SENSITIVITY, RESISTANCE, AND TREATMENT OF SALMONELLA PATHOGENS TO ETIS-2 COMPLEX PREPARATION AND OTHER TYPES OF ANTIBIOTICS

Djurakulov O. K.
Basic doctoral student, Veterinary Research Institute, Tuberculosis Laboratory, Respublic of Uzbekistan, Samarkand region, Tailak district, Charogban CNC, village New Tailak 1, building 67.
oybekdjurakulov435@gmail.com

Annotation:
This article provides information that the indicators of sensitivity to antibiotics in relation to aqueous and oil emulsions of various concentrations of the drug ETIS-2 to the causative agent of salmonella enteritidis were carried out in laboratory conditions.

Keywords: S. Enteritidis, S. Typhimurium, S. Dublin, antibiotic, strain, GPA (meat peptone agar) and GPQ (meat peptone broth), ETIS-2 complex preparation, sensitivity, resistance, pathogen, concentration, ratio, dilution.

Relevance of the Topic: Currently, salmonellosis remains a significant issue in both veterinary and medical fields, not only in our country but worldwide. The pathogens *Salmonella Enteritidis, Salmonella Typhimurium,* and *Salmonella Dublin* are commonly found in agricultural animals, causing economic damage to livestock farming. It is well established in scientific research that these Salmonella serovars can lead to foodborne epidemics affecting both animals and humans [1].
Various groups of sulfonamides, nitrofuran preparations, and antibiotics are used to prevent and treat salmonellosis. Scientists from the tuberculosis research laboratory at VITI have developed a complex preparation, ETIS-2, composed of pharmacopoeial medicinal substances. The use of ETIS-2 eliminates the need for other antibiotics or alternative treatments [12].

Our study aims to investigate the sensitivity and resistance of different Salmonella strains, as well as other bacterial species, to varying concentrations of antibiotics and the ETIS-2 preparation.

Research Objective: The objective of this study is to examine the effects of the ETIS-2 preparation and certain antibiotics on *Salmonella Enteritidis* pathogens, compare the effectiveness of these treatments in combating salmonellosis, and analyze hematological changes in the treated sheep.

Literature Review: Salmonellosis is an acute infectious disease primarily affecting young animals in a septic form. It is characterized by fever, gastrointestinal dysfunction, and diarrhea. Calves are most susceptible between 3-4 weeks and up to 4 months of age, piglets up to 4 months, lambs at all ages, poultry in their early days of life, and foals can be infected even in utero by specific pathogens such as *S. pullorum* and *S. gallinarum* [5].

The causative agent belongs to the *Salmonella* group and exhibits significant polymorphism within the microbial cell. It stains well with aniline dyes and grows effectively on GPA and GPQ media. Biochemically, it does not produce indole, releases hydrogen sulfide, and does not coagulate milk. It remains unchanged in lactose and sucrose but produces gas and acid in glucose, mannitol, and maltose. The microorganism secretes a potent endotoxin and demonstrates varying sensitivity and resistance to antibiotics and sulfonamides [6].

In cases of disease outbreak, clinical examination and thermometry are conducted, and animals are categorized into the following groups:

1. Healthy
2. Suspected cases
3. Confirmed infected
4. Recovered animals.

Each group must have its own designated feeders, shepherds, and equipment. Proper organization of nutritious and high-quality feeding is essential. For treatment, the use of levomycetin, sintomycin, and tribrissen is recommended. If pneumonia

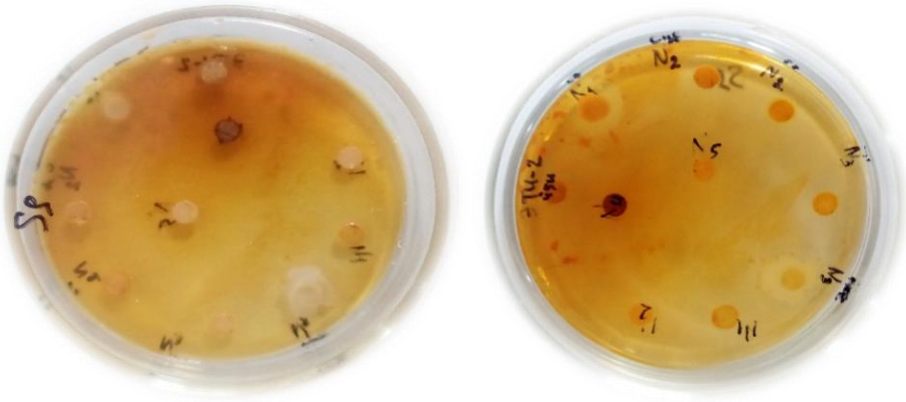
complications arise, a combination of antibiotics and sulfonamides **(**norsulfazole, disulfan, etazol, sulfadine, sulfadimezine**)** has been proven to be highly effective [6]. Among the nitrofuran group, furazolidone, furacin, and furazoline have shown high therapeutic efficacy. Antitoxins or hyperimmune blood serums used against salmonellosis also yield significant therapeutic results. Determining the sensitivity of pathogens to different drugs enhances the effectiveness of treatment strategies, and this task is assigned to laboratories specializing in infectious diseases [7].

For prescribing antibiotics to infected animals, certain clinical symptoms must be present, such as purulent sputum, changes in blood test results (increase in leukocytes and neutrophils), and elevated inflammatory markers like C-reactive protein (CRP)**.** Bacteriological cultures from body fluids are examined, and based on the identified colonies, the appropriate antibiotic is selected. Incorrect or mixed use of antibiotics during this period may not affect microorganisms but instead cause adverse effects on the liver, kidneys, and intestines, leading to various complications [8].

Scientists from the VITI Tuberculosis Laboratory have developed the ETIS-2 complex preparation**,** composed of pharmacopoeial medicinal substances, to combat bacterial infections. This preparation has been successfully used to eradicate tuberculosis in many farms across the country, preventing significant economic losses and reducing the risk of human transmission [11]. As a formulating agent and adjuvant**,** vitamin-enriched vegetable oil **(**Trivit or Tetravit**)** has been included. Considering the effects of the medicinal components on different microorganisms, the effectiveness of the preparation in treating various infectious and non-infectious diseases has been studied under laboratory and production conditions. The method of treating bacterial diseases in livestock using this preparation is now being implemented in livestock farms across the country [12]

The combination of components within the ETIS-2 complex preparation gives it an advantage over other bacteriostatics. This combination provides both a synergistic effect (where one drug enhances the effect of another) and a prolongation effect (extending the duration of the drug's action). The preparation can be administered to all types of animals from 10 days of age, regardless of their physiological condition [12].

Research Object and Methodology: Between 2022 and 2023**,** scientific research was conducted in the Microbiology and Tuberculosis Laboratories of the Veterinary Scientific Research Institute (VITI) using the *S. Enteritidis* strain from the



1. (No. 1) The 1:10 ratio oily emulsion of ETIS-2 preparation - **sensitive**.
2. (No. 2) The 1:100 ratio aqueous solution of ETIS-2 preparation - **low sensitivity.**
3. (No. 2) The 1:100 ratio oily emulsion of ETIS-2 preparation - **sensitive.**
4. (No. 3) The 1:50 ratio (aqueous) ETIS-2 preparation - **low sensitivity.**
5. (No. 3) The 1:50 ratio (oily) ETIS-2 preparation - **low sensitivity.**
6. ETIS-2 preparation in its basic concentration - **highly sensitive.**
7. (No. 1, aqueous) The 1:10 ratio aqueous solution of ETIS-2 preparation - **not sensitive.**
8. (No. 2, oily) Ditrim 1:10 ratio oily solution - **not sensitive.**
9. (No. 4, aqueous) Nitox 1:10 ratio solution - **not sensitive.**
10. (No. 5, aqueous) Enroflan 1:10 ratio solution - **sensitive.**

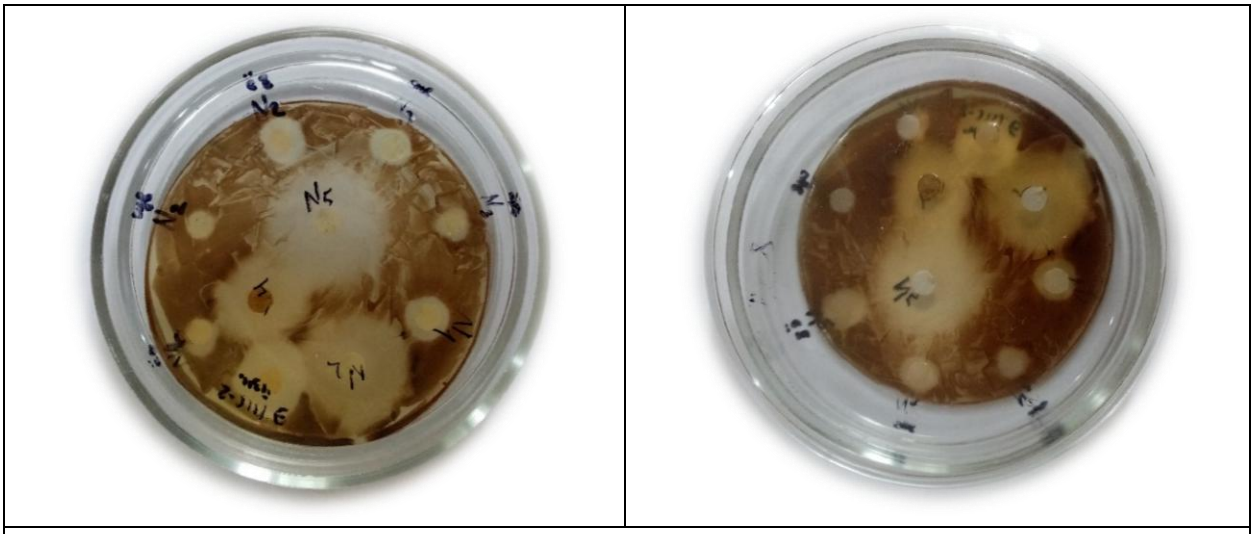
Figure 1: Antibiotic susceptibility of 1-day-old Salmonella pathogens prepared from Salmonella-Shigella strain.

Microorganism Collection stored at the Regional Diagnostic Laboratory. Due to the strain's lyophilized state and storage at -80°C, it was differentiated on Salmonella-Shigella (SS) agar, Bismuth Sulphite agar, and Blood Agar Base (Infusion Agar Base) before experimentation.

During the studies carried out in the Microbiology Laboratory of VITI, antibiotic discs were prepared and used to assess the sensitivity of the S. Enteritidis pathogen to four types of antibiotics: Enroflan, Nitox, Ditrim, and ETIS-2 complex preparation (in both aqueous and oily emulsions). The disk diffusion method was

employed on Salmonella-Shigella agar, Bismuth Sulphite agar, and Blood Agar Base (Infusion Agar Base) to determine antimicrobial activity.

The cultures with antibacterial agent discs were incubated at 37°C for 24 hours. Antibiotic sensitivity was determined according to the sensitivity categories (if the growth area of the bacteria with the disc installed is 1,5-2,5 cm, it is considered sensitive; if up to 1.5 cm, it is less sensitive; and if there is no growth area, it is considered resistant). The growth zone of each colony was compared to determine this [3].



1. 1:10 ratio oily emulsion of ETIS-2 preparation – **sensitive,**
2. 1:100 ratio aqueous solution of ETIS-2 preparation – **less sensitive,**
3. 1:100 ratio oily emulsion of ETIS-2 preparation – **less sensitive,**
4. 1:50 ratio (aqueous) of ETIS-2 preparation – **not sensitive,**
5. 1:50 ratio (oily) of ETIS-2 preparation – **less sensitive,**
6. Main concentration of ETIS-2 preparation – **highly sensitive,**
7. (No.1) 1:10 ratio aqueous solution of ETIS-2 preparation – **sensitive,**
8. (No.2 oil) Ditrim 1:10 ratio oily solution – **sensitive,**
9. (No.4 water) Nitoks 1:10 ratio solution – **sensitive,**
10. (No.5 water) Enroflan 1:10 ratio solution – **sensitive.**

Figure 2: Antibiotic sensitivity of Salmonella pathogens grown on Bismuth Sulphite Agar medium.

The aqueous and oily emulsions of ETIS-2 preparation were diluted at ratios of 2, 10, 50, and 100. Additionally, the colonies of Salmonella were studied based on standard microbiological methods, including colony morphology, biochemical characteristics, and Gram staining.

RESULTS OF THE RESEARCH.

To determine antibiotic sensitivity using the disk-diffusion method, our studies involved the use of ETIS-2 preparation, Ditrim, Nitoks, and Enroflan antibiotics in diluted aqueous and oily emulsions on Salmonella pathogens. Their effect on the S.enteritidis strain was determined (Table 2).

Table 1

Antibiotic sensitivity of S. enteritidis strain grown on different media in the presence of ETIS-2 preparation and other antibiotics.

No.	Preparation Name	Dilution Level	Effect on		
			Sensitivity of Salmonella pathogens grown on Bismuth Sulphite Agar medium.	Sensitivity of Salmonella pathogens grown on Salmonella Shigella Agar medium.	Sensitivity of Salmonella pathogens grown on Blood Agar Base (Infusion Agar Base) medium.
1	ETIS-2 (Oily Emulsion)	1:1	Sensitive	Sensitive	Sensitive
		1:10	Sensitive	Less Sensitive	Less Sensitive
		1:50	Less Sensitive	Less Sensitive	Less Sensitive
		1:100	Not sensitive	Less Sensitive	Less Sensitive
2	Ditrim	1:10	Sensitive	Sensitive	Sensitive
		1:50	Less Sensitive	Less Sensitive	Less Sensitive
3	Nitoks	1:10	Less Sensitive	Less Sensitive	Sensitive
		1:50	Not sensitive	Not sensitive	Less Sensitive
4	Enroflan	1:10	Sensitive	Sensitive	Sensitive
		1:50	Less Sensitive	Less Sensitive	Less Sensitive

According to the results of Table 1, according to the sensitivity of the S. enteridis strain grown on Bismuth Sulphite Agar, it was found that: Salmonella pathogens are sensitive to the oil emulsion of the ETIS-2 complex preparation in a ratio of 1:1 and 1:10, the 1:50 emulsion is less sensitive, and the 1:100 oil emulsion is not sensitive.

Salmonella pathogens are sensitive to the oil emulsion of the Ditrim preparation in a ratio of 1:10, the 1:50 emulsion is less sensitive. Salmonella pathogens are sensitive to the oil emulsion of the Nitox preparation in a ratio of 1:10, the 1:50 emulsion is not sensitive. Enroflan preparations are sensitive to the oil emulsion of the Enroflan preparation in a ratio of 1:10, the 1:50 emulsion is less sensitive.

According to the sensitivity of *S.enteridis* grown on a Salmonella Shigella nutrient medium: ETIS-2 complex preparation was found to be sensitive to the 1:1 and 1:10 oil emulsion of the 1:50 emulsion, and 1:100 oil emulsion. Ditrim preparation was found to be sensitive to the 1:10 oil emulsion of the 1:50 emulsion, and 1:100 oil emulsion. Nitox preparation was found to be sensitive to the 1:10 oil emulsion of the 1:50 emulsion, and 1:10 emulsion, respectively. Enroflan preparation was found to be sensitive to the 1:10 oil emulsion of the 1:50 emulsion, and 1:10 emulsion, respectively.

According to the sensitivity of S. enteridis grown on blood agar base (Infusion agar base), it was found that: the oil emulsion of the ETIS-2 complex preparation in a ratio of 1:1 and 1:10 is sensitive to the causative agent of salmonella, the 1:50 emulsion is less sensitive, and the 1:100 oil emulsion is less sensitive. The oil emulsion of the Ditrim preparation in a ratio of 1:10 is sensitive to the causative agent of salmonella, the 1:50 emulsion is less sensitive. The oil emulsion of the Nitox preparation in a ratio of 1:10 is sensitive to the causative agent of salmonella, the 1:50 emulsion is less sensitive. The oil emulsion of the Enroflan preparation in a ratio of 1:10 is sensitive to the causative agent of salmonella, the 1:50 emulsion is less sensitive.

Materials and Research Methods

The scientific research on the effect of the ETIS-2 preparation against salmonellosis was conducted at the Microbiology and "Study of Young Animal Diseases" laboratories' vivarium using 6 sheep. For this purpose, a one-day culture of *Salmonella Enteritidis* strain grown on meat peptone agar (GPA) was prepared into a suspension using a physiological solution. The *Salmonella Enteritidis* strain, obtained from the Microorganisms Collection, was tested for its pathogenicity in 9 marine pigs in the Tuberculosis Laboratory. For this, the McFarland Standard

International, developed in France, was used to compare and prepare the suspension. The suspension was diluted to a concentration of 1.92×10^{-4} mol/L $BaSO_4$ and then sterilized to determine the pathogen's pathogenicity in 6 sheep (Table 2).

In the experiment, 3 sheep from Group 1 were administered 2 ml of the *Salmonella Enteritidis* strain with an LD_{50} of 2.5×10^9 CFU (LD_{50}) into the abdominal cavity. In Group 2, 3 control sheep were also administered the same dose of *Salmonella Enteritidis* strain (Table 1). The general condition, physiological and clinical state (body temperature, heart rate, and respiratory rate), as well as hematological parameters of the sheep in the experiment, were continuously monitored before and after inoculation.

The goal of our research is to study the effect of the ETIS-2 complex preparation on *Salmonella Enteritidis* pathogens, compare the effectiveness of the preparation in treating the disease, and analyze the hematological changes in the treated sheep's organism.

In the experiment, Group 1 sheep (infected with salmonellosis) were treated with the ETIS-2 complex preparation after the clinical signs of the disease appeared following infection. The treatment involved administering 5.0 ml subcutaneously per

Table 2

Results of the Experiment on the Effect of ETIS-2 Preparation Against Sheep Salmonellosis

№	Pathogen Name	Infection Method and Dose	Method	Num-ber of Sheep	ETIS-2 Dose (100 kg/ 5 ml)	Number of ETIS-2 Injections (Subcutaneous)					Result
						Day 1	Day 2	Day 3	Day 4	Day 5	
1	Salmonella Enteritidis experiment	LD_{50}2,5x10^9 KXB	Abdo-minal cavity	3	2-3 ml	I	II	III	IV	V	100% Cured
2	Salmonella Enteritidis control	LD_{50}2,5x10^9 KXB	Abdo-minal cavity	3	-	control					Sick
3	Intact control (healthy) group	-	-	-	-	-					Healthy

100 kg of body weight. For treatment, the ETIS-2 complex preparation was injected subcutaneously once a day at a dose of 3 ml per head for 7 days. The control group did not receive the preparation (see Table 2).

In the experiment, blood samples were taken from the jugular vein of the sheep on days 3, 6, and 9 after infection, and hematological parameters were measured using a photometric method. For this, 0,2 ml of blood from the experimental, control, and intact groups of sheep was collected into a test tube and analyzed using MINDRAY BC-20, MINDRAY BA-88A, MINDRAY BS 30s hematology equipment (manufactured in China).

The aim of our research is to study the effects of the ETIS-2 complex preparation on Salmonella Enteritidis pathogens, compare the effectiveness of the preparation in treating the disease, and analyze hematological changes in the treated sheep.

In Group 1 (experimentally infected with salmonellosis), 36 hours after infection, the initial clinical signs of the disease appeared, including an increase in body temperature (+40,3°C), weakness, and reduced appetite. In the following days, these signs worsened, and diarrhea was observed in two sheep on days 3-4 of the experiment. After the clinical signs of illness appeared in the experimental sheep, the ETIS-2 complex preparation was administered subcutaneously once a day at 3 ml per head for 7 days.

Research Results

In the conducted studies, the initial clinical signs of the disease were observed in both the experimental Group I and the control Group II, 36 hours after infection. In the experimental animals, an increase in body temperature (+41,6°C), weakness, and reduced appetite were detected. In the following days, these clinical signs worsened, and diarrhea was observed in the sheep during days 3-4 of the experiment. After the signs of illness appeared in the experimental sheep, the ETIS-2 complex preparation was administered subcutaneously once a day at a dose of 3 ml per head for 7 days (see Table 2). On the third day of treatment, the body temperature of the sick sheep returned to normal (+38,4°C), appetite was restored, and diarrhea stopped. During the 6th-7th days of treatment and the following period, no signs of illness were observed in the experimental sheep.

In the control group, the initial signs of illness appeared 36 hours after infection. The clinical signs observed included an increase in body temperature (+40,9°C), an increased heart rate, difficulty breathing, general weakness, reduced rumination, and decreased appetite. In the following days, these signs worsened, and diarrhea and blood clots in the feces were observed in two sheep on days 3-4 of the experiment. In this group, the Salmonella Enteritidis strain exhibited typical virulence characteristics, and the sheep showed complete manifestations of typical salmonellosis symptoms.

In the intact Group III, no signs of illness were observed, and these sheep did not undergo treatment with the ETIS-2 preparation (see Table 2).

According to the hematological examination results, in the experimental Group I, after the sheep were infected with Salmonella and the clinical signs of the disease began to appear, the hemoglobin level was 6,4±0,24 x10 g/L, the erythrocyte count was 7,21±0,34 $x10^{12}$ g/L, the leukocyte count was 15,9±0,70 $x10^{9}$/L, and the lymphocyte count was 81,4±3,99 %$x10^{9}$/L. The obtained results indicated a decrease in hemoglobin and erythrocyte levels, along with an increase in leukocyte and lymphocyte counts. The hematocrit value decreased to 22,5±1,06 $x10^{-2}$L/L on the 3rd day after infection. Anemia was observed in the experimental sheep.

As a result of the hematological examination (see Table 3), in Group I, on the 9th day of the experiment, the hemoglobin level increased to 9,5±0,28 x10 g/L, erythrocytes reached 9,82±0,41 $x10^{12}$ g/L, leukocytes increased to 11,9±0,47 $x10^{9}$/L, and lymphocytes increased to 69,4±2,22 %$x10^{9}$/L. The hematocrit level decreased to 29,6±1,24 $x10^{-2}$L/L on the 9th day of the experiment. The results indicate that anemia (a decrease in red blood cells) was observed in the experimental sheep during the first 3 days after infection.

Table 3

Hematological Examination Results of Blood Samples from Sheep Infected with Salmonella

№	Group Name and Inventory Numbers	Hemoglobin, x10 g/L			Erythrocytes, x10¹² g/L			Leukocytes, x10⁹/L			Lymphocytes, %x10⁹/L			Hematocrit, x10⁻² L/L		
Physiological Norm		**9-15**			**9-15**			**4,0-12,0**			**40-75 2x9**			**27-45**		
Group I (Experimental Group)		Day 3	Day 6	Day 9	Day 3	Day 6	Day 9	Day 3	Day 6	Day 9	Day 3	Day 6	Day 9	Day 3	Day 6	Day 9
1	Right ear painted	6,9±0,24	8,6±0,46	9,6±0,28	7,31±0,31	9,87±0,35	9,82±0,33	15,2±0,73	13,6±0,45	12,1±0,47	81,3±3,82	75,9±3,42	70,4±3,73	22,1±0,62	26,7±1,31	29,2±1,72
2	Left ear painted	6,6±0,18	8,7±0,41	9,1±0,17	7,14±0,34	9,62±0,16	9,76±0,51	16,5±0,56	12,8±0,73	11,4±0,33	80,5±3,46	74,8±2,02	68,3±1,50	23,4±0,87	27,2±0,79	30,1±1,11
3	Forehead area painted	6,4±0,27	9,5±0,31	9,9±0,23	7,16±0,30	9,84±0,53	9,88±0,21	15,9±0,57	13,1±0,56	12,3±0,65	82,4±2,64	74,7±3,29	69,5±3,54	21,9±1,01	28,1±1,04	29,4±1,26
M±m		**6,4±0,24**	**8,9±0,41**	**9,5±0,28**	**7,21±0,34**	**9,78±0,36**	**9,82±0,41**	**15,9±0,70**	**13,2±0,58**	**11,9±0,47**	**81,4±3,99**	**75,1±3,53**	**69,4±2,22**	**22,5±1,06**	**27,3±1,07**	**29,6±1,24**
Group II (Experimental Group)		***Day 1***	***Day 3***	***Day 29***	***Day 1***	***Day 3***	***Day 29***	***Day 1***	***Day 3***	***Day 29***	***Day 1***	***Day 3***	***Day 29***	***Day 1***	***Day 3***	***Day 29***
1	Right side of the neck painted	6,8±0,26	6,5±0,28	6,4±0,19	7,81±0,34	6,51±0,23	6,24±0,21	14,8±0,71	15,4±0,51	16,7±0,65	83,9±3,91	82,9±3,73	86,1±4,56	25,4±0,71	22,3±1,09	21,8±1,29
2	Left side of the neck painted	6,9±0,19	6,8±0,32	6,9±0,13	7,43±0,33	6,78±0,12	6,46±0,34	15,2±0,52	15,9±0,91	17,5±0,51	81,5±3,50	86,7±2,34	88,2±1,94	23,2±0,86	21,5±0,62	20,2±0,75
3	Chest area painted	6,7±0,28	6,4±0,21	6,3±0,14	7,65±0,32	6,74±0,36	6,88±0,14	15,8±0,57	16,2±0,70	16,9±0,90	84,5±2,70	86,1±3,79	86,9±4,43	22,8±1,05	20,7±0,77	19,9±0,86
M±m		**6,8±0,22**	**6,6±0,21**	**6,5±0,32**	**7,63±0,28**	**6,68±0,13**	**6,53±0,30**	**15,3±0,69**	**15,8±0,59**	**17,1±0,65**	**83,1±3,74**	**85,2±4,01**	**87,1±3,66**	**23,8±0,83**	**21,5±0,82**	**20,6±0,95**
Group III (Intact Group)		***Day 3***	***Day 6***	***Day 9***	***Day 3***	***Day 6***	***Day 9***	***Day 3***	***Day 6***	***Day 9***	***Day 3***	***Day 6***	***Day 9***	***Day 3***	***Day 6***	***Day 9***
1	Right front leg painted	9,7±0,37	9,5±0,41	9,8±0,28	9,73±0,46	9,52±0,33	9,41±0,32	10,4±0,50	10,9±0,36	11,2±0,43	61,8±2,90	62,2±2,80	60,7±3,22	32,5±0,91	31,2±1,53	31,8±1,88
2	Left front leg painted	9,3±0,225	9,1±0,43	9,2±0,17	9,61±0,42	9,59±0,16	9,63±0,50	11,5±0,39	10,7±0,61	11,3±0,33	59,7±2,57	59,6±1,61	57,5±1,27	31,4±1,16	32,6±0,95	32,9±1,22
3	Left abdomen side painted	9,4±0,39	9,2±0,30	9,3±0,21	9,58±0,40	9,37±0,51	9,42±0,20	10,9±0,39	10,5±0,45	11,4±0,60	61,8±1,98	58,5±2,57	59,8±3,05	29,8±1,37	31,3±1,16	30,7±1,32
M±m		**9,5±0,41**	**9,3±0,38**	**9,4±0,46**	**9,64±0,45**	**9,49±0,35**	**9,49±0,37**	**10,9±0,48**	**10,7±0,57**	**11,3±0,44**	**61,1±2,87**	**60,1±2,22**	**59,3±2,49**	**31,2±1,19**	**31,7±1,24**	**31,8±1,24**

In the control group II sheep, after being infected with Salmonella and when the clinical signs of the disease appeared, on the 3rd day of the experiment, the hemoglobin level was 6,8±0,22 x10 g/L, erythrocytes were 7,63±0,28 $x10^{12}$ g/L, leukocytes were 15,3±0,69 $x10^{9}$/L (decreased), and the lymphocyte count increased to 83,1±3,74 $\%x10^{9}$/L. The hematocrit value decreased to 23,8±0,83 $x10^{-2}$L/L on the 3rd day after infection. These results indicate the development of anemia in the sheep.

In the intact Group III sheep, on the 3rd day of the experiment, the hemoglobin level was 9,5 x10 g/L, erythrocytes were 9,64±0,45 $x10^{12}$ g/L, leukocytes were 10,9±0,48 $x10^{9}$/L, lymphocytes were 61,1±2,87 $\%x10^{9}$/L, and hematocrit was 31,2 $x10^{-2}$L/L. Throughout the experiment, no significant changes were detected in their values.

In the intact Group III sheep, on the 9th day of the experiment, the hemoglobin level was 9,5±0,46 x10 g/L, erythrocyte count was 9,94 $x10^{12}$ g/L, leukocyte count was 10,6±0,40 $x10^{9}$/L, lymphocyte count was 59,1±2,48 $\%x10^{9}$/L, and hematocrit

was 30,2±1,39 x10^{-2}L/L. Throughout the experiment, no significant changes were observed in their values (see Table 3).

Thus, according to the results of the conducted research, in the sheep treated with the ETIS-2 complex preparation, the hematological examination results showed that after infection with Salmonella pathogens, when the clinical signs of the disease began to appear, a decrease in hemoglobin, erythrocyte, and hematocrit levels, along with an increase in lymphocyte and leukocyte counts, was observed in both the experimental and control groups.

Conclusions

1. The water and oily emulsions of the ETIS-2 complex preparation exhibited bactericidal and bacteriostatic effects in Salmonella, Shigella, Bismuth Sulphite, and Blood agar base (Infusion agar base) agar media, as determined by the disk diffusion method.
2. The Salmonella pathogen is sensitive to the 1:1 and 1:10 ratios of the oily emulsion of ETIS-2 complex preparation. The 1:50 and 1:100 ratios of the oily emulsion, however, showed lower sensitivity to the Salmonella pathogen.
3. In sheep treated with ETIS-2, hematological examinations revealed that after infection with Salmonella pathogens, when the clinical signs of the disease began to appear, there was a decrease in hemoglobin, erythrocyte, and leukocyte levels, an increase in lymphocyte count, and a decrease in hematocrit. These indicators indicated the development of anemia in the sheep.
4. After the sheep in the experiment were infected with the Salmonella Enteritidis strain and the clinical signs of the disease fully appeared, they were treated with the ETIS-2 complex preparation. The treatment involved administering 3 ml per head subcutaneously once a day for 7 days. On the 3rd day of treatment, the sick sheep's body temperature returned to normal (+38,4°C), their appetite was restored, and diarrhea ceased. On the 6th and 7th days of treatment, as well as in the following period of the experiment, no signs of illness were observed in the sheep.
5. When treating salmonellosis, the use of the ETIS-2 complex preparation eliminated the need for other types of antibiotics or treatments.

6. The combination of components in the ETIS-2 complex preparation resulted in an advantage over other bacteriostatic agents. This combination provides a synergistic (where one drug enhances the effect of the other) and a prolonged (extends the duration of the drug's effect) outcome. The preparation can be used on all types of animals, regardless of their physiological condition, starting from 10 days of age.

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