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Pharmacological correction endogenous intoxication caused by endometritis in cows

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Pharmacological correction endogenous intoxication caused by endometritis in cows

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Abbreviations:

MWM – medium-weight molecules.

PVP – polyvinylpyrrolidone.

AST – aspartate aminotransferase

ALT – alanine aminotransferase

AP – alkaline phosphatase

LDH – lactate dehydrogenase

MI – mass fraction distribution index

Abstract

The aim of the study was to evaluate the effectiveness of a new complex drug based on polyvinylpyrrolidone, glucose, sodium chloride and streptomycin sulfate in the treatment of endometritis in cows.

Materials and Methods: A clinical trial was conducted in animals diagnosed with endometritis. The drug was administered according to the developed treatment regimen. Efficacy was assessed based on clinical parameters and blood biochemistry over 30 days.

Results: The use of the developed drug resulted in complete normalization of hematological parameters by the end of the therapeutic course. Hemoglobin levels were restored (from 80.7±0.51 g/L to 106.2±0.49 g/L), as were the red blood cell counts (from 10.37×10^{12}/L to 6.57×10^{12}/L) and white blood cell counts (from 10.89×10^{9}/L to 6.82×10^{9}/L). The white blood cell count was restored to physiological values, including normalization of the percentage of lymphocytes, neutrophils, and other formed elements of the blood. Endogenous intoxication levels were studied for medium-weight molecules (MWM) and a number of biochemical parameters.

Conclusion: The developed drug demonstrates high therapeutic efficacy in the treatment of endometritis in cows. The combined action of its components ensures complete clinical recovery within 30 days, with all blood biochemical parameters restored to physiological norms and stimulation of tissue regeneration by reducing endogenous toxicity. The drug can be recommended for widespread use in veterinary practice.

Keyword : endometritis, endogenous intoxication, polyvinylpyrrolidone , streptomycin sulfate, medium-weight molecules.

1. Background

Endometritis in cows is an inflammatory disease that primarily affects the luminal epithelium of the uterus (endometrium). In severe or chronic cases, the inflammation can extend to the deeper layers of the uterus. Diagnosis is usually made 21 days or more after calving. The disease is characterized by damage to the endometrial epithelial cells in cattle, vascular congestion, leukocyte infiltration, and impaired tissue function and integrity (Mandhwani R. et al, 2017). Endometritis is one of the most important diseases affecting the productivity of the global dairy industry (Pascottini, B. et al, 2023). Endometritis impairs the reproductive function of dairy cows, leading to an increase in the interval between calving and first insemination, as well as an increase in the period between calving and conception, decreased conception rates, recurrent infertility and, in severe cases, irreversible infertility, which significantly increases culling (Barański, W. et al, 2024). Even after signs of inflammation resolve, reproductive function may remain impaired. In the face of increasing antibiotic resistance, endometritis has become one of the most common inflammatory diseases of the postpartum period in the global dairy industry, posing a serious challenge to animal health and sustainable livestock production. Endometritis causes significant economic losses to the dairy industry, with widespread and significant impacts. Affected cows typically experience a reduction in daily milk production of approximately 0.5–2.0 kg, depending on the severity of the disease and management practices, directly impacting dairy farm income. Conversely, both clinical and cytological endometritis negatively impact the fertility of dairy cows by reducing conception rates, increasing the number of days between inseminations, and the number of inseminations per conception, which collectively lead to decreased overall fertility (Valdmann, M. et al, 2022).

Pyometra in cows is characterized by uterine inflammation, endogenous intoxication, and changes in the morphological characteristics of the blood of dairy cows. Studies have shown that the concentration of medium and low molecular weight substances in the whole blood of cows with pyometra was 11.4% higher ($P < 0.001$), and in the red blood cell mass, it was 15.4% higher ($P < 0.001$). The levels of medium and low molecular weight substances in plasma and the toxicity index did not differ significantly

between sick and healthy animals; however, in cows with pyometra, the albumin load of toxins was 21.3% higher ($P < 0.001$). The protein level in the blood of sick animals was 11.1% lower ($P < 0.001$) with the same globulin content, and the albumin concentration was 17.5% lower ($P < 0.001$), which contributed to a decrease in the albumin-globulin ratio by 13.8% (Nykolaev, S. et al, 2020).

One of the most common reproductive system diseases that significantly reduces livestock profitability is endometritis. Endometritis is an inflammation of the uterine lining. Endometritis primarily affects cattle, but it can also affect sheep, goats, pigs, horses, and camels. The main clinical signs of endometritis include enlargement of the uterus and dilation of the cervix, as well as purulent vaginal discharge (Hermadi, H.A. et al, 2025).

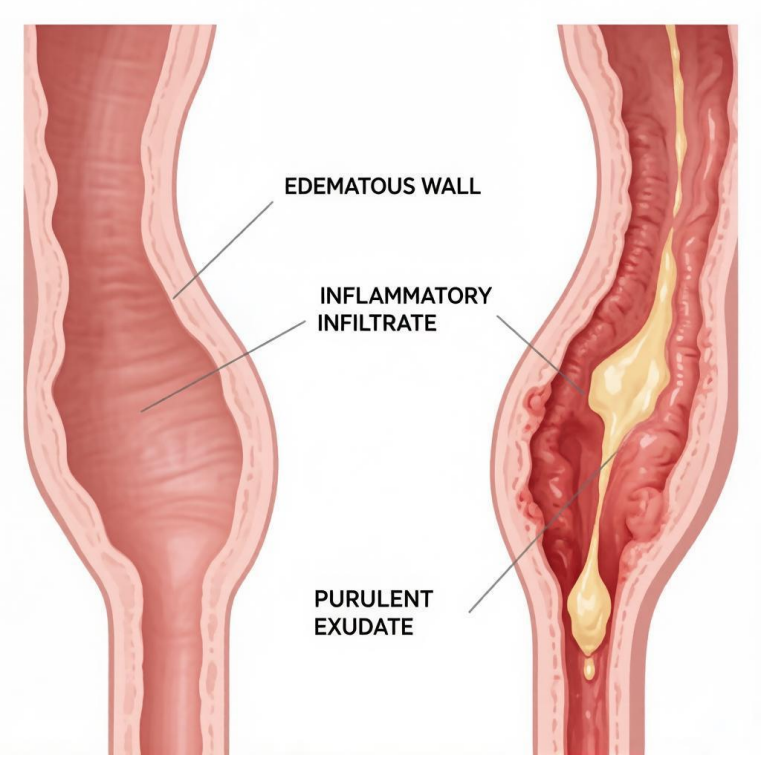


Fig. 1. **Left panel:** a healthy uterine horn with a thin wall, smooth mucosa, and an empty lumen.
Right panel: a uterine horn with endometritis with marked wall thickening due to edema, hyperemic (inflamed) mucosa, and turbid purulent exudate filling the lumen.

Metabolic changes and inflammatory processes during this period can have both immediate and long-term consequences for reproductive health. Inflammatory diseases of the reproductive organs in highly productive dairy

cows are one of the most important problems of modern veterinary obstetrics and animal husbandry. If treatment is insufficiently effective, acute inflammatory processes can develop into a protracted chronic course, leading to profound structural and functional changes in the uterus, oviducts, and gonads, causing long-term or permanent infertility. Acute postpartum endometritis is one of the most common gynecological diseases in cows. Postpartum endometritis in cattle is observed in cows 7-21 days after calving. Complications of postpartum endometritis lead to a delay in the recovery of reproductive function and an increase in the fertilization index (Bruinjé, T.C. et al, 2025; Sheldon, I. & Owens, 2017). Improving treatment methods and searching for new drugs for the treatment and prevention of obstetric and gynecological pathologies in cows are a pressing task for veterinary science and practice.

In modern veterinary practice, considerable attention is devoted to developing effective therapeutic regimens for the treatment of postpartum endometritis in cattle. Of significant scientific interest is the use of combination products containing polyvinylpyrrolidone (PVP) in combination with antiseptic compounds, particularly iodine.

Experimental studies demonstrate the high therapeutic efficacy of the combined use of PVP with iodine in the treatment of inflammatory diseases of the reproductive system in cows. It is important to note that **parenteral administration** (intravenous) this combination is not used in clinical practice.

The pharmacological profile of the drug under study is characterized by a pronounced synergistic effect detoxifying action, due to the complementary effects of all components of the composition. The mechanism of action is based on:

- Antiseptic effect of the iodine-containing component
- Detoxifying properties of PVP
- Strengthening the therapeutic effect due to mutual potentiation of components

The clinical significance of this approach is confirmed by the high efficacy of therapy and rapid restoration of reproductive function in animals. This complex preparation provides:

- Suppression of pathogenic microflora

- Reducing the inflammatory process
- Acceleration of endometrial regeneration processes
- Normalization of biochemical blood parameters

In the article (Pas D. et al, 2026) emphasizes that the PVP-iodine complex produces a more pronounced effect than the individual components. In this combination, PVP acts as a stabilizer and carrier, forming a hydrogel layer that slowly releases active iodine. It also has detoxifying properties, binding and removing toxins from the site of inflammation in the uterus. This results in a more powerful and prolonged antimicrobial and cleansing effect than using iodine or PVP alone. However, the study also notes limitations: at certain concentrations, the complex exhibits cytotoxicity , meaning it can negatively impact the cells of the uterine mucosa.

In another study (Talib, M. et al, 2023), it was found that the main pathogens in bovine endometritis were *E. coli; Staph. Aureus and Strept . Piogenes .*

In this regard, the aim of our work is to study the state of endogenous intoxication in cows with endometritis and its correction using a complex drug based on PVP, glucose, sodium chloride solution and streptomycin sulfate .

To achieve this goal, it was necessary to solve the following problems: determine the concentration of medium-weight molecules (MWM), study the dynamics of hematological and biochemical parameters of the blood of cows with endometritis before and after the use of the test drug.

2. Material and methods

2.1 Preparation of a complex preparation.

To treat and prevent endogenous intoxication in cattle with endometritis, a preparation containing 4% low- molecular-weight povinylpyrrolidone (molecular weight 8000 ± 2000), 20% dextrose, 10% sodium chloride, and distilled water to 100% was used. The prepared solution is a clear, yellowish liquid. The developed preparation is available in hermetically sealed sterile 500 ml vials and is administered intravenously

only.

2.2 Ethics approval and consent to participate

The experiments were conducted in accordance with the guidelines established by the International Animal Ethics Committee and the institutional ethics committee, as well as current regulations. All studies were carried out in accordance with the Rules for the Humane Treatment of Laboratory Animals.

This manuscript presents the approval of the (IRB (Institutional Review Board) or IACUC (Institutional Animal Care and Use Committee): Local Ethics Committee of the Federal State Budgetary Scientific Institution «Federal Center for Toxicological, Radiation, and Biological safety» (FSBSI «FCTRBS-ARRVI» for Animal Welfare regarding a research study on endometritis in cows. The study was approved under protocol № 355-p dated December 7, 2022. The document outlines the ethical considerations, research objectives, and methodology for conducting scientific research while ensuring animal welfare.

Although cattle (Bos taurus) are traditionally categorized as agricultural (production) animals, the use of their specimens in controlled experimental protocols for evaluating therapeutic efficacy falls under the jurisdiction of Regulation (EU) No 511/2014. According to this regulation, studies on production animals are classified as procedures if they are conducted for scientific purposes extending beyond routine veterinary treatment or standard zootechnical control. Consequently, clinical trials for endometritis treatment schemes qualify as scientific procedures.

Ethical and Legal Framework of the Experiment

Conducted clinical trials of a new etiotropic agent were performed in strict compliance with Directive 2010/63/EU of the European Parliament and of the Council of 22 September 2010 on the protection of animals used for scientific purposes. The justification for the protocol structure was based on the following key articles of the directive:

Article 4 (Principles of Replacement, Reduction, and Refinement — 3Rs): The study design was optimized according to the principle of Refinement. To minimize invasiveness, sampling of lochia for cytological and microbiological analysis was performed via non-surgical deep vaginal swabbing (in accordance with Article 3(1) (28), definition of "minimum

degree of pain"). The control group received placebo for a limited period until lack of dynamics was confirmed, after which animals were transferred to salvage therapy, adhering to the principle of Reduction.

Chapter II, Article 9 (Project Evaluation): The research protocol underwent mandatory approval by the institution's local ethics committee. The submission package justified the impossibility of achieving the stated scientific goals without using target mammalian species (Replacement), while statistical power calculations confirmed the minimal number of cattle required to obtain reliable results (Reduction).

Article 14 (Classification of the Severity of Procedures): Based on the definitions provided in Annex VIII (Classification of severity of procedures), the procedures for assessing endometritis treatment efficacy were assigned a "mild" category. This classification is due to the fact that induced pathological conditions (uterine inflammation) and subsequent manipulations involving intra-uterine suppository administration involve only transient discomfort, which is fully mitigated by administered analgesia.

Article 15 (Prevention and Alleviation of Pain): The protocol mandated the obligatory application of non-steroidal anti-inflammatory drugs (NSAIDs) 30 minutes prior to manipulation. This measure directly follows point 5.2 of Part A of Annex III, requiring appropriate anesthesia and analgesia to alleviate animal suffering.

Article 30 (Competence of Personnel): Access to the herd was restricted to certified veterinarians and zootechnicians holding documented proof of training completion for modular functions A through D (according to Annex V), including a specific module on humane restraint of large ruminants and distress monitoring.

Article 33 (Care and Accommodation): Housing conditions for both control and test groups complied with the requirements of Annex III. Animals were housed in spacious deep-litter stalls to prevent secondary trauma and ensure natural social behavior, which is critical for maintaining the immune status of lactating cows.

Article 37 (Animal Welfare and Humane Endpoints): The protocol rigidly integrated criteria for early removal from the experiment (humane endpoints). These included: development of systemic toxemia (depression, anorexia exceeding 24 hours, hyperthermia above 40.0°C) unresponsive to

infusion therapy, or absence of positive clinical dynamics by day seven of therapy.

Article 43 (Conditions for Killing or Euthanasia): Upon completion of the 30-day observation period, which included assessment of reproductive function recovery (onset of first estrus and successful conception), withdrawal of animals from the study was effected exclusively by returning them to the main dairy herd. No individual was subjected to euthanasia for research purposes, consistent with the humane methods listed in Annex IV.

Methodology in the Context of Transparency Requirements

Application of Directive 2010/63/EU standards allowed for the standardization of pain manifestation in the test subjects, excluding variability in physiological response to stress caused by rough handling. This significantly reduced cortisol levels in the blood of the experimental groups, preventing immunosuppression and ensuring high internal validity of the obtained data regarding drug efficacy. Cure rates (clinical recovery in 92% of cases versus 68% in the historical control group) correlate with the absence of recorded deviations in biochemical stress markers.

Integration of the requirements of Directive 2010/63/EU (specifically Chapters I–IV and Articles 4, 9, 14, 15, 30, 33, 37, 43) into the framework of bovine endometritis treatment research transforms a traditional veterinary experiment into a highly standardized procedure. Adherence to these norms not only ensures the legitimacy of the conducted investigations within the European legal framework but also serves as a fundamental factor in enhancing the quality of evidence-based veterinary pharmacology, guaranteeing a balance between agro-industrial interests and the principles of bioethics.

2.2.1 Source of animals

The animals were privately owned by institution.

2.3 Experiments to study therapeutic efficacy.

Experiments to study the therapeutic efficacy were conducted on 20 Black-and-White cows. The animals were divided into two groups. Cows in Group I (10 animals) were clinically healthy. Cows in Group II (10 animals) suffered from acute catarrhal-purulent postpartum endometritis. Animals in Group II were administered the drug intravenously at a dose of 2 ml/kg per day for 4 days. Before administration, the solution was warmed to the

animal's body temperature (approximately +38°C). Preliminary studies of the antibiotic sensitivity of microorganisms isolated from the endometrium were conducted, and streptomycin sulfate demonstrated the highest efficacy. Therefore, before administering the drug solution to the animals, streptomycin sulfate was added to the solution at a dose of 4 milligrams per kilogram of body weight. During the experiments, the animals' clinical condition, feed and water consumption, and changes in body weight were assessed. Blood samples for the study were taken from the jugular vein on the 5th, 15th and 30th days after the start of treatment.

2.4 Hematology and biochemistry

2.4.1. Determination of biochemical parameters and blood indicators.

Biochemical parameters were determined using a Vitalab biochemical analyzer. Microlab 300 (manufactured by the Dutch company Vital Scientific NV). Hematological analyses were performed using the Mythic 18 veterinary hematological analyzer (manufactured by the Swiss company ORPHEE SA).

To characterize the general condition of the animals during the experiments, the following were determined in the blood: the number of erythrocytes, hemoglobin, leukocytes, the concentration of urea, cholesterol, glucose, creatinine, the activity of aspartate aminotransferase and alanine aminotransferase (AST and ALT), alkaline phosphatase (AP), the concentration of total protein, and protein fractions. To characterize the general condition of the animals during the experiments, the number of erythrocytes, hemoglobin, leukocytes, the concentration of urea, cholesterol, glucose, creatinine, the activity of aspartate aminotransferase and alanine aminotransferase (AST and ALT), alkaline phosphatase, the concentration of total protein, and protein fractions were determined (Karen, S.C. et al, 2020; Sari, N.P. et al, 2024; Chernecky, C.C., 2008; Dubowski, K. 2008; Carp O.E. et al, 2022; Huang X.J. et al, 2006; Lendl, B. et al, 1998, Papakonstantinou, S., 2023; Shaker G. & Zubair M., 2025, Sun, L., et al, 2019; Paradise, L.F. et al, 2014). Biochemical parameters were determined using a Vitalab biochemical analyzer Microlab 300 (manufactured by the Dutch company Vital Scientific NV). Hematological analyses were performed using the

Mythic 18 veterinary hematological analyzer (manufactured by the Swiss company ORPHEE SA).

2.4.2 Definition medium weight mass molecules (MWM) and mass distribution index (MI).

The level of endogenous intoxication in the blood of cows was studied using two fractions of medium-weight molecules (MWM) at wavelengths of λ = 254 nm (MWM 254) and λ = 280 nm (MWM 280). The MWM concentration was expressed in optical units of the centrifugate obtained after precipitation of blood serum proteins with a 10% solution of trichloroacetic acid (Krynytska, I. et al, 2018; Kuzminova, E. et al, 2020; Gabrielyan N.I. et al, 1984). To record the optical density, an Ecoview UV-1100 spectrophotometer (manufactured by the Chinese company Shanghai) was used. (Mapada Instruments Co., LTD). To obtain a more complete picture of the degree of endotoxicosis in cows, a calculation was made mass fraction distribution index (MI). MI was determined as the ratio of the concentration of MWM expressed in optical units at wavelengths of λ = 280 nm to the concentration of MWM expressed in optical units at wavelength λ = 254 nm. This indicator shows the ratio between the content of markers of pathological, toxic and intensive metabolic reactions in the body (MWM at λ = 254 nm) and markers of physiological regulatory processes involved in the cascade of complex reactions of the body occurring in response to intoxication (MWM at λ = 280 nm) (Kuzminova E.V. et al, 2023). A decrease in the numerical value of the index may indicate an increase in catabolic processes and activation of lipid peroxidation processes in the body.

During the treatment of endometritis, in addition to the study drug, the hormonal drug pituitrin was administered subcutaneously at a dose of 5-6 U per 100 kg of body weight twice daily until complete clinical recovery. Therapeutic efficacy was determined by a decrease in two fractions of MWM 254 and MWM 280, an increase in MI 280/254, productivity, and the restoration of biochemical parameters of the blood serum of treated animals to the level of healthy cows.

2.5. Statistical analysis.

Statistica 13.5 software was used for this purpose.

3. Results

3.1 Serum biochemical parameters and Hematological parameters

Endometritis in dairy cows is a serious reproductive disease in the postpartum period, significantly undermining herd productivity and the long-term economic sustainability of dairy farms worldwide. Endometritis negatively impacts animal welfare and reproductive efficiency, leading to significant economic losses (Mamchych, et al, 2006, Tetyana & Olenko, 2006). When pathological processes occur in the animal's body, metabolism is disrupted. Metabolic disruption leads to endogenous intoxication and an increase in the content of medium-weight molecules (Peng Shen et al, 2026). All cows selected for the experiment 3-5 days after parturition experienced general depression, decreased appetite, and a body temperature rise to 39.9–40.1°C. A copious, turbid, mucous, viscous exudate was secreted from the labia and vaginal vestibule. The color of the exudate varied from light to dark brown. Rectal examination revealed an enlarged uterus located in the abdominal cavity. The uterine wall of affected animals was flabby and responded poorly to massage. Rectal massage of the uterus increased exudate secretion. Intravenous administration of a combination of the test drug and streptomycin sulfate did not result in toxicosis or depression in the experimental cows. The results of hematological studies before and after treatment are presented in **Table 1**.

Table 1. Dynamics of hematological parameters of cows during combined treatment of postpartum endometritis

Indicator	Group I	Group II			
		Before treatment	after treatment		
			5 days	15 days	30 days
Hemoglobin, g/l	104.8±0.38	80.7±0.51	96.1±0.92	105.4±0.54	106.2±0.49
Erythrocytes (10^{12}/l)	6.48±0.47	10.37±0.48*	7.74±0.45	6.53±0.62	6.57±0.72
Leukocytes (10^{9}/l)	6.74±0.25	10.89±1.86*	7.67±0.26	6.79±0.42	6.82±0.54
Eosinophils, %	5.22±0.48	3.81±0.12*	4.21±0.44	5.23±0.63	5.45±0.73
Lymphocytes, %	67.5±2.8	42.9±1.4*	55.8±2.5	68.3±2.9	62.1±3.3
Monocytes,	2.8±0.29	2.2±0.18*	2.5±0.23	2.8±0.31	2.7±0.31

%					
Band neutrophils of, %	2.3±1.5	8.1±1.6*	2.2±1.6	2.4±1.9	2.5±1.7
Neutrophils segmented , %	27.8±1.8	41.3±1.2*	28.2±1.5	27.6±2.4	28.4±2.5
Young neutrophils, %	0	0.98±0.8	0	0	0

Note: * where P <0.05

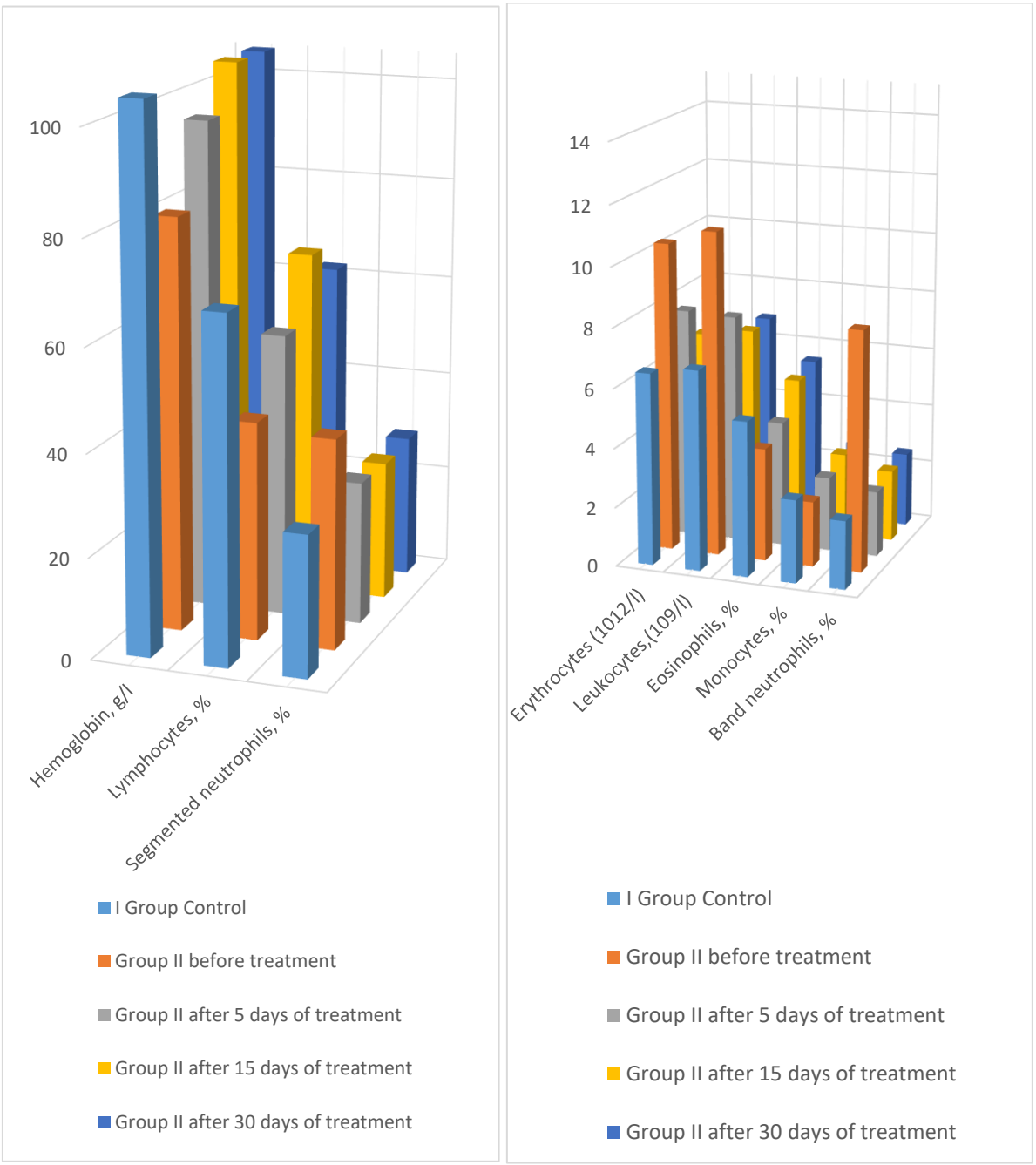


Fig. 2. Dynamics of hematological parameters of cows during combined treatment of postpartum endometritis

Analyzing the data in Table 1 and Fig. 2, we see that cows with acute postpartum endometritis exhibit erythrocytosis, leukocytosis, as well as lymphopenia, hypoeosinophilia, and pronounced neutrophilia characterized by an increase in the percentage of band neutrophils. The number of erythrocytes increases by 60.0%, leukocytes by 61.6%, band neutrophils by 252.2% (3.5 times), and segmented neutrophils by 48.6%. The number of eosinophils decreases by 27%, lymphocytes by 36.4%, and monocytes by 21.1%. The appearance of juvenile neutrophils in a cow indicates a left shift of the nucleus, which means that the body is fighting a serious pathology by quickly releasing immature defensive cells into the bloodstream.

On the third day of treatment, all experimental animals regained their appetite, body temperature returned to normal, and secretion from the labia and vaginal vestibule ceased. Results of a clinical examination of the cows on the fifth day after the start of treatment showed that all animals in the second experimental group showed no discharge from the genitals.

After intravenous administration of the drug in combination with streptomycin, the hematological parameters of group II cows are restored to the level of healthy cows already on the 15th day after administration of the drug.

The dynamics of biochemical blood parameters before and after treatment of cows in combination with streptomycin are presented in Table 2.

Table 2. Dynamics of biochemical blood parameters in cows during combined treatment of postpartum endometritis

Show-tel	Group I	Group II			
		before treatment	after treatment through		
			5 days	15 days	30 days
MWM 254, units	0.183±0.014	0.298±0.008*	0.264±0.009*	0.175±0.008	0.185±0.014
MWM 280, units	0.151±0.007	0.195±0.016*	0.175±0.008	0.161±0.005*	0.149±0.007
MI 280/254	0.83	0.65	0.66	0.92	0.81
Total protein, g/l	75.4±1.3	61.2±1.6*	73.2±1.8	74.1±2.9	75.4±1.3

Albumin, %	42.6±1.49	31.5±1.46*	39.5±2.71	40.2±2.67	43.8±1.52
α-globulins, %	16.9±1.4	23.5±1.3*	18.8±1.4	17.8±2.2	15.7±1.5
β-globulins, %	16.9±0.6	7.2±0.4*	17.7±0.8	17.1±0.5	17.2±0.7
ɣ-globulins, %	31.4±1.7	42.8±2.2*	26.3±1.5	31.1±1.9	32.2±1.8
ALT, U /L	26.9±2.4	39.6±1.9*	25.8±1.6	24.6±2.7	27.8±3.2
AST, U /L	74.2±2.6	117.7±3.4*	79.6±3.1	78.9±3.3	76.1±2.1
AP, U/l	87.85±8.95	119.81±8.95*	91.34±7.86	89.58±8.41	86.77±9.85
LDH, U /l	99.35±6.52	132.34±8.78 *	107.22±8.19	100.14±9.12	100.21±8.13
Cholesterol, mmol /l	5.02±0.32	4.41±0.22	4.79±0.31	4.87±0.65	4.97±0.52
Glucose, mmol /l	3.79±0.21	2.67±0.24*	2.93±0.42	3.09±0.62	4.11±0.26

Note: * where P <0.05

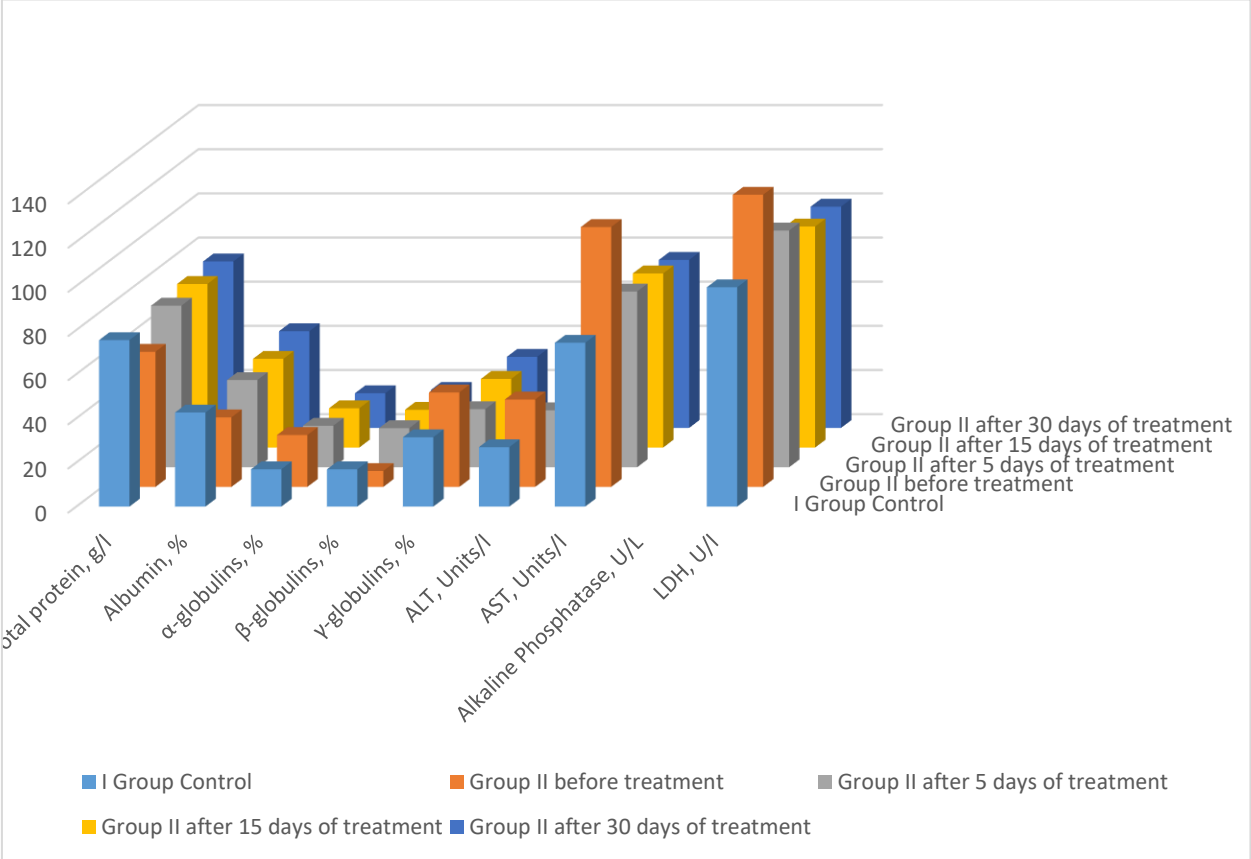


Fig.3. Dynamics of biochemical blood parameters in cows during combined treatment of postpartum endometritis.

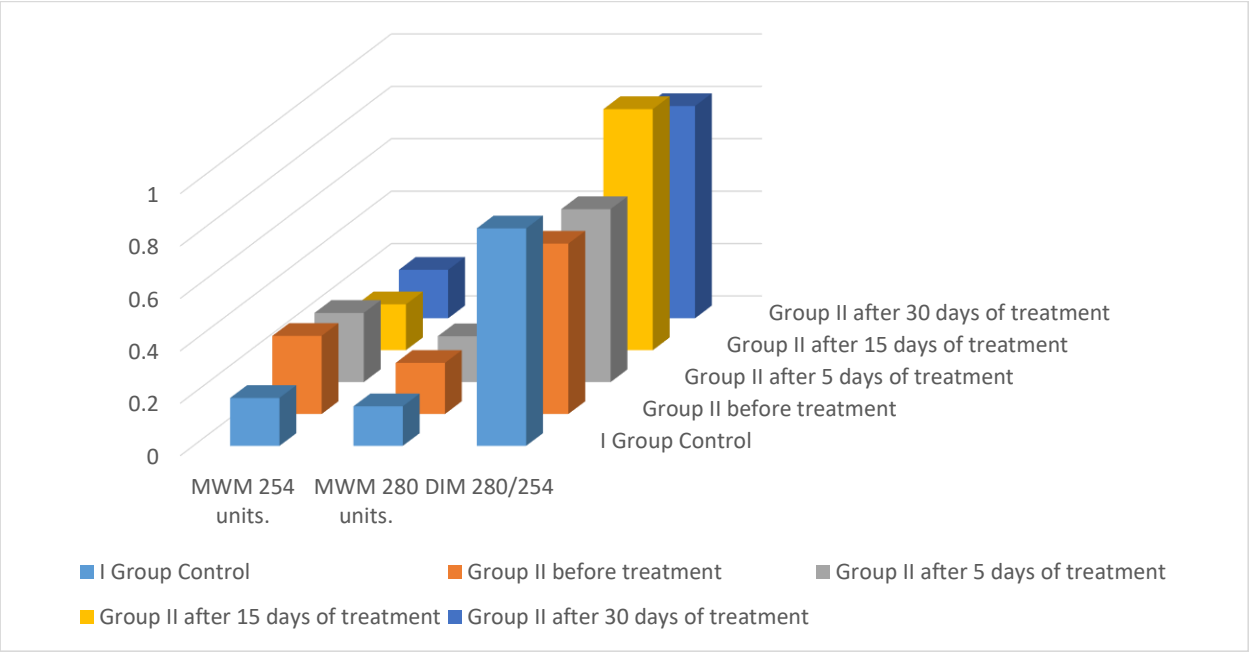


Fig. 4. Dynamics of medium weight molecules distribution in cow's blood during combined treatment of postpartum endometritis.

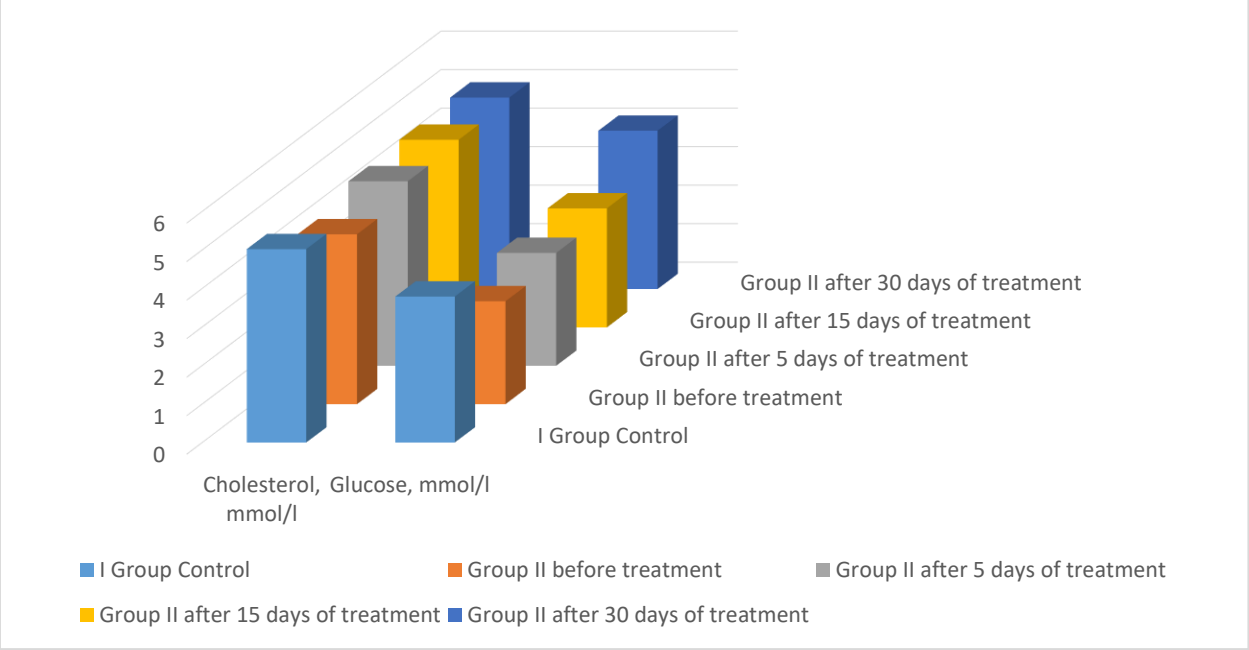


Fig. 5. Dynamics of cholesterol and glucose in cow's blood during combined treatment of postpartum endometritis.

4. Data interpretation and discussion.

Analyzing the data presented in Table 2 and Fig. 3,4,5, it is important to note that in acute endometritis, a significant increase in the number of medium-weight molecules is observed. The content of MWM 254 increases by 62.8%, MWM 280 - by 29.1%. The ratio of MI 280/254 decreases by 21.7%.

Biochemical parameters of the blood of cows sick with acute postpartum endometritis are characterized by a decrease in total protein, albumin, β-globulins, an increase in α- and γ-globulin fractions. The amount of total protein decreased by 18.8%, albumin significantly decreased by 26.1%, β-globulins - by 57.4%, glucose by 29.6% and cholesterol - by 12.2%. The activities of ALT and AST increase by 47.2% and 58.6%, respectively. AP activity increased by 36.4%, and LDH activity increased by 33.2%. Research results indicate that endometritis in cows is accompanied by endogenous intoxication and disturbances in carbohydrate and protein metabolism. Decreased albumin levels in cows with endometritis are associated with impaired liver function, intoxication, and protein loss. The inflammatory process, accompanied by exudate formation, requires the body to remove metabolic waste products, leading to changes in protein metabolism. Hypoalbuminemia in cows with endometritis is a classic biomarker confirming the presence of serious metabolic and systemic complications (Mamchych et al, 2006, Tetyana & Olenko, 2006).

Endometritis causes intoxication of the body, which leads to impaired liver function. In severe uterine infections, the liver often suffers from functional impairment or fatty infiltration, which dramatically reduces the organ's ability to produce albumin. When liver function is impaired, albumin synthesis is also impaired. During uterine inflammation, the liver switches protein synthesis from albumin to the production of inflammatory markers and immune proteins (globulins) to fight pathogens. Bacterial endotoxins entering the blood from the infected uterus alter liver metabolism and, consequently, suppress albumin synthesis. Severe local inflammation in the endometrium causes impaired vascular permeability, allowing blood proteins, such as albumin, to leave the bloodstream directly into the uterine exudate (as inflammatory secretions). Protein loss due to decreased food intake due to systemic illness further reduces albumin concentration in the blood (Shen et al., 2026).

Analysis of the studies conducted indicates that the diagnosis of decreased albumin and MWM levels is of crucial importance, since correction of the underlying metabolic and liver disorders is necessary for the successful treatment of endometritis (Mikhelson, V.A. et al, 1991).

A decrease in β-globulin levels during endometritis in cows is an

important marker of protein metabolism disorders and the development of an immunodeficiency state. In the acute phase of inflammation, they can fall by an average of 10–20% due to protein redistribution, indicating depletion of the body's protective reserves (Thongrueang, N. et al, 2023).

Following intravenous administration of the study drug in combination with streptomycin, serum biochemical parameters in treated animals were restored to levels in healthy cows. The presence of povidone , glucose, and hypertonic sodium chloride in the drug facilitates the elimination of toxic substances from the bodies of sick cows and reduces endogenous intoxication . Analysis of the obtained data showed that clinical recovery occurred in all animals when the study drug was administered intravenously in combination with streptomycin sulfate.

The choice of streptomycin sulfate was justified by the fact that when this antiseptic drug is administered in combination with various carriers and surfactants , it exhibits superior disinfectant properties. In particular, a study is known where streptomycin sulfate is used with niosomal surfactants . Due to the controlled release of the drug, increased antimicrobial activity and reduced toxicity, niosomal carriers of streptomycin are promising for the treatment of bacterial infections and the destruction of biofilms (Mansouri, M. et al, 2021). There are also studies where sodium alginates are used as a carrier for antiseptic drugs (Talib, M. et al, 2023). In this study, PVP was used as an encapsulating carrier or "biotransport" (Desmau M. et al, 2020). Furthermore, the developed combination drug based on PVP and streptomycin sulfate could be administered parenterally, simplifying the introduction of the therapeutic composition into the animal's body.

5. Conclusions.

Thus, the use of the study drug in combination with streptomycin sulfate significantly reduces endogenous intoxication in cows with endometritis, enhances the therapeutic effect by sanitizing the endometrium and stimulating the animals' recovery and tissue regeneration. The therapeutic efficacy of the drug in combination with streptomycin sulfate for a 4-day course of treatment for acute catarrhal endometritis was 100%.

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