

# Research Journal of Pharmaceutical, Biological and Chemical Sciences

## The Effectiveness Of Probiotic-Sorption Compounds In The Complex Treatment Of Sepsis In Cats.

Pavel A Rudenko<sup>1\*</sup>, Victoria B Rudenko<sup>1</sup>, Andrey A Rudenko<sup>2</sup>, Oksana N Khokhlova<sup>1,3</sup>, Vitaly A Kazakov<sup>1</sup>, Dmitriy I Rzhavskiy<sup>1</sup>, and Igor A Dyachenko<sup>1,3</sup>.

<sup>1</sup>Branch of Shemyakin-Ovchinnikov Institute of Bioorganic Chemistry of the Russian Academy of Sciences, prospect of Science 6, Pushchinocity, 142290, Russia.

<sup>2</sup> Moscow State University of Food Production, Volokolamsk highway 11, Moscowcity, 125080, Russia.

<sup>3</sup>Pushchino Research Center of the Russian Academy of Sciences, prospect of Science 3, Pushchinocity, 142290, Russia.

### ABSTRACT

The purpose of this work is to study the effectiveness of probiotic-sorption compounds "Dilaxil" and "Sorbelakt" in the treatment of cats with sepsis. 48 cats with sepsis, as they entered the veterinary clinic of Lugansk, were, by the method of envelopes, distributed into groups B1, B2 and B3. Sick cats were homogeneous by sex, age, time of admission to veterinary clinics from the moment of the occurrence of the disease, by the causes of the onset and development of the disease, the severity of the course and the expressiveness of the pathological process. Cats with sepsis were treated with various regimens, evaluating their effectiveness. Probiotic-sorption compounds "Dilaxil" and "Sorbelakt" in the complex intensive care of cats with sepsis have a positive effect on the course of the inflammatory process in general, and on individual links of the pathogenetic process: the healing process of the primary purulent focus, the microflora, intoxication and the general clinical improvement. This is indicated by a decrease in the average time for the appearance of granulations by 6.19 days, an average time for the healing of wounds of the primary lesions by 9.91 days, as well as an acceleration in the time for overall clinical improvement by 5.78 days when compared with animals of group B1.

**Keywords:** surgical infection, sepsis, cats, probiotics.

*\*Corresponding author*

## INTRODUCTION

Recently, the problem of the formation of poor-quality micro biocenosis in various forms of surgical infection, which arise as a result of a decrease in the therapeutic efficacy of traditional medicines due to their uncontrolled and unsystematic use, is becoming more and more urgent. This, in turn, led to an increase in the resistance of pathogens of surgical infection to them, the emergence of pathogenicity and an increase in the virulence of microorganisms, the emergence of new mutational forms of bacteria. The colonization by individual representatives of conditionally pathogenic microorganisms of various biotopes of the body, not characteristic of their existence, also increased [1-5].

The role of conditionally pathogenic bacteria in the formation of microbiocenosis of ecological niches in purulent-inflammatory diseases of varying severity in cats is poorly understood [6]. Therefore, improving the methods of diagnosis, prevention and treatment of cats with sepsis is an urgent problem, and its solution will increase the effectiveness of the fight against surgical infections in this species of animals. Sepsis is a severe inflammatory process that occurs when pathogenic microorganisms and their toxins spread through the bloodstream or lymphatic bed from the primary purulent focus to other organs and tissues of the body, accompanied by severe clinical course and the development of infectious multiple organ failure [7, 8]. The state of natural detoxification systems (liver function), disorders of the systemic and regional blood flow, impaired microcirculation play a significant role in the pathogenesis of sepsis [9]. Progressive disruption of immunological protection and impaired barrier function of the intestinal wall leads to an increase in the phenomenon of translocation of bacteria and toxins through the damaged intestinal wall into the bloodstream, additional activation of inflammatory cytokines and the progression of inflammatory manifestations, the development of polyorgan dysfunction syndrome [10-13].

In recent years, probiotics, bacterial preparations from living microbial cultures, have been widely used for the prevention and treatment of infectious diseases. Their use causes an increase in the body's resistance, favorable metabolic changes, as well as an antagonistic effect on the micro flora harmful to the animal. Probiotics do not cause adverse reactions, have no contraindications to use, have a positive effect on the microbiocenosis of the microorganism [14-16]. At the same time, in veterinary practice, still probiotic preparations are used only for the correction of dysbacteriosis and the fight against acute and chronic intestinal infections [17-19]. The development and use of probiotic preparations for the correction of microbiocenosis in surgical infections, including sepsis in animals, is still poorly understood. Based on the above, the correction of micro biocenosis in sepsis in cats with the help of probiotic-sorption compounds obtained by us, as well as an assessment of their effectiveness, is a relevant area for research.

## MATERIALS AND METHODS

This study was reviewed and approved by the Expert Council, as well as the bioethical commission of the Faculty of Veterinary Medicine, Lugansk National Agrarian University, Lugansk. The maintenance of cats, experiments and manipulations with them were carried out in accordance with the legislation and international bioethical norms, the provisions of the IV European Convention on the Protection of Vertebrate Animals used for experimental and other scientific purposes.

Animals, which were diagnosed with sepsis, were subsequently distributed by envelopes into groups B1, B2 and B3. The groups formed from cats suffering from sepsis were homogeneous both by sex and age, the terms of admission to veterinary clinics from the moment of the onset of the disease, and by the causes of the onset and development of the disease, the severity and expressiveness of the pathological process.

The treatment regimens for cats with sepsis are shown in Table 1. In animals of all experimental groups, therapeutic activities had two directions: treatment of the primary suppurative focus and general intensive care.

**Table 1: Treatment of cats with sepsis(n=48)**

Animal groups	Treatment regimens	
Control group(B <sub>1</sub> ),	Treatment of primary purulent focus	Surgical treatment of purulent focus. Sanitation of cavities with 1% dioxidine solution; ointment

n=12		"Levomekol"
	General intensive care	Antibacterial therapy. Detoxification therapy (rehydration therapy)
1 experienced group (B <sub>2</sub> ), n=17	Treatment of primary purulent focus	Surgical treatment of 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)
2 experienced group (B <sub>3</sub> ), n=19	Treatment of primary purulent focus	Surgical treatment of purulent focus. Sanitation of cavities with 1% aqueous suspension of Dilaxil; or application of the probiotic-sorption drug "Dilaxil"
	General intensive care	Antibacterial therapy. Detoxification therapy (rehydration + probiotic sorption therapy)

Surgical treatment of the primary purulent focus consisted in dissecting tissues, opening purulent cavities, pockets and creating free access to all wound sites, an essential element for a complete surgical treatment. In the course of the operation, purulent exudate was carefully evacuated, non-viable tissues were dissected and the exudate was allowed to flow freely (drainage of the wound).

Animals of all experimental groups with abdominal sepsis were subjected to extensive laparotomy, the evacuation of purulent exudate, the habilitation of the abdominal cavity, the suturing of the laparotomy wound and the filing of tubular polyvinyl chloride drains. Through these drains, 2 times a day, the abdominal cavity was sanitized to cats of group B<sub>1</sub> with 1% dioxidine solution, animals of group B<sub>2</sub> with 1% aqueous suspension of aerosil A-300, and animals of group B<sub>3</sub> with 1% aqueous suspension of Dilaxil preparation.

General intensive care in all experimental groups included antibacterial therapy and detoxification therapy.

Antibacterial therapy was carried out in 2 stages: Stage 1 - empirical prescription of a combination of broad-spectrum antimicrobial agents, Stage 2 continued or changed the antibiotic therapy regimen based on bacteriological studies taking into account the antibiotic sensitivity of the isolated microflora. At stage 1, cephalosporin of the 3rd generation was prescribed - ceftriaxone (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 5 days). At the 2nd stage, 17 (35.4%) sick animals became aware of the need to replace the antibiotic therapy regimen, taking into account the determination of the sensitivity of the isolated microflora from the primary focus to antibiotics. At the same time, 15 (31.2%) cats with sepsis used cephalosporin IV generation cefepime (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 course of abdominal sepsis (in patients with postoperative peritonitis) - gatifloxacin (intravenously at a dose of 15-20 mg / kg in dilution with 0.9% sodium chloride at a dilution of 1:10, 1 time per day for 5 days) in combination with metronidazole. The main route of administration of antibiotics was the parenteral (saphenous vein of the forearm) route of administration.

In animals B<sub>1</sub>-B<sub>3</sub> of the experimental groups, rehydration therapy consisted of intravenous drip of a solution of sodium chloride 0.9% at a dose of 10 ml / kg + 5% glucose solution at a dose of 10 ml / kg + reosorb elact at a dose of 5 ml / kg + refortan at a dose 2.5 ml / kg. In addition, animals of the B<sub>2</sub> group used sorption (oral administration of Aerosil A-300 2 times a day), and cats B<sub>3</sub> with probiotic-sorption (oral administration of the probiotic-sorption preparation "Sorbelact" 2 times a day) therapy.

Probiotic-sorption compound "Dilaxil" is intended for the treatment of purulent wounds in cats. At the same time, one gram of compound contains production strains of *L. acidophilus* No. 24 and *L. rhamnosus* No. 26, each with 2.5 billion m. respectively, which are immobilized on the sorbent - aerosil-300. Probiotic-sorption compound "Sorbelakt" is intended for the correction of dysbiotic disorders in small animals. At the same time,

one gram of compound contains production strains of *L. plantarum* "Victoria" No. 22 and *L. acidophilus* No. 24, 2.5 billion cubic meters each. respectively, which are immobilized on the sorbent - aerosil-300 [20].

For microbiological studies, peripheral blood was collected from cats in the B1-B3 groups prior to treatment, as well as on the 5th day of therapy. Qualitative and quantitative microbiological studies were also carried out from samples of purulent exudate selected from the primary purulent foci of cats with sepsis. In addition, the cat B1, B2 and B3 groups prior to treatment, as well as on the 7th and 14th day, collected the contents of the rectum for the quantitative determination of microorganisms, as well as blood for immunological studies and the study of the cytokine profile.

The obtained research results were processed statistically and presented in the form of tables. All calculations were done on a personal computer using the statistical program STATISTICA 7.0 (Stat Soft, USA).

### RESULTS AND DISCUSSION

When analyzing the distribution of cats with sepsis, by etiological factors, it was found that sepsis most often occurred as a result of the development of peritonitis in cats - in 29 (60.4%) and osteomyelitis - in 10 (20.8%) animals of the total number of cases. It should be noted that the causes of abdominal sepsis were rupture of the uterus with pyometra - 13 (44.9%), post operative peritonitis - at 9 (31.0%), perforation of the hollow organ as a result of penetrating wounds - 5 (17.2%), as well as intestinal foreign bodies - in two (6.9%) cases out of the total number of cats with peritonitis - 29 (100.0%) animals. Osteomyelitis in cats occur red as a complication of poorly performed osteosynthesis - 8 (80.0%) and in bone fractures - in two (20.0%) animals of the total number of cases. Much less frequently in cats with sepsis, cellulitis was recorded - 6 (12.5%) and purulent arthritis - 2 (4.2%) animals. In one (2.1%) animal, the etiology of sepsis has not been established. The effectiveness of the treatment of cats in experimental groups with sepsis is presented in table 2.

**Table 2: The effectiveness of the treatment of cats with sepsis(n=48)**

Criteria for evaluating treatment		Animal groups		
		Control group (B <sub>1</sub> ), n=12	1 experienced group (B <sub>2</sub> ), n=17	2 experienced group (B <sub>3</sub> ), n=19
Local	Necessityforrepeatednecrotomy, abs. number (%)	3 (25,0)	2 (11,7)	1 (5,3)
	The average time of occurrence of granulations, days	11,71±0,56	8,23±0,30	5,52±0,21
	The average time of wound healing, 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 blood culture on the 5th day of treatment, abs. number (%)	7 (58,3)	6 (35,3)	4 (21,0)
	The number of complications abs number (%)	7 (58,3)	5 (29,4)	3 (15,7)
	Mortalityrate, abs. number (%)	5 (41,6)	4 (23,5)	2 (10,5)

The data in the table shows that the most effective treatment was for sepsis in cats of the B3 group, as indicated by a decrease in the average time of appearance of granulations by 6.19 days, an average time of healing for wounds of primary lesions by 9.91 days, and an acceleration of the time for overall clinical improvement by 5 , 78 days when compared with animals of group B1.

With repeated sampling of peripheral blood on the 5th day of treatment for adequate bacteriological monitoring of the effectiveness of the proposed therapeutic measures, it was found that the isolation of hemo cultures of micro organisms was recorded: in cats B1 - 7 (58.3%), in cats B2 - 6 (35.3 %), and in cats of the B3 group - only in 4 (21.0%) cases of the total number of animals. It should be noted that the lowest mortality rate was observed in animals of the B3 group, namely, in two (10.5%) animals of the total number of sick cats. Animals of this group also had the lowest number of post-septic complications, namely, only 3 (15.7%) of the

total number of patients with sepsis in the group of animals. A detailed description of the post septic complications in cats during the treatment of sepsis is given in Table 3.

**Table 3: The nature of post septic complications in cats of the control and experimental groups**

Nature of the complications	Control group (B <sub>1</sub> ), n=12		1 experienced group (B <sub>2</sub> ), n=17		2 experienced group (B <sub>3</sub> ), n=19	
	Amount, abs.ch. (%)	Killed, abs.ch. (%)	Amount, abs.ch. (%)	Killed, abs.ch. (%)	Amount, abs.ch. (%)	Killed, abs.ch. (%)
From the primary outbreak	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)	–
Multiple 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 in 3 (20.0%), and mening oencephalitis - 2 (20.0%) of the total number of cases. In cats with sepsis, prior to treatment, an apathetic or comatose serious general condition was noted. In animals, basically, there was no motor activity, and also reactions to external irritations were reduced. We recorded fever with pronounced chills, weakened vegetative functions, icterus or anemia of the visible mucous membranes, shortness of breath, anorexia, cachexia, dehydration, decreased skin elasticity, hyperthermia, tachycardia, tachypnea. The skin of sick cats in non-pigmented areas of the body had a pale-icteric color, and in some animals - with minor hemorrhages. Sometimes hemorrhages have also been noted on the mucous membranes of the oral cavity and conjunctiva.

It is worth noting that in 11 (22.9%) cases of the total number of experimental animals that died during the treatment, hypothermia was observed (1-2 days before death) (from 34.8 to 35.6 ° C). The occurrence of stable hypothermia in cats with severe sepsis indicates decompensation of animal functions, which is confirmed by other clinical and laboratory parameters. In addition, two (4.2%) cats had stiffness in the neck muscles, stupor and clonic-tonic convulsions a day before death, and Cheyne-Stokes respiration was observed an hour before the lethal outcome. These animals died as a result of the development of mening oencephalitis.

Dyspnea on initial examination with respiratory rate more than 50 times per minute was noted in 58.3; 64.7 and 42.1% of cats of groups B<sub>1</sub>, B<sub>2</sub> and B<sub>3</sub>, respectively. It should be noted that 4 (33.3%), 9 (52.9%) and 9 (47.4%) animals from groups B<sub>1</sub>, B<sub>2</sub> and B<sub>3</sub> respectively, observed tachycardia with a heart rate above 220 beats per minute.

When monitoring local clinical signs, it was found that the surrounding tissues around the primary lesions were hyperemic, swollen, with gray areas of necrosis, painful on palpation, with an increase in skin temperature in the area of damage. An insignificant amount of liquid, gray color, and more often hemorrhagic with an unpleasant smell of purulent exudate, was released from the primary lesions, and the dead tissue had a gray tint. The prognosis for sepsis, in most cases, was poor.

**CONCLUSION**

Thus, probiotic-sorption compounds "Dilaxil" and "Sorbelact" in the complex intensive care of cats with sepsis have a positive effect on the course of the inflammatory process as a whole, and on individual links of the pathogenetic process: the healing process of the primary purulent focus, microflora, intoxication and the like, as indicated by the decrease in the average time of appearance of granulations by 6.19 days, the average time of healing of wounds of the primary lesions by 9.91 days, as well as the acceleration of the time of

general clinical improvement and 5.78 days when compared with animals of group B1. The use of probiotic-sorption compounds in the complex treatment of surgical infections in animals, in particular, and in cats, is an evolutionarily reasonable approach that requires further study in order to determine indications for widespread use in surgical practice.

#### REFERENCES

- [1] Fukuyama Y, Kawarai S and Tezuka T. The palliative efficacy of modified moha paste for controlling canine and feline malignant skin wounds. *J. Vet. Q.* 2016; 1: 1-7
- [2] Skube S et al. Characterizing surgical site infection signals in clinical notes. *Stud. Health Technol. Inform.* 2017; 245:955-59
- [3] Martínez Clet et al. Prevention of the wound infection: little changes, huge results. *Cir. Pediatr.* 2017; 30(3):138-41
- [4] Pletz MW, Hagel S and Forstner C. Who benefits from antimicrobial combination therapy? *Lancet Infect. Dis.* 2017; 17(7):677-78
- [5] Krezalek MA et al. The intestinal microbiome and surgical disease. *Curr. Probl. Surg.* 2016; 53(6): 257-93
- [6] Kumru IH et al. Severe abdominal dog bite wounds in a pregnant cat. *J. Feline Med. Surg.* 2007; 3: 499-502
- [7] Minasyan H. Sepsis and septic shock: Pathogenesis and treatment perspectives. *J. Crit. Care.* 2017; 40:229-42
- [8] Ryan T, Coakley JD and Martin-Loeches I. Defects in innate and adaptive immunity in patients with sepsis and health care associated infection. *Ann. Transl. Med.* 2017; 5(22):447
- [9] Grek A and Arasi L. Acute liver failure. *AACN Adv Crit. Care.* 2016; 27(4):420-429
- [10] Ruiz-Tovar J et al. Effect of the abdominal fascial closure with triclosan-coated sutures in fecal peritonitis, on surgical site infection, and evisceration: a retrospective multi-center study. *Surg. Infect.* 2018; 19(1): 61-64
- [11] Berg RD. Bacterial translocation from the gastrointestinal tract. *Adv. Exp. Med. Biol.* 1999; 473:11-30.
- [12] Azhar N and Vodovotz Y. Innate immunity in disease: insights from mathematical modeling and analysis. *Adv. Exp. Med. Biol.* 2014; 844:227-43
- [13] Ono S et al. Mechanisms of sepsis-induced immunosuppression and immunological modification therapies for sepsis. *Ann. Gastroenterol. Surg.* 2018; 2(5): 351-358
- [14] Sharma B et al. Role of probiotics on gut permeability and endotoxemia in patients with acute pancreatitis: a double-blind randomized controlled trial. *J. Clin. Gastroenterol.* 2010; 3: 243-247
- [15] Semenov E.I. et al. Screening drugs-potential immunomodulators for T-2 mycotoxicosis. *Bali Medical Journal.* 2017; 6(2): 110-114.
- [16] Alok A et al. Probiotics: A new era of biotherapy. *Adv. Biomed. Res.* 2017; 6:31.
- [17] Wynn SG. Probiotics in veterinary practice. *J. Am. Vet. Med. Assoc.* 2009; 234(5) 606-613
- [18] German AJ, Halladay LJ and Noble PJ. First-choice therapy for dogs presenting with diarrhoea in clinical practice. *Vet. Rec.* 2010; 167(21):810-814
- [19] Gómez-Gallego C et al. A canine-specific probiotic product in treating acute or intermittent diarrhea in dogs: A double-blind placebo-controlled efficacy study. *Vet. Microbiol.* 2016; 197:122-128
- [20] Rudenko PA and Murashev AN. Technological process of production of complex probiotic-sorption preparations "Dilaxil" and "Sorbelakt". *Biopharmaceutical Journal.* 2017; 9.6: 40-45.