	7.94 ± 0.17**	10.74 ± 0.45	11.21 ± 0.56	8.12 ± 0.44**	11.15 ± 0.48	11.63 ± 0.14
Leukocytes, $10^9/L$	17.41 ± 0.98**	12.84 ± 0.63	10.73 ± 0.95	17.08 ± 1.14**	10.74 ± 0.36	10.34 ± 2.16	17.63 ± 1.19**	10.13 ± 0.61	9.62 ± 0.36
Basophils, %	0	0.23 ± 0.07	0	0	0	0	0	0	0
Eosinophils, %	5.73 ± 1.59**	5.27 ± 1.11	5.05 ± 0.83	5.44 ± 1.32*	2.73 ± 0.24	2.69 ± 0.34	5.12 ± 1.37*	2.63 ± 0.96	2.59 ± 0.64
Neutr young	0.83 ± 0.14*	0.77 ± 0.53	1.24 ± 0.42	0.86 ± 0.23*	0.52 ± 0.08	0.64 ± 0.13	0.82 ± 0.21*	0.41 ± 0.13	0.44 ± 0.18
ophils, stick-nucleated	4.24 ± 0.48*	4.73 ± 1.16	4.15 ± 1.82	4.41 ± 0.97*	4.46 ± 0.87	4.39 ± 0.64	4.32 ± 0.57*	4.35 ± 0.51	4.56 ± 0.22
% segmented nuclear	49.27 ± 2.78	44.14 ± 3.91	34.22 ± 2.32	48.84 ± 3.46**	36.53 ± 3.43	36.14 ± 3.48	49.01 ± 3.11*	36.47 ± 2.28	35.75 ± 1.71
Lymphocytes, %	37.93 ± 3.43**	42.45 ± 2.47	53.18 ± 3.13	38.38 ± 4.12**	53.12 ± 2.82	53.85 ± 2.96	38.51 ± 2.89**	53.92 ± 3.12	54.82 ± 2.47
Monocytes, %	2.24 ± 0.04**	2.65 ± 0.39	2.44 ± 0.37	2.36 ± 0.09*	2.74 ± 0.27	2.47 ± 0.21	2.28 ± 0.23**	2.46 ± 0.69	2.42 ± 0.43

Notes: * – $P < 0.05$; ** – $P < 0.01$ – pairwise comparison with respective pre-treatment group (day 0) with Bonferroni correction; Treatment 1 group was administered "Quinosan" (contains the active ingredient decoquinat), Treatment 2 group was administered "Baycox" 5% (contains the active ingredient toltrazuril), Treatment 3 group was administered "Brovaseptol" (contains norsulfazole, sulgin, trimethoprim, oxytetracycline hydrochloride and tylosin tartrate).

The use of a combined preparation containing norsulfazole, sulgin, trimethoprim, oxytetracycline hydrochloride and tylosin tartrate (study group 3) resulted in an increase in the number of red blood cells by 25.2%, a decrease in the total number of leukocytes and eosinophils by 41.9% and 52.1%, respectively. The number of agranulocytes also changes, in particular, the number of young neutrophils decreased by half – by 50.2%; the number of rod neutrophils increased by 2.3%, and segmented neutrophils, on the contrary, significantly increased by 26.8%. Also, the number of lymphocytes and monocytes increased by 29.6% and 8.3%, respectively, compared with the results of the study of lambs with *Eimeria* before treatment.

Analyzing the results of morphological studies of the blood of lambs with *Eimeria* treated with various chemotherapeutic agents, the following was found. On the 14th day of treatment in the 1st experimental group (treatment was carried out with decoquinat), a significant increase in the number of red blood cells by 22.4%, the number of young neutrophils by 38.3%, lymphocytes and monocytes by 28.6% and 8.6%, respectively, was detected. At the same time, there was a decrease in the total number of leukocytes by 38.3%, eosinophils by 12.2%, and rods and segmented neutrophils by 2.3% and 30.5%, respectively, compared with the pre-treatment values.

The following changes in the hematological profile of blood were observed in lambs treated with toltrazuril (experimental group 2) in appropriate doses. In particular, a significant increase in the number of red blood cells by 25.9%, neutrophils by 2.3%, as well as lymphocytes and monocytes by 29.5% and 10.9%, respectively, was recorded. At the same time, normalization of leukocyte counts was also noted. Thus, the total number of leukocytes decreased by 40.8% compared to the beginning of treatment, the number of eosinophils by 52.8%, the number of young and segmented neutrophils decreased by 25% and 26.5%, respectively.

The most significant and significant changes in the morphological parameters of the blood of lambs with *Eimeria* were noted during their treatment with a combined preparation containing norsulfazole, sulgin, trimethoprim, oxytetracycline hydrochloride and tylosin tartrate (experimental group 3). In particular, there was an increase in the number of red blood cells by 28.4%, the number of neutrophils by 6.6%, and an increase in the number of lymphocytes and monocytes by 30.8% and 9.1%, respectively. There were also significant changes in other leukocyte subpopulations: a decrease in the number of eosinophils by 54.5%, young and segmented neutrophils by 50.0% and 27.3% was noted. The total number of leukocytes also significantly decreased compared to the beginning of treatment – by 44.8%.

Analyzing the effect of antiemeriosis drugs on the morphological state of the peripheral blood of sick lambs, it should be noted that the fastest

recovery of blood parameters to the level of healthy animals was recorded when using the combined drug "Brovaseptol". The least effective was the drug based on decoquinat – "Quinosan".

Biochemical changes in the blood serum of sick animals directly depend on the pathogen, the place of its parasitization, the method of feeding, the peculiarities of its effect on the host and the course of the underlying disease, which is the basis of the evolutionary strategy of parasite-host interaction (Karapehlivan et al., 2007).

According to the results of biochemical tests of the blood serum of lambs with *Eimeria*, a decrease in the content of total protein by 36.1% and albumin by 13.1% was found compared to biochemical studies of biological material from healthy lambs. A decrease in the level of total protein and albumin may indicate a violation of the protein-synthesizing function of the liver, as well as being due to insufficient intake of proteins with feed due to damage to the digestive tract and impaired absorption of nutrients. At the same time, an increase in the content of globulins in the blood serum of diseased lambs by 11.9% was noted. Hyperglobulinemia may indicate an increased synthesis of globulins in the body against the background of *Eimeria* damage, as an immunological reaction of the body to the presence of protozoan parasites in the digestive tract. The albumin-globulin ratio or de Ritis coefficient was reduced, indicating dysproteinemia and dystrophic changes in the liver.

The hemoglobin content also decreased in the serum of diseased animals by 32.2%, indicating significant blood loss due to impaired vascular integrity of the digestive tract. A decrease in glucose content by 27.8% was observed, which is the cause of impaired absorption and intake of nutrients from the intestines.

According to the results of the study of alanine aminotransferase (ALT) and aspartate aminotransferase (AST), there was an increase by 43.4% and 33.1% respectively in the activity of these enzymes in the blood of lambs affected by *Eimeria*. The increase in the activity of these enzymes is evidence of the reaction of the central detoxification organ – the liver – to the products of inflammation and metabolism of *Eimeria*, which enter the internal environment of the body of sick lambs. A statistically insignificant decrease in the level of gamma-glutamyl transferase (GGT) was also noticed (Table 3).

Determining the effect of antiemeriosis drugs on the biochemical parameters of the blood of sick lambs, it was found that on the 7th day of treatment, with the use of decoquinat, an increase in total protein by 15.7%, hemoglobin by 11%, albumin by 3.2%, glucose by 5.6% and GGT activity by 6.1% was noted. A decrease in globulin content by 13.7%, as well as the activity of ALT and AST enzymes by 17.3% and 16.3%, respectively, was also recorded in comparison with the biochemical parameters of blood serum of lambs free of the *Eimeria* pathogen (Table 4).

Table 3
Biochemical parameters of the blood of lambs with and without *Eimeria* ($x \pm SE$, $n = 40$)

Hematological parameters	Lambs free from <i>Eimeria</i> oocysts – control ($n = 10$)	Lambs with <i>Eimeria</i> , before treatment ($n = 30$)
Total protein, g/L	65.52 ± 0.96	62.39 ± 0.57**
Hemoglobin, g/L	124.03 ± 2.74	84.06 ± 0.69*
Albumin, g/L	31.67 ± 0.35	27.23 ± 1.13*
Globulins, g/L	33.96 ± 2.28	35.13 ± 2.14**
De Ritis coefficient	1.01 ± 0.15	0.77 ± 0.19*
Glucose, mmol/L	3.86 ± 0.72	2.84 ± 0.23**
ALT, U/L	28.47 ± 1.71	50.24 ± 2.85*
AST, U/L	54.62 ± 3.74	81.68 ± 3.62**
GGT, U/L	42.18 ± 2.03	36.18 ± 2.73**

Notes: see table 1; ALT – aminotransferase, AST – aminotransferase, GGT – gamma-glutamyl transferase.

The following biochemical changes in the blood serum were observed during the treatment with toltrazuril of sick lambs affected by *Ei-*

Table 4
Biochemical parameters of the blood of lambs with *Eimeria* before and after treatment with three chemotherapy drugs on days 7 and 14 ($x \pm SE$, $n = 30$)

Biochemical parameters	Treatment 1 ($n = 10$)			Treatment 2 ($n = 10$)			Treatment 3 ($n = 10$)		
	day 0	day 7	day 14	day 0	day 7	day 14	day 0	day 7	day 14
Total protein, g/L	62.3 ± 0.6**	61.9 ± 0.6	62.5 ± 1.7	63.0 ± 2.1**	61.9 ± 1.5	54.8 ± 1.4	62.3 ± 1.1**	63.0 ± 0.3	62.3 ± 0.9
Hemoglobin, g/L	84.0 ± 2.7*	94.4 ± 3.2	101.2 ± 2.8	85.8 ± 2.5*	104.3 ± 2.6	118.7 ± 3.1	90.3 ± 3.2*	116.1 ± 3.6	120.3 ± 3.2
Albumin, g/L	27.2 ± 1.1*	28.1 ± 1.2	29.3 ± 1.5	28.4 ± 2.1**	27.9 ± 1.6	29.0 ± 1.5	28.9 ± 1.8*	28.5 ± 2.1	30.5 ± 1.2
Globulins, g/L	35.1 ± 2.1**	33.8 ± 1.9	33.2 ± 2.9	34.6 ± 2.4*	34.0 ± 2.8	33.3 ± 2.3	33.5 ± 2.5**	34.2 ± 2.1	31.8 ± 1.7
De Ritis coefficient	0.812 ± 0.094**	0.958 ± 0.192	0.923 ± 0.161	0.836 ± 0.156**	0.812 ± 0.213	0.954 ± 0.121	0.867 ± 0.273**	0.817 ± 0.247	0.929 ± 0.141
Glucose, mmol/L	2.82 ± 0.23**	3.16 ± 0.17	3.23 ± 0.57	2.86 ± 0.36**	2.91 ± 0.46	3.24 ± 0.66	2.95 ± 0.22**	3.12 ± 0.69	3.43 ± 0.97
ALT, U/L	50.2 ± 2.8*	41.5 ± 2.1	39.2 ± 2.9	51.9 ± 4.1*	46.8 ± 2.2	43.1 ± 3.1	48.6 ± 3.1*	38.6 ± 3.8	33.5 ± 2.8
AST, U/L	81.7 ± 3.6**	68.4 ± 2.2	65.7 ± 4.2	82.1 ± 4.8**	68.6 ± 3.8	58.5 ± 3.6	79.2 ± 3.6**	65.3 ± 3.7	60.5 ± 2.2
GGT, U/L	36.2 ± 2.7**	38.5 ± 1.8	38.9 ± 2.5	38.5 ± 3.1**	37.9 ± 1.8	38.6 ± 1.8	37.8 ± 1.6**	37.5 ± 1.2	39.5 ± 1.2

Notes: see Tables 2 and 3.

The treatment of the experimental group of lambs with toltrazuril revealed an increase in total protein by 23.5%, albumin by 6.2%, hemoglobin by 29.2%, glucose by 10.8%, and GGT activity by 6.4%. The level of globulin content was reduced by 5.1%, as well as the activity of AST and ALT enzymes by 14.7% and 28.4%, respectively, compared to the biochemical parameters of blood serum of healthy lambs of the control group. Studying the effect of the combined drug "Brovaseptol" on the biochemical parameters of blood serum of *Eimeria*-affected lambs, an increase in the content of total protein, albumin and hemoglobin by 33.7%, 10.8% and 30.2%, respectively, glucose content by 15.7% and GGT activity by 8.4% was found. A decrease in globulin levels by 9.2% and ALT and AST activity by 33.2% and 26.2%, respectively, was found.

It is worth noting that the restoration of biochemical parameters of the blood serum of lambs with *Eimeria* to the level of blood serum of healthy animals was fastest when treated with the combined drug "Brovaseptol". The lowest effect on the biochemical parameters of blood serum of *Eimeria*-affected animals was produced by the drug based on decoquinate – "Quinosan".

Discussion

The most common and significant parasites of the sheep digestive tract are *Eimeria* (Bartels et al., 2010). These parasitic protozoa are the cause of diarrhea, anemia, dehydration, and growth retardation, and are characterized by high morbidity and mortality (Ghanem & El-Raof, 2005). In *Eimeria*, significant hematological changes in the morphological parameters of the blood are noted, in particular, a decrease in the number of red blood cells and hemoglobin is recorded (Ghanem & El-Raof, 2005; Anumol et al., 2012). In addition, the parasitization of unicellular parasites leads to damage to the intestinal wall, its inflammation and, as a result, inflammatory processes characterized by significant changes in the hematological profile, in particular, a sharp increase in the total number of leukocytes (Salem, 2017). In the study, total erythrocyte count and hemoglobin concentration were significantly decreased in heavy *Eimeria* spp. in-

meria: an increase in the content of total protein, albumin and hemoglobin by 23.1%, 2.5% and 19.4%, respectively; glucose content and GGT activity by 3.4% and 4.7%, respectively. At the same time, a decrease in globulin content by 3.1%, as well as ALT and AST activity by 6.7% and 15.9%, respectively, was recorded.

The use of a combined antiemeriosis drug based on sulfonamides and antibiotics for the treatment of lambs was reflected in the biochemical state of the latter as follows: the content of total protein, albumin and hemoglobin increased by 29.3%, 7.2% and 17.4%, respectively, the content of glucose by 9.8%, and the activity of GGT by 7.1%. A decrease in serum globulin content by 2.5% was also recorded, and ALT and AST activity decreased by 23.1% and 20.1%, respectively.

Determining the biochemical parameters of the blood serum of lambs with *Eimeria* on the 14th day of treatment with decoquinate, a significant increase in the content of total protein, albumin and hemoglobin by 22.5%, 7.1% and 17%, respectively, was found. There was also an increase in glucose content by 11.5% and GGT activity by 7.1%. The content of globulins decreased by 5.4%, similarly, the activity of ALT and AST by 22.1% and 19.6%, respectively.

Total leucocyte count and granulocyte percentage were significantly elevated in mildly infected sheep while, lymphocyte percentage was increased in cases of heavy infection. Total proteins significantly decreased in case of heavy infection (Abdulmageed et al., 2022). The results of our studies of the morphological parameters of the blood of lambs with *Eimeria* are consistent with the studies of scientists who have studied this issue. Due to the results of biochemical studies, a decrease in the content of total protein and albumin, an increase in the number of globulins, as well as an increase in the activity of serum enzymes in diseased animals were noticed (Zajac & Conboy, 2006). Changes in these parameters can be explained by a decrease in appetite and in the intestinal wall's ability to absorb nutrients, as *Eimeria* causes the loss of intestinal epithelial cells, which exfoliate, leading to bloody diarrhea (Sheikh et al., 2005). The above studies are also consistent with our results. Various chemotherapeutic agents are used to control *Eimeria* in small ruminants, including sulfonamides, monensin, lasalocid ionophore, antibiotics, amprolium, toltrazuril and diclazuril (Taylor et al., 2003; Platzer et al., 2005).

According to the results of research, Mahmoud et al. (2005) found that different anticimerosal agents affect the morphological and biochemical parameters of the blood of diseased lambs in different ways. The most effective were sulfonamides and amprolium: an increase in the number of red blood cells, hemoglobin content and a significant decrease in the total number of leukocytes were found during the treatment of animals. Treatment with toltrazuril was less effective. Such changes in the hematological profile, according to the authors, reflect changes in the body and are harbingers of animal recovery.

In particular, the results of treatment of *Eimeria* in lambs with aprotium and sulfadimethoxine showed satisfactory treatment results. Thus, according to the results of three weeks of therapy, the changed parameters of blood parameters almost returned to those of healthy animals. However, the highest and most stable results were obtained with sulphadimethoxine treatment than with aprotium (Ghanem & El-Raof, 2005).

Due to the results of our research, it was found that the applied preparations based on decoquinate, toltrazuril and a combined preparation con-

sisting of norsulfazole, sulgin, trimethoprim, oxytetracycline hydrochloride and tylosin tartrate had a therapeutic effect, which was reflected in changes in the morphological and biochemical parameters of the blood of lambs with *Eimeria*. However, a more stable result, which was closest to the results of blood tests of healthy animals, was observed with the use of a combined preparation based on sulfonamides and antibiotics. Thus, the results of our studies are fully consistent with the findings of previous studies. In our opinion, the therapeutic effect of sulfonamides is enhanced by the antibacterial effect of antibiotics which suppress the secondary microflora of the digestive tract since the secondary microflora plays a leading role in the development of complications of *Eimeria* in lambs (Catchpole & Gregory 1985).

Conclusion

When lambs were affected by the *Eimeria* pathogen, significant changes in morphological and biochemical blood parameters were observed, which were associated with the effect of unicellular parasites on the intestinal wall, damage to the mucous membrane of the digestive tract, dehydration, and the effect of inflammation and metabolic products of *Eimeria* on the animals' body. Chemotherapeutic drugs based on decoquinat, toltrazuril, and a combined drug containing norsulfazole, sulgin, trimethoprim, oxytetracycline hydrochloride, and tylosin tartrate were used to treat *Eimeria*. It was noted that the therapeutic effect was reflected in the morphological parameters of the blood: an increase in the number of red blood cells, stick neutrophils, lymphocytes and monocytes; a decrease in the total number of leukocytes, eosinophils, young and segmented neutrophils. Also, changes were noted in the biochemical composition of the blood serum of diseased animals: an increase in the content of total, albumin, hemoglobin, glucose, as well as the activity of gamma-glutamyl transferase; a decrease in the content of globulins and the activity of aspartate aminotransferase and alanine aminotransferase, compared with the biochemical parameters of the blood serum of lambs that were free of *Eimeria*. It was found that all applied *Eimeria* treatment regimens were quite effective. However, the most stable effect on the restoration of blood parameters to those of healthy animals was observed with the use of the combined drug "Brovaseptol", which contains sulfonamides and antibiotics. Obviously, due to this combination of chemotherapeutic substances, it is possible to affect the *Eimeria* and secondary microflora, which has a significant impact on the development of the pathological condition of animals.

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