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Experimental and Clinical Justification of the use of Probiotic-Sorption Drugs in Veterinary Surgery

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ABSTRACT
The wide range of therapeutic effects of silicon dioxide (reduction of endogenous intoxication, normalization of intestinal microbiocenosis, reduction of systemic inflammatory response, activation of detoxification function) makes its use as a matrix in the production of pharmacological drugs for the treatment and prevention of surgical infection by giving an interesting direction for scientific research. The article provides experimental and clinical justification for the use of complex probiotic-sorption drugs in veterinary surgery in the treatment of various forms of surgical infection.
Based on the results of the conducted research, the solution of an urgent scientific problem about the mechanisms of formation of microbiocenoses, improvement of methods of diagnosis, prevention and treatment of cats with surgical infections have been achieved. It is established that purulent-inflammatory processes in cats develop against the background of dysbiotic disorders of the microbial ecosystem of the intestinal tract, which has a certain prognostic value. The introduction to treatment regimens of probiotic-sorption drugs proved to be pathogenetically justified, which is confirmed by experimental and clinical studies.
Key words: Veterinary Surgery, Silicon Dioxide, Sorbent, Probiotic, Surgical infection, Cats.
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INTRODUCTION
The role of veterinary medicine in modern society is high, primarily in providing mankind with safe food and protecting human health from anthropozoonous diseases; protecting the environment from bio- contamination and the animals from infection; treating sick animals; conducting customs veterinary control. The profession of veterinary medicine becomes prestigious and important in protecting humanity and the biosphere from pollution, epizootics of infectious diseases, fulfilling the most noble mission in society.[1,2,3,4,5,6]
Treatment of purulent-inflammatory processes and to date remains, one of the most complex and urgent problems in surgery. Over the past decades, an increase in the number of purulent-inflammatory diseases and postoperative infectious complications in surgical patients has been registered.[7,8,9,10] Despite the introduction of modern methods of treatment; development of new generations of antibiotics; the use of therapeutic schemes significant Arsenal of pharmacological agents with antimicrobial, necrolytic, analgesic, stimulating and sorption; continuous improvement; methods of asepsis and antisepsis, the number of cases of complications of surgical infection is not only diminished, but rather increased. This leads to search for new, more effective methods of fighting purulent-inflammatory processes of soft tissues.[7]
The use of sorbents as application materials in the treatment of wounds and purulent soft tissue lesions has been known for a long time. Even a few millennia ago in Egypt, they used "soot from the walls over the hearths." Charcoal and ashes of burned bones were applied to wounds in those ancient times to clean them and stimulate healing. In Cossack medicine, the use of ash, river silt and leaf pressing for the treatment of wounds is known. Over time, these methods were forgotten.[11,12,13,14]
Recently, there has been an accelerated development of high technologies using nanoparticles of certain chemicals in various fields of scientific and economic activity. This happens due to the fact that nanotechnology provides a unique opportunity to manipulate matter at the level of one or several nanometers, which actually determines the control of physical, chemical and biological processes at the atomic and molecular levels. The large area of the active surface formed by nanoparticles, with their ultra-small size, determines several important physical and chemical properties.[15,16,17] Over the past 20-30 years, methods for the synthesis of numerous adsorbents have been developed, their structure, adsorption and biomedical properties have

been studied, and their effectiveness in the treatment of various diseases has been shown. Industrial production of a number of medical sorbents has been launched for the removal of toxic substances and microorganisms in the gastrointestinal tract (enterosorption), for blood detoxification (hemosorption), as well as for the treatment of external pathological conditions-wounds, burns, frostbite, trophic ulcers and others (application sorption). Currently, sorption drugs are used independently or in combination with additional treatment methods in almost all areas of medicine – surgery, therapy, Oncology, cardiology, pulmonology, and infectious diseases.[12,14,18,119,20,21,22,23] In animal breeding, silicon-containing minerals are used to strengthen the bone skeleton of animals.[24]

The essence of application sorption is the separation of toxic metabolites, microbial cells and bacterial toxins from wounds and purulent cavities in direct contact with the surface of the sorbent. When using sorbents, chemical and biologically active substances are sorbed from the wound, which are contained in large quantities in the wound exudate and the zone of perifocal inflammation. In addition, sorption preparations that have pronounced hydrophilic properties provide exudate evacuation from the wound, dry the wound surface, and remove edema of damaged tissues.[8,9,25,26,27,28,29,30]

Hydrophilic silicon-containing sorbent silicon dioxide (SiO_2) has a number of advantages over other sorbents: low toxicity, no destruction of histological structures of internal organs; in addition, it is not absorbed through the mucous membranes and, of course, its cheapness. In many ways, the wide application of silicon dioxide is determined by the possibility of setting specific properties by modifying the structural construction of this compound. Chemical modification of the surface of silicon dioxide allows the formation of particles that have an almost perfect spherical shape and an extremely diverse surface – from 50 to 380 m^2 per 1 g of substance. Such unique properties explain sufficiently wide possibilities of using these materials in Biomedicine and biotechnology.[14,31,32,33,34]

Silicon dioxide is a highly dispersed colloidal silica, characterized by high hydrophilic properties, osmotic activity, the ability to bind a large amount of water, adsorb proteins, has an antitoxic, antibacterial, antiproteinase and anti-inflammatory effects. In addition, it has high immuno-stimulating and anti-allergic effects. Silicon, along with oxygen, carbon, nitrogen, hydrogen, phosphorus and calcium, is among the vital elements. Significant amounts of silicon are found in hair, nails, skin, thyroid, adrenal, and pituitary glands. Silicon is responsible for skin elasticity, hair shine, and bone strength. Silicon participates in the formation of connective tissue in the body, which performs a supporting and protective function. In addition, silicon participates in the construction and functioning of blood vessels, where it is a part of elastin.[35,36,37]

High hydrophilic activity refers to the main properties of silicon dioxide. When considering the properties of the sorbent, purulent exudate consists of 90% water as well as the fact that inflamed and injured tissues develop edema with subsequent trophic disorders have a great importance. In addition, silicon dioxide has a high osmotic activity, that is, the ability to direct the flow of liquid from the walls of the purulent focus into the cavity, thereby providing detoxification of the wound and the body as a whole.[14] It is well known that wound purulent exudate contains a large amount of protein. Most microbial toxins, such as 7α, 7β, 7δ, 7ε toxins, 7ζ-hemolysins, Staphylococcus toxin, exotoxins A and S, cytotoxin, hemolysin (phospholipase C) and Pseudomonas aeruginosa proteases, also have a protein nature. Also, the fimbriae of Proteus and Pseudomonas aeruginosa consist of protein substrates, which ensure their adhesion to the wound surface. Silicon dioxide is a unique substance among sorbents for its protein-binding properties (it can bind up to 655 mg/g from a lyophilized plasma solution, and a colloidal solution-up to 1150 mg / g of protein).[29]

It should be noted that silicon dioxide has a unique ability to sorption of microorganisms. At the same time, it actively absorbs representatives of both gram-positive and gram-negative microflora up to 10^{10} CFU/g, which avoids the selection of resistant strains. It is essential that the sorbent particles bind several microorganisms to their surface immediately and, as a result of this agglutinating action, form quite large conglomerates that are easily removed during surgical treatment of the wound. In addition, the composition of such conglomerates complicates the penetration of microflora into the surrounding tissues. Due to the binding of hemoglobin by the sorbent in the wound and preventing its decomposition, a certain deficiency of iron is created, which is necessary for the growth of microorganisms and it leads to limit the implementation of their pathogenic properties. Interesting, from our point of view, there is data about increasing the sensitivity of wound microbiota to antibiotics and antiseptics after their contact with silicon dioxide. This phenomenon is caused by the interaction of the sorbent with R-plasmids of the microflora, which are the leading factors in the transfer of antibiotic resistance.[25,27]

Silicon dioxide, which is stimulating the fibrinolytic activity of the contents of the wound surface, can reduce the adhesion of the gauze dressing. This reduces injury of tissues during bandaging, which promotes improved outcomes in treatment. Silicon dioxide is also an effective hemostatic agent due to the stimulation of mononuclear phagocytes, monocytes and neutrophils in the lesion. In this case, there is a release of thromboplastic factors from these cells that activate platelets, which leads to contribute the formation of fibrin clots, and also accelerate the processes of the first phase of blood clotting.[38,39,40,41,42]

One of the main mechanisms of action of silicon dioxide as an enterosorbent undoubtedly is its effect on the conditionally pathogenic and pathogenic intestinal microflora. The direct action should include the binding of bacteria with their subsequent elimination from the body with feces; indirect-refers to the creation of adverse conditions for the life of microorganisms (the concentration of bacteria on the sorbent creates a local shortage of nutrients for them; concentrated on silicon dioxide, the microbiota increases the antigenic effect, thereby enhancing the immune response of the body, binding of hemoglobin leaves them without the necessary iron, etc.). Oral administration of the sorbent significantly reduces the translocation of minor microflora from the intestine to the internal environment of the body, thereby preventing the generalization of the infectious process.[12,40,41,42,43] Silicon dioxide also has the ability to bind substances of a protein nature, namely microbial Exo-and endotoxins, antigens and allergens, toxins and hydrolysis products of endogenous origin. The sorbent when administered orally also binds low-molecular weight substances such as oligopeptides with medium and low molecular weight, protein putrefaction products, cholesterol, bile acids, bilirubin, etc. It should be noted that silicon dioxide has a certain detoxification effect during enterosorption, which is manifested decrease in the level of MWM and LO products in biological fluids of the body, normalization of immunobiological reactivity, increase of resistance to hypoxia, as well as a decrease the intensity of inflammatory processes of different localization.[47,48,49,50,51,52,53,54]

A new promising direction is the development and use of sorbents for immobilization of various drugs which is on it. Immobilization of various pharmaceutical products on a sorbent allows you to get effective drugs that have a wide range of actions. These properties are realized as the released immobilized substances on it.[55,56,57]

However, the possible mechanisms of interaction between nanoparticles and biological objects remain unclear. The development of nanotechnology is actually taking place against the background of a lack of practical knowledge about the impact of nanoparticles on the health of both animals and humans. Thus, due to the wide range of therapeutic effects of silicon dioxide (reduction of endogenous intoxication, normalization of intestinal microbiocenosis, reduction of systemic inflammatory response, activation of detoxification function), its use as a matrix in the production of pharmacological drugs for the treatment and prevention of surgical infection is pathogenetically justified and is an interesting direction for scientific research.

MATERIALS AND METHODS

A search was conducted in various biotopes (skin biopsy, oral contents, fecal samples and peripheral blood samples) of 18 clinically healthy cats that were in the shelter for homeless animals Yasinovatsky Machine Building Plant JSC in Yasinovataya, Donetsk oblast, promising strains of lactic acid microorganisms-candidates for probiotic drugs.

Promising strains were selected based on the characteristics of their marker biological properties: sensitivity to antibiotics, adhesive activity and antagonistic properties. During the research, high biological properties were determined in the strains of *L. plantarum "Victoria" No. 22, L. rhamnosus No. 26* and *L. acidophilus No. 24.*

When creating probiotic-sorption preparations, we chose silicon dioxide as the matrix. We have chosen a strategy for creating two drugs for effective treatment and prevention of surgical infection in cats. The first – for local use in purulent-inflammatory soft tissue pathologies in the first phase of the wound process, the second-as an enterosorbent to fight dysbacteriosis, neutralize intestinal translocation of microorganisms and, as a result, prevent surgical infection.

Developed probiotic sorption drugs "Draxil" and "Sorbilact" for correction of microbiocenosis in cats. One gram of probiotic-sorption preparation "Sorbilact" contains production strains of *L. plantarum "Victoria" No. 22* and *L. acidophilus No. 24* of 2.5 billion cubic meters, respectively, which are immobilized on Aerosil-300 (silicon dioxide with a surface of 300 m^2 per 1 g of the substance). One gram of probiotic-sorption drug "Draxil" contains production strains of *L. acidophilus No. 24* and *L. rhamnosus No. 26* for 2.5 billion MK. respectively, which are immobilized on Aerosil-300 (silicon dioxide with a surface of 300 m^2 per 1 g of the substance).

To assess the effectiveness of probiotic-sorption drugs "Draxil" and "Sorbilact" in the treatment of cats with accidental purulent wounds, animals were divided into four groups by the envelope method – 1 experimental (A_1, n=16), 2 experimental (A_2, n=16), 3 experimental (A_3, n=21) and control (comparison group, A_0, n=11). PHO of purulent foci was performed on animals of all four groups. Surgical treatment consisted of dissecting tissues, opening purulent cavities, inflections, pockets, removing non-viable tissues and purulent exudate, as well as creating a reliable drainage of the wound. At the beginning, as well as in the course of treatment, a clinical examination of animals and wounds was performed, which determined their shape, size, condition of the walls, edges and bottom, consistency, quantity, color and smell of wound exudate, the nature of granulation and epithelization.

Treatment of animals was carried out taking into account the phase of the wound process. The treatment regimen for cats with accidental purulent wounds is shown in (TABLE 1). The control group included animals whose owners refused treatment. For cats of group A_1 in the first phase of the wound process 2 times a day, a gauze drainage was introduced into their wound cavity, impregnated with a hydrophilic ointment "Levomekol", and in the absence of a cavity, its application was performed.

TABLE 1: Treatment regimen for cats with accidental purulent wounds (n=64)

Phases of the wound process	Animal groups			
	Control group (A_0), n=11	1st experimental group (A_1), n=16	2nd experimental group (A_2), n=16	3rd experienced group (A_3), n=21
Locally				
The 1st phase. Self-cleanings	Surgical treatment of wounds	Surgical treatment of the wound. Ointment "Levomekol"	Surgical treatment of the wound. Application of Aerosil A-300	Surgical treatment of the wound. Lace probiotik-sorption of the drug "Draxil"

2nd phase. Filling with granulation	–	Salve "Solcoseril" (1 time a day)	
3rd phase. Epithelialization	–	Salve "Solcoseril" (according to indications, 1 time per day)	
By mouth			
1st, 2nd, 3rd phases	–	Aerosil A-300	Probiotik-sorption of the drug "Sorbilact"

To animals of group A_2 in the first phase of the wound process 2 times a day were applied Aerosil A-300, a layer of no more than 3 mm. To cats of group A_3 in the first phase of the wound process 2 times a day on the wound surface was applied probiotic-sorption drug "Draxil", also a layer of no more than 3 mm. In the future, if possible, to animals A_1-A_3 experimental groups were applied a bandage.

On animals of groups A_1-A_3 in the second and according to indications in the third phase of the wound process was used salve "Solcoseril" one time a day. In addition, animals of the second experimental group, throughout the treatment, once a day orally prescribed Aerosil A-300, at a dose of 1 g., and cats of the 3 experimental group – probiotic-sorption drug "Sorbilact" at a dose of 1 g.

Animals who were admitted to veterinary medicine clinics and were given a preliminary diagnosis of sepsis, were later distributed into groups B_1, B_2 and B_3 using the envelope method. Groups of patients with sepsis cats were homogeneous as for age and sex, date of admission to veterinary clinics since the outbreak of the disease, and the causes and development of disease, the severity and expressiveness of pathological process.

Treatment regimens for cats with sepsis are shown in table 2. In animals of all experimental groups, therapeutic measures had two directions: treatment of the primary purulent focus and General intensive therapy.

TABLE 2: Treatment regimen for cats with sepsis (n=48)

Groups of animals	Treatment regimen	
Control group (B_1), n=12	Treatment of primary purulent focus	Surgical treatment of a purulent focus. Sanitation of cavities with 1% dioxin solution or "Levomekol" ointment
	General intensive care	Antibacterial therapy. Detoxification therapy (rehydration therapy)
1st experimental group (B_2), n=17	Treatment of primary purulent focus	Surgical treatment of a purulent focus. Sanitation of cavities with 1 % aqueous suspension of Aerosil A-300; or application of Aerosil A-300
	General intensive care	Antibacterial therapy. Detoxification therapy (rehydration + sorption therapy)
2nd experimental group (B_3), n=19	Treatment of primary purulent focus	Surgical treatment of a purulent focus. Sanitation of cavities with 1 % aqueous suspension of "Draxil" or application of probiotic-sorption drug "Draxil"
	General intensive care	Antibacterial therapy. Detoxification therapy (rehydration + probiotic-sorption therapy)

Surgical treatment of the primary purulent focus consisted of dissecting tissues, opening purulent cavities, pockets, and creating free access to all areas of the wound – a necessary element for full surgical treatment. During the operation, the purulent exudate was carefully evacuated, non-viable tissues were excised, and the exudate was freely drained (wound drainage).

Animals of all experimental groups with abdominal sepsis underwent extensive laparotomy, evacuation of purulent exudate, abdominal sanitation, suturing of the laparotomic wound and suturing of tubular PVC drains. Through these drains, the abdominal cavity was sanitized 2 times a day for cats of group B_1 – 1 % solution of dioxin, for animals of group B_2-1 % aqueous suspension of Aerosil A-300 (silicon dioxide with a surface of 300 m2 per 1 g of the substance), and for animals of group B_3 – 1% aqueous suspension of the drug "Draxil".

General intensive therapy in all experimental groups included antibacterial therapy and detoxification therapy. Antibacterial therapy was performed in two stages: stage 1 – empirical administration of a combination of broad-spectrum antimicrobials, stage 2-continuation or change of the antibiotic therapy regime based on bacteriological studies, taking into account the antibiotic sensitivity of the isolated microflora. At first stage, cephalosporin III generation – Ceftriaxone was prescribed (intramuscularly at a dose of 75-100 mg/kg 1 time per day for 5-7 days) in combination with metronidazole (at a dose of 7-10 mg/kg intravenously drip 1 time per day for 5 days). At second stage, in 17 (35.4 %) of sick animals needed to replace the antibiotic therapy regimen, taking into account the sensitivity of the microflora isolated from the primary focus to antibiotics. At the same time, 15 (31.2 %) cats with sepsis were treated with cephalosporin IV generation cefepim (intramuscularly at a dose of 50 mg/kg 2 times a day for 5-7 days) in combination with metronidazole, and 2 (4.2 %) animals with extremely severe abdominal sepsis (in patients with postoperative peritonitis) – Gatifloxacin (intravenously at a dose of 15-20 mg/kg in dilution with 0.9% sodium 1:10 1 times a day for 5 days) in combination with metronidazole. The main route of administration of antibiotics was the parenteral (subcutaneous vein of the forearm) route of administration.

In animals of B_1-B_3 experimental groups, rehydration therapy consisted in intravenous drip of sodium chloride 0.9% in a dose of 10 ml/kg + 5% glucose solution; at a dose of 10 ml/kg of Reosorbilact; at a dose of 5 ml/kg + refortan; at a dose of 2.5 ml/kg. In addition, to animals of group B_2 were applied sorption (oral Aerosil A-300, 2 times a day) and to the cats of B_3 group probiotika-sorption (oral appointment of probiotic-sorption of the drug "Sorbilact" 2 times a day) therapy.

At the next stage of the work, the prevention of postoperative purulent-inflammatory complications in cats was improved. During the experiment, the animals were divided into four groups C_0, C_1, C_2 and C_3 by using the envelope method, according to their admission to the state and private clinics of veterinary medicine in Luhansk for routine surgery – ovariohysterectomy. Schemes for preventing the occurrence of surgical infection in cats are presented in the (TABLE 3).

TABLE 3: Scheme of prevention of surgical infection in cats (n=474)

Animal groups	Schemes of preventive measures
Control group (C_o), n=67	–
1st group of animals (C_1), n=162	Antibacterial therapy
2nd group of animals (C_2), n=108	Antibacterial + sorption therapy
3rd group of animals (C_3), n=137	Antibacterial + probiotic-sorption therapy

Antibacterial therapy in all experimental groups included Ceftriaxone. To animals of the C_2 group was also given the sorbent Aerosil A-300 (silicon dioxide with a surface of 300 m^2 per 1 g of the substance) at a dose of 1 g per day. Cats of the C_3 group were prescribed probiotic-sorption drug "Sorbilact" at a dose of 1 g per day.

RESULTS AND DISCUSSION

During studying the pathogenetic features of the course of aseptic and purulent-inflammatory processes, we developed the hypothesis for the development of surgical infection in this type of animal. The mechanisms of forming the surgical infection in cats are shown in the FIG 1.

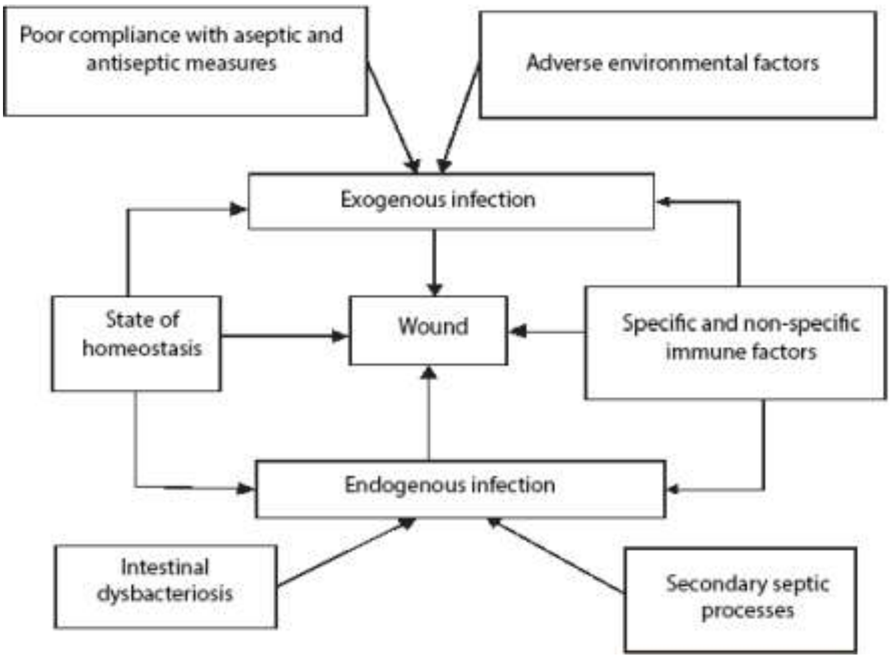

FIG. 1: Mechanisms of formation of surgical infection

Sources of contamination of any wound can be both external (exogenous infection) and internal (endogenous infection) factors. Main external sources of infection of the wound surface are the veterinary clinic personnel, surgical instruments contaminated with microorganisms, suture and dressing material, also air and surfaces of medical equipment elements. The presence of adverse environmental factors decreases of the immunobiological reactivity of the animal's organism, exhaustion, having accompanying diseases etc. are also needed for the development of infection. Preventive and antiepizootic measures aimed at preventing the occurrence of exogenous infection in cats during the postoperative period should be based on comprehensive preoperative examination of an animal and assessment of its condition, compliance of modern aseptic and antiseptic measures (treatment of

hands, the surgical field, sterilization of surgical instruments, suture material, disinfection of operation room, etc), as well as providing adequate postoperative care.
The endogenous infection of an operating wound can be caused by the own microflora of an animal that penetrates into the injured tissues from the places of permanent (translocation of microorganisms from the places of permanent colonization with quantitative or qualitative disruption of the intestinal microbial ecosystem) or temporary (representatives of the microbiocenosis from the primary focus of infection) colonization. The development of endogenous infection is also affected by a number of adverse environmental factors as well as decrease in specific and non-specific factors of protection of animal body, the presence of accompanying diseases, etc.
Studying pathogenetic features of the course aseptic and purulent-inflammatory processes of various degrees of severity in cats, identification of the role of intestinal dysbiosis in the course of various forms of surgical infection, provided prerequisite of justification by using probiotic-sorption medicines in the treatment and prevention of this group of pathologies.
Preclinical studies have established by its appearance, biochemical properties, safety, lack of extraneous admixtures, that medicines «Draxil» and «Sorbilact» are stable compositions and do not change their biological, therapeutic and preventive properties. They have a prolonged effect as evidenced by the low rate of desorption of lactobacilli in the first three hours of contact with saline. Probiotics-sorption medicines are not toxic, do not have pyrogenic, allergenic and irritating properties.[14]
In order to justify the effectiveness of probiotic-sorption medicines «Draxil» and «Sorbilact» in the treatment of cats with accidental purulent wounds, we conducted a comprehensive clinical and laboratory study in 64 cats that were admitted to the veterinary clinics in Luhansk. When analyzing anamnestic data of sick cats, it was found that mostly purulent wounds were located in the head – 26 (40,6 %), neck – 14 (21,9 %), withers – 8 (12,5 %) and in the region of thoracic limbs– 7 (10,9 %) from the total amount of experimental animals. Purulent wounds in animals were mostly registered in the age from 1 to 5 years – 39 (60,9 %) and from 5 to 10 years – 23 (35,9 %) from the total amount of sick cats. It is necessary to notice that the vast majority – 47 (73,5 %) from cases were outbred cats. It should be mentioned that most injured cats were males, namely 48 (75,0 %) animals from the total amount of experimental animals. Besides that, we noticed clearly expressed seasonality of purulent wounds in cats. Most often purulent wounds were registered in the spring months, namely in March – 17 (26,7 %), in April – 14 (21,9 %) and in May – 12 (18,7 %) cases from the total amount of experimental animals.
In case of accidental purulent wounds in cats, we mainly registered a satisfactory general condition. In some animals a slight decrease in appetite was observed, which did not affect their fatness; in 3 (12 %) cats with purulent wounds, that did not heal for a long time, was noticed a decrease of body weight. The examined animals showed the reliable ($p<0,001$) increasing of general temperature of the body by 1,02 times, compared with the control group (38,5±0,06 °C). It should be mentioned that temperature of the body in 60,0 % of an animals was subfebrile, in 16,0 % of cases – febrile.
In the early stages of wound process (self-cleaning phase), we observed an intensive release of liquid wound exudate. The edges, walls and surrounding tissues around the wound during the initial examination were swollen, had dough-like consistency, hyperemic in non-pigmented areas of the skin, moderately painful, with increased local temperature. Due to the enzymatic melting of avitalized tissues, in the wound cavity was accumulated a small amount of purulent exudate of a whitish or yellowish colour (FIG. 2. A). As the wounds were cleared of necrotic tissues and purulent exudate, the general condition of animals improved, locally decreased the edema of tissues, on the bottom of the wound were registered islands of granulation tissue, which were better developed in cats of the group A_3 (FIG. 2. B).

a b

FIG. 2: Purulent wound: a – self-cleaning phase; b - granulation

Clinical results of treatment of cats with accidental purulent wounds in the control and experimental groups are shown in the (TABLE 4) and on the picture 3. Data from the table and the picture shows that using probiotic-sorption medicines in the treatment of cats with purulent wounds significantly accelerates their healing.

TABLE 4: Criteria of evaluating the course of the wound process in cats during their treatment with different schemes.

Clinical characteristics	Control group (A_0), n=11	1 experimental group (A_1), n=16	2 experimental group(A_2), n=16	3 experimental group(A_3), n=21
Disappearing of hyperemia, days	9,45±0,57	3,75±0,21 ***	2,75±0,21 ***	1,90±0,18 ***
Decrease of edema, days	11,45±0,57	4,62±0,34 ***	3,75±0,33 ***	2,90±0,18 ***
Cleansing of the wounds and granulation formation, days	13,45±0,57	5,62±0,34 ***	4,75±0,33 ***	3,76±0,22 ***
Beginning of epithelization, days	23,90±0,41	11,62±0,34 ***	9,93±0,28 ***	7,76±0,23 ***
Complete healing of the wounds, days	33,27±0,50	20,62±0,34 ***	17,93±0,28 ***	14,76±0,22***

Remark: *** - $p<0,001$ comparing with animals of the control group.

The average period of wound cleaning and granulation formation in animals of the group (A_3) was 3.6 times faster than in cats of the control group ($p<0.001$).

a b

FIG. 3: Cat «Gosha», outbred, 2 years. Lacerated wound in the neck area (3 experimental group) a – view of the purulent wound before the primary surgical treatment; b – application of the medicine «Draxil»

This caused early beginning of growth along the periphery of the epithelial border, which occurs 3,1 times faster in cats of the 3 experimental group, compared to animals of the group A_0 ($p<0,001$). It should be mentioned that complete healing of wound with scar formation occurred in groups of animals A_1, A_2 and A_3 1,6, 1,9 and 2,3 times faster, respectively, than in cats of the control group ($p<0,001$).

Further, we present a comparative assessment of the results of treatment of cats with sepsis, with using of traditional treatment scheme (animals of the group B_1) in combination with application and enterosorption using aerosol A-300 (silicon dioxide with a surface 300 m^2 per 1 g of substance) (animals of the group B_2), as well as in combination with probiotic-sorption medicines «Draxil» and «Sorbilact» (animals of the group B_3).

For the most accurate presence of the most important sources of translocation of microorganisms and their toxins, generalization of the infectious process in each specific clinical case, we, primarily, analyzed the distribution of cats with sepsis by etiological factors. The results of the analysis are shown at the FIG 4.

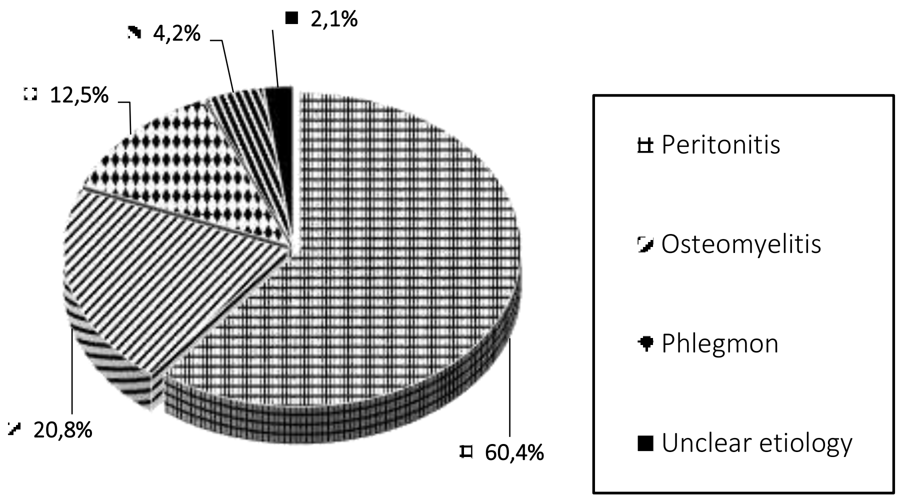

FIG. 4: Disease, which caused the development of sepsis

The data of the picture shows that sepsis occurred more often as the result of the development in cats peritonitis – in 29 (60,4 %) and osteomyelitis – in 10 (20,8 %) animals from the general amount of cases. It should be noticed, that the reasons of occurrence of the abdominal sepsis were uterine ruptures with pyometre – 13 (44,9 %), postoperative peritonitis - 9 (31,0 %), perforation of the hollow organ as a result of penetrating wounds – 5 (17,2 %), as well as foreign bodies in the intestines – in two (6,9 %) cases from the total amount of cats with peritonitis – 29 (100,0 %) cases. Osteomyelitis occurred in cats as a complication of poorly performed osteosynthesis – 8 (80,0 %) and in bone fractures – in two (20,0 %) animals of the total amount of cases. Significantly less often in cats with sepsis were registered phlegmons – 6 (12,5 %) and purulent arthritis – 2 (4,2 %) animals. In one (2,1%) animal etiology of sepsis occurrence was not established.

The effectiveness of treatment of cats in experimental groups with sepsis is shown in the (TABLE 5).

TABLE 5: Effectiveness of treatment of cats with sepsis (n=48)

Criteria for the evaluation of treatment		Groups of animals		
		Control group (B_1), n=12	1 experimental group (B_2), n=17	2 experimental group (B_3), n=19
Local	Need for repeated necrectomies, ab. number(%)	3 (25,0)	2 (11,7)	1 (5,3)
	The average time of appearance of granulation tissue, days	11,71±0,56	8,23±0,30	5,52±0,21
	Average wound healing time, days	22,14±0,40	16,07±0,26	14,23±0,21
General	Overall clinical improvement, days	14,42±0,57	12,00±0,25	8,64±0,17
	Isolation of the hemoculture for 5 days of treatment, ab. number (%)	7 (58,3)	6 (35,3)	4 (21,0)
	Number of complications, ab. number (%)	7 (58,3)	5 (29,4)	3 (15,7)
	The case-fatality rate, abs. number (%)	5 (41,6)	4 (23,5)	2 (10,5)

The data of the table shows that the most effective treatment of sepsis was in cats of the group B_3, as indicated by the decrease of the average time of granulation formation to 6,19 days, average time of healing wounds of the primary focus to 9,91 days, as well as decrease of terms of general clinical improvement to 5,78 days when compared with animals from the group B_1.

During repeated sampling of peripheral blood on the 5th day of the treatment for adequate bacteriological monitoring of effectiveness of the proposed therapeutic measures, it was found that isolation of microbial hemocultures were registered: in cats B_1 – in 7 (58,3 %), in cats B_2 – in 6 (35,3 %), in cats of B_3 group – only in 4 (21,0 %) cases of the total amount of the animals. It should be noted that we registered the lowest mortality rate in cats of the group B_3, namely in two (10,5 %) animals of the total amount of sick cats. In animals of this group was also registered the lowest number of post-septic complications, namely in 3 (15,7 %) from the total amount of animals with sepsis in the group.

A detailed description of post-septic complications in cats during the treatment of sepsis is given in (TABLE 6).

TABLE 6: Character of post septic complications in cats of control and experimental groups.

Character of complications	Control group(B_1), n=12		1 experimental group (B_2), n=17		2 experimental group (B_3), n=19	
	Amount ab. nuber. (%)	Died, ab. number (%)	Amount ab. nuber. (%)	Died, ab. number (%)	Amount ab. nuber. (%)	Died, ab. number (%)
From the primary focus	1 (14,3)	–	–	–	–	–
Pneumonia	–	–	1 (20,0)	–	2 (66,7)	2 (100,0)
Meningoencephalitis	1 (14,3)	1 (20,0)	1 (20,0)	1 (25,0)	–	–
Septic shock	1 (14,3)	–	1 (20,0)	1 (25,0)	1 (33,3)	–
Multi-organ failure	4 (57,1)	4 (80,0)	2 (40,0)	2 (50,0)	–	–
Total	7 (100,0)	5 (100,0)	5 (100,0)	4 (100,0)	3 (100,0)	2 (100,0)

According to these data, it was found that the most frequent complications in cats with sepsis were multiple organ failure – 6 (40,0 %), pneumonia and septic shock – 3 (20.0%), and meningoencephalitis – 2 (20,0 %) from the total number of cases. It should be noted that in cats with sepsis before the treatment was registered apathetic or comatose general condition. The animals, in general, had no motor activity, reactions to the external irritations were reduced. In cats with sepsis were registered fever with strongly pronounces chills, weakening of vegetative functions, icteric or anemic appearance of the mucous membranes, shortness of breath, anorexia, cachexia, dehydration, decreased skin elasticity, hyperthermia, tachycardia, tachypnea. The skin of sick cats on the unpigmented areas of the body had a pale icteric colour, in some animals with small hemorrhages. Sometimes hemorrhages were noticed on the mucous membranes of the oral cavity and conjunctiva. It should be mentioned that in 11 (22,9 %) cases of the total amount of experimental animals that died during the treatment, hypothermia was observed 1-2 days before the fatal outcome (from 34,8 to 35,6° C). In our opinion, the occurrence of the stable hypothermia in cats with severe sepsis indicates about the decompensation of animal body functions, which was confirmed by other clinical and laboratory indicators. Besides that, in two (4,2 %) cats, the day before death were registered neck muscle rigidity, stupor and tonic-clonic convulsions and 1 hour before the fatal outcome Cheyne-Stokes breathing was observed. These animals died as a result of the development of meningoencephalitis. Dyspnea at the initial examination with a respiratory rate of more than 50 times per minute was observed in 58.3; 64.7 and 42,1 % cats of the groups B_1, B_2 and B_3 respectively. It should be noticed, that in 4 (33,3 %), 9 (52,9 %) and 9 (47,4 %) animals from the groups B_1, B_2 and B_3 respectively was observed tachycardia with a heart rate more than 220 beats per minute.

During the research of general clinical indicators (rectal temperature of the body, pulse, respiration) in the treatment of the animals with sepsis, it was established that cats of the B_3 group on the 7th day of therapy already had the stabilization of the clinical condition. We registered a highly reliable ($p<0.001$) decrease in body temperature, pulse and respiration by 1.05; 1.35 and 1.75 times, respectively. It should be mentioned, that in a comparative analysis of the general clinical indicators of animals from the other experimental groups relative to the group B_1, on the 7th day of the treatment in cats of the group B_3 it was observed a highly reliable decrease in rectal body temperature ($p<0,001$,, pulse ($p<0,01$) and respiration ($p<0,001$) in 1,06; 1,16 and 1,81 times, respectively.

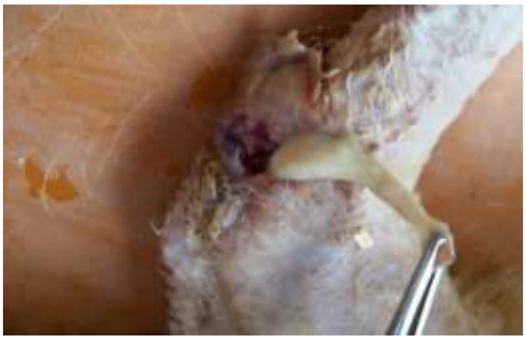

FIG. 5: Tissue necrosis in sepsis in the area of the primary focus, complicated by a bone fracture

During the monitoring of local clinical signs in experimental cats with sepsis, it was registered that the surrounding tissues around the primary focus were hyperemic, swollen, with grey areas of necrosis, painful on palpation, with high temperature of the skin in the area of the injury. A small amount of grey-coloured liquid and more often - hemorrhagic with unpleasant smell purulent exudate were released, necrotic tissues had grey tone (FIG. 5.). The prognosis for sepsis in most cases is adverse.

Therefore, on the basis of the complex research it was established, that probiotic-sorption medicines «Draxil» and «Sorbilact», which were proposed by us, during the comprehensive therapy of the cats with sepsis have a good influence both on the course of the inflammatory process in general, and on the separate parts of the pathogenesis: the process of healing of the primary purulent focus, microflora, intoxication, etc.

The priority of preventive measures in the postoperative period is determined, first of all, by the fact that the percentage of severe purulent-inflammatory complications in cats, which in some cases can lead to the fatal outcome, is quite high. Therefore, based on the careful examination of the pathogenetic features of the course of aseptic and purulent-inflammatory processes in cats, as well as the development of probiotic-sorption medicines for the correction of microbiocenosis in this type of animals, we made an experiment to improve the prevention of surgical infection.

The results of the effectiveness of various preventive measures to prevent the development of surgical infection in cats are presented in the (TABLE 7).

TABLE 7: Effectiveness of prevention of surgical infection in cats (n=473)

Group	n	Absence of postoperative complications		Normalization of the physiological state, days	Terms of wound healing, days	Number of purulent complications		Duration of purulent -inflammatory process, days
		Absolute number	%			Absolute number	%	
C_o	67	51	76,2	6,49±0,55	12,62±0,90	16	23,8	15,50±0,97
C_1	162	148	91,4	3,98±0,15	8,51±0,28	14	8,6	10,85±0,64
C_2	108	101	93,5	3,16±0,11	7,50±0,22	7	6,5	8,85±0,63
C_3	136	134	98,6	1,86±0,05	5,92±0,07	2	1,4	5,50±0,50

When we set up a randomized control trial, animals, who were admitted to the public and private veterinary clinics for the planned operation – ovariohysterectomy, were divided into four groups C_0, C_1, C_2 and C_3. In the group C_0 - there were animals whose owners refused an postoperative treatment; cats of the group C_1 - after surgery were prescribed a III-generation cephalosporin antibiotic – Ceftriaxone; animals of the group C_2 during the postoperative period were prescribed Ceftriaxone and oral using of sorbent aerosol A-300 (silicon dioxide with a surface of 300 m^2 per 1 g of the substance); cats of the group C_3 were prescribed Ceftriaxone with probiotic-sorption medicine «Sorbelact», made by us, that was prescribed per os. It should be mentioned, that animals of the all four groups in the postoperative period had standard debridement of the wounds.

The data from the table suggests, that the most effective method of preventing the occurrence of the postoperative purulent-inflammatory complications in cats is scheme that included antibacterial and probiotic-sorption therapy (group C_3). This is evidenced by a low level of occurrence of the postoperative complications – only in two (1,4 %) animals, as well as highly reliable ($p<0,001$) decrease of the period of normalization of the physiological condition from 6,49±0,55 to 1,86±0,05 days and period of the wound healing from 12,62±0,90 to 5,92±0,07 days by 3,5 and 2,1 times, respectively, when compared with the animals without prescribed postoperative treatment (group C_o).

It should be noticed, that the number of complications of surgical infection we observed in animals from the group C_1 – 8,6 % (χ^2=9,67; $p<0,05$), in animals from the group C_2 – 6,5 % (χ^2=10,97; $p<0,001$) and in animals from the group C_3 – 1,4 % (χ^2=27,90; $p<0,001$), when compared with the animals, whose owners refused postoperative preventive measures (group C_0).

Therefore, prevention of the endogenous infection of the surgical wound is effectively carried out when cats are prescribed in the postoperative period antibacterial therapy in combination with probiotic-sorption medicine «Sorbilact».

CONCLUSION

Therefore, according to the results of the conducted research, the solution of an actual scientific problem about the mechanisms of formation of microbiocenosis; improvement of diagnostic methods; prevention and treatment of cats with surgical infections have been reached. It was established, that purulent-inflammatory processes in cats occurred against the background of dysbiotic disorders of the microbial ecosystem of the intestinal tract, which has specific diagnostic value. The introduction of probiotic-sorption medicines to the treatment schemes proved to be pathogenetically justified, which is confirmed by experimental and clinical researches.

It is shown, that medicines «Draxil» and «Sorbilact» during the treatment of cats with purulent wounds are effective. Their use positively effects on the cleaning of the wound surface from the purulent exudate, reduces the time of the beginning of epithelization of wounds and their complete healing. The average period of wound cleaning and granulation formation in animals of the group (A_3) is 3.6 times faster, than in cats of the control group ($p<0.001$). This causes the early start of growth on the periphery of the epithelial border of wounds, which occurs 3.1 times faster in cats of the experimental group A_3, compared to the A_0 group.

The article also provides the data that medicines «Draxil» and «Sorbilact» during the complex intensive therapy in cats with sepsis have a positive effect both on the course of the inflammatory process as a whole and on the specific parts of the pathogenetic process. It is shown by the decrease in the average time of the granulation occurrence by 6,19 days, the average time of the healing of primary foci by 9,91 days and also time of the general clinical improvement by 5,78 days.

It was established, that the prevention of the surgical infection is effective when cats are prescribed antibacterial therapy with the probiotic-sorption medicine «Sorbilact» in the postoperative period. This is evidenced by the low level of the occurrence of postoperative complications – only in two (1,4%) animals, as well as decrease of the period of normalization of the physiological condition and the wound healing period in 3,5 and 2,1 times, respectively.

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CONFLICT OF INTEREST

The authors have no conflict of interest.

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