

## Analgesic effectiveness of new nanosilver drug

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The article provides data on the study of antimicrobial activity and analgesic efficacy of the medicine Mastitnano-BelGAU, which includes silver nanoparticles, copper nanoparticles, arginine, dexpanthenol, and distilled water. Based on the study of antimicrobial activity of the drug Mastitnano-BelGAU it was defined higher antimicrobial activity against clinical polyresistant strains of the genus *Staphylococcus* at a concentration of 10<sup>4</sup> cell/mL of samples 1 and 2, where respectively the concentration of the active substance of silver nanoparticles was 0.15 and 0.12 mg/mL. The tested samples of the remedy Mastitnano-BelGAU were characterized by higher antibacterial properties against the clinical strain *R. aeruginosa* 185, in contrast to the strain of *E. coli* 197. In the study of analgesic activity of the drug Mastitnano-BelGAU, it was found that it exhibits a significant long-term (within four hours) analgesic effect on the model of the pathogenic process induced by carrageenan. The most pronounced changes in pain sensitivity were recorded 60-120 min after the application of Mastitnano-BelGAU.

**Keywords:** Mastitnano-BelGAU; Dexpanthenol; Antimicrobial and analgesic activity; Mastitis; Cattle

### Introduction

The choice of treatment for cows with mastitis depends on the type of mastitis, its course and the general condition of the animal. For this purpose, physical, pathogenetic, etiologic, and symptomatic therapy for severe illness are used. Mastitis is a disease not only of the mammary gland, but of the whole animal's body, therefore, treatment should be comprehensive, aimed at eliminating the inflammatory process in the mammary gland and restoring the normal physiological state of the whole organism. Physiotherapeutic methods for treating cows with mastitis include the use of cold (dousing with cold water, applications of cold clay, cold compresses), heat (rubbing camphor alcohol or oil, ointments and liniment with an irritating effect, paraffin therapy, ozokerite therapy), quantum therapy (ultraviolet, thermal, laser irradiation, iontophoresis, treatment with ultrasound, electromagnetic field/UHF) and massage of the udder (Markiewicz et al., 2013). The use of cold in combination with Logvinov novocaine blockade and intravenous administration of 10% sodium chloride solution and 40% glucose solution promotes rapid recovery of cows with acute serous mastitis and positively affects their hematological parameters (Vojtenko et al., 2013).

Pavlov (2006), Abdessemed & Avdeenko (2014) used laser radiation in the treatment of cows with serous and catarrhal mastitis. The entire surface of the affected quarter or biologically active udder points located in the center of the quarter and at the base of the milking were subject to irradiation. The therapeutic efficacy in treating cows with a STP-5 laser device was 80.0%. A similar indicator in the treatment with novocaine blockade was 65.0, and with the use of the drug mastilex – 60.0%. After laser therapy, morpho-biochemical and immunological blood parameters after recovery approached the level of clinically healthy animals (Suhin, 1997). Scientists (Antipina & Konopel'cev, 2010) investigated the effect of laser radiation, antibiotics, and novocaine blockade on the nonspecific reactivity of the body and the histostructure of the mammary gland of cows with serous mastitis. The effect of laser radiation, mastisan-B and novocaine blockade according to D. D. Logvinov on the histostructure of the mammary gland was observed. It has been confirmed that laser radiation has a positive effect on the glandular tissue of the udder compared with the less effective action of antibiotics. Laser therapy contributed to the rapid restoration of the histological structure of the udder parenchyma of diseased cows – proliferation and alteration processes ceased, the secretory function of glandular tissue was restored, and secretory processes in the alveolar epithelium normalized. Whereas during the treatment with Mastisan-B, the processes of atrophy in separate places of the particles were preserved. With novocainotherapy, compensatory reactions in the glandular tissue intensified, proliferation and alteration decreased (Antipina & Konopel'cev, 2010; Chumikov & Ivashchenko, 2013).

Electrophysical methods include electroanalgesia. The use of electroanalgesia in animal husbandry along with an analgesic effect is accompanied by stimulation of the nervous system, especially the processes of regulation of autonomic functions in the body controlled by it. A consequence of this effect is an increase in tissue trophism and an increase in natural resistance (Glazunova et al., 2013). Taking into account the numerous studies of the physical properties, chemical composition and biological effects of beekeeping products on animals, apitherapy has found its application in veterinary practice (Sobczak & Kantyka, 2014; Vishchur et al., 2016; Kovalskiy et al., 2018; Vishchur et al., 2019). To treat cows with subclinical and clinical forms of mastitis, the author (Zeng et al., 2012) used a 3% aqueous emulsion of propolis intracisternally in the affected portion of the udder. According to research results, a 3% aqueous emulsion of propolis has anti-inflammatory and immunomodulating, bactericidal action. Other scientists (Baryshev, 2016; Postoienco et al., 2016) provide experimental data on the effect of the "Antimast" preparation for intracisternal administration, which contains bee propolis, bee extract, beeswax, castor oil, on the level of lipid peroxidation products and the state of the antioxidant defense system in cows subclinical form of mastitis. "Antimast" ointment is recommended for the prevention and treatment of various forms of mastitis, nipple cracks, inflammatory processes and skin diseases of cattle. The drug "Biogel-10" for the treatment of cows with mastitis contains 20% alcohol extract of propolis, sodium carboxymethyl cellulose, is intended for intracisternal use in various forms of mastitis (Danilov & Vorob'ev, 2012).

The drug "Mastilin" has an antimicrobial, anti-inflammatory, analgesic effect. Silver colloid easily penetrates the cells of microorganisms - pathogens and exhibits bactericidal and bacteriostatic effects. Propolis, which is part of the drug and consists mainly of flavonoids, together with an antimicrobial effect with a predominant effect on gram-positive microorganisms, has an anti-inflammatory effect (du Preez, 2000; Bovkun et al., 2015).

The authors (Modin, 2010; Antipina & Konopel'cev, 2010) developed a method for treating cows with mastitis patients using ozonated fish oil obtained by bubbling the ozone-oxygen mixture intracisternally. It is proved that the introduction of ozonized fish oil intracisternally causes the activation of local protection factors.

Specialists of St. Petersburg Institute of Pharmacy CJSC have developed an original standardized preparation "Aflogileks", which is an extract from the liver of cod fish species. The drug was developed for the treatment of inflammatory and allergic processes in two dosage forms "Aflogylex-0.02% gel" and "Aflogylex-0.1% solution". It contains as an active pharmaceutical ingredient a peptide-phospholipid complex, free amino acids and trace elements (Na, K, Ca, Mg, Fe, Cu, Zn), which play a significant role in the metabolic processes of animals (Skomarova & Rasputina, 2006; Rybakova, 2012).

For the treatment and prevention of these diseases of the mammary gland of farm animals, biologically active substances (BAS) are used. Among natural biostimulants, vitamin preparations are used, in particular, a food preparation of microbial carotene, derivatives of humic acids of peat – sodium humate (huminate), hydrohumate (Chursin, 2008; Bezuglova & Zinchenko, 2016). The use of a stimulating tissue preparation with immunostimulating properties (STP) during the start-up period and dead wood prevents serous mastitis in cows. The preparation contains hydrolysates from tissues of fish, plant and animal origin (Komarov & Belkin, 2015). Scientists (Zimnikov et al., 2011; Pereira et al., 2011; Glazunova et al., 2013) have proposed the use of hirudotherapy for the treatment of mastitis. The method consists of replanting leeches on the skin of a sick quarter of the udder, with an exposure of 25–30 minutes, for 3 days, with an interval of 24 hours.

Many drugs have been proposed for the etiotropic treatment of mastitis, among which the most widely used are: antibiotics; combined antibiotics (broad spectrum, a combination of two or more); combination drugs (antibiotics + sulfanilamides, antibiotics + nitrofurans); sulfonamides; nitrofurans; antiseptics; iodine-containing drugs (as antiseptics) (Persson et al., 2011). A comprehensive treatment regimen, which is based on the intravenous administration of thiotriazolin in combination with an application on the skin of an udder of an ointment containing a 30% solution of dimexide (40 ml), anestezin (5 g), menthol (3 g), lanolin (200 g), provides a decrease in the number of cases of cow disease with mastitis (Hansson et al., 2011; De Vlieghe et al., 2012).

Currently, world vaccines have been developed for carrying out preventive measures against this disease (Hovinen & Pyorala, 2011; Jacobs & Siegford, 2012). After the treatment of animals with mastitis and vaccination of cows with the Startvak vaccine, a decrease in the number of somatic cells in milk was noted, and the incidence of subclinical and clinical mastitis decreased by almost 4 times in a farm (Mass et al., 2016).

The positive results of the biocidal and therapeutic effect of staphylococcal toxoid vaccine using glutaraldehyde and alkyldimethylbenzylammonium chloride were used to increase the biocidal effect of ofloxacin and tetracycline, reduce the dose of antibiotics and make an ointment for treating patients with mastitis, which significantly reduced the duration of treatment (Evglevskij & Tagirmirzoev, 2015; Komarov, 2015; Komarov & Belkin, 2015; Guccione et al., 2016; Mass et al., 2016).

It is worth noting that the use of antimicrobial agents for the treatment of mastitis in cows is not enough. This leads to the emergence of resistant strains of microorganisms, especially antibiotics, resulting in reduced therapeutic efficacy of anti-mastitis drugs based on them. In addition, after treatment, the presence of residual amounts of antibiotics in milk is noted. In this regard, it becomes technologically unsuitable and harmful to human health. Intramammary drugs for use in veterinary medicine must be sterile, intended for introduction into the mammary gland through the mammary nipple canal. They are two main categories of drugs used for animals lactating, and drugs intended for use in animals after a period of lactation or non-lactating, for the treatment or prevention of infection (Mass et al., 2016).

Intrathoracic drugs for use in veterinary medicine are solutions, emulsions, suspensions or soft drugs, containing one or more APIs in an appropriate solvent. Suspensions may form a precipitate that must be rapidly dispersed by shaking, forming a suspension stable enough to provide the necessary dose for use. Emulsions can exfoliate, however, when agitated, they are easy to recover. Suspension – liquid LF containing as a dispersed phase one or more powdered powdered substances distributed in a liquid dispersion medium. Dispersed systems with a liquid dispersion medium and a solid dispersed phase, the segments of which are large enough, therefore not able to diffuse, do not have osmotic pressure, they do not detect unauthorized Brownian motion. In suspensions, the particles precipitate relatively quickly (sedimentation) or float, sticking together to floc aggregates (flocculation).

The main factors of the physical stability of suspensions are hydrophilicity (wettability) or hydrophobicity (non-wettability with water), size, shape, specific gravity, surface charge density of the solid phase, as well as density, viscosity, surface activity of the dispersion medium, which are regulated by surfactants, high molecular weight compounds (HMC) electrolytes, which ensure the wettability of the dispersed phase, an increase in the viscosity of the dispersion medium, and the formation of a zeta potential solid at the liquid - solid interface, which makes able the LF stability.

Increasing the stability of suspensions of hydrophobic substances is achieved by adding a hydrophilic colloid (stabilizer) to the solution, which provides insoluble substances with wettability properties. are more likely to exhibit a protective effect in natural or synthetic HMC suspensions. HMC solutions not only themselves have greater stability, but also transmit this ability to hydrophobic parts. As surfactants, they reduce the surface energy supply in the system, form adsorption shells and hydrated layers on the

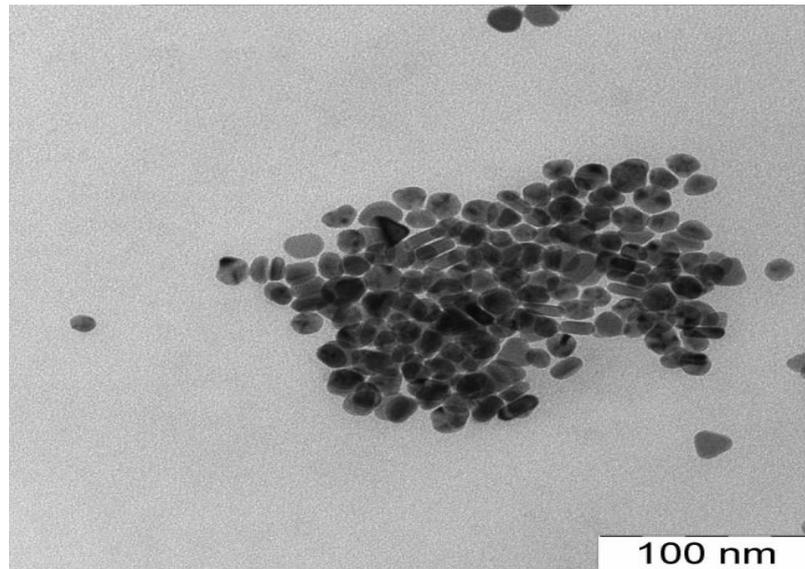
surface of solid hydrophobic particles, and also cover them with long chain-like macromolecules. As stabilizers in suspensions, natural or synthetic HMCs are used. The ratio between the solid phase of the suspension and the protective HMC depends on the degree of hydrophobicity of the substance and the hydrophilic properties of the protective substance.

The main DRs in sterile suspensions are represented by the following groups: surfactants (ensuring the wetting of hydrophobic compounds and stabilization of suspensions), components of the buffer system (adjusting the pH of the medium), antimicrobial preservatives (providing protection against microbial contamination), antioxidants (providing protection against oxidative degradation), suspending agents (stabilization of suspensions) and others (Khariv et al., 2017; Holubiev et al., 2017; Slivinska et al., 2018; Gutyj et al., 2018; Sobolev et al., 2018; Klosova et al., 2019; Palchykov et al., 2019; Zazharskyi et al., 2019; Kiserer et al., 2019). Therefore, the urgent problem of veterinary medicine is the development of drugs that would have a high therapeutic effect and would not negatively affect human health when ingested in milk.

The aim of the study was to investigate the antimicrobial activity and analgesic effectiveness of the newly developed drug Mastitnano-BelGAU, which contains silver nanoparticles, copper nanoparticles, organin, dexpanthenol, distilled water.

## Material and Methods

The antimicrobial activity of six samples of the Mastitnano-BelGAU preparation containing silver nanoparticles as the active pharmaceutical ingredient was investigated. The average size of silver nanoparticles was  $16 \pm 5$  nm (according to TEM) (Figure 1).



**Figure 1.** Silver nanoparticles ( $16 \text{ nm} \pm 5$ ) according to TEM.

The drug Mastitnano-BelGAU in various concentrations of the active substance in silver nanoparticles (1 – 0.15 mg/mL, 2 – 0.12 mg/mL, 3 – 0.1 mg/mL, 4 – 0.09 mg/mL, 5 – 0.05 mg/mL, and 6 – 0.002 mg/mL) was tested for clinical multiresistant strains of microorganisms Sigma (USA). *Staphylococcus aureus* 421, *S. epidermidis* 439, *Escherichia coli* 197, *Pseudomonas aeruginosa* 185 strains characterized by multiple antibiotic resistance were used as test objects.

The studied cultures of various types of microorganisms were grown on Muller-Hinton medium at 37°C for a day. A microbial suspension was prepared in sterile physiological saline (5.0 cm<sup>2</sup>) at concentrations of 10<sup>6</sup>, 10<sup>4</sup> cfu/mL using a DENSIMAT densitometer instrument and McFarland standards (manufactured by bioMerieux, France). The selected staphylococcal strains were characterized by high levels of oxacillin resistance, which are caused by the production of the MESA encoded penicillin binding protein PSB2, which was proved by latex agglutination method using Slidex MRSA Detection kit (manufactured by BioMerieux, France). The sensitivity of the test strains to the studied drug Mastitnano-BelGAU was studied using sterile disks, which were impregnated with the drug in the form of a soft drug containing silver nanoparticles. For inoculation, prepared microbial suspensions of the above cultures of two concentrations were used. The standard inoculum was pipetted onto the surface of the Muller-Hinton medium uniformly distributed over the surface of the medium, the excess was pipetted out and dried. Then, with the help of sterile tweezers, discs impregnated with samples of the studied drug were placed. As a control, sterile discs without impregnation with Mastitnano-BelGAU were used. The results were evaluated by the diameter of the zones of growth inhibition of the studied strains around the disks impregnated with the drug after 24 hours of incubation in an incubator at 37°C. Depending on the diameters of the zones of growth inhibition of the studied microorganisms around the disks, the strains belonged to sensitive, moderately stable, or resistant (resistant).

A study of the analgesic activity of the drugs Mastitnano-BelGAU and Dexpanthenol was carried out by cutaneous application to the plantar surface of the hind right limb of white rats using an eye glass rod. The exposition of the preparations (within 120 sec) was carried out under conditions of soft (manual) fixation of rats in a horizontal position in air, without touching the extremities of any surface. The prophylactic and therapeutic regimen for the application of drugs was applied, twice applying the cream and ointment to rats of the corresponding groups prior to the administration of carrageenan with an interval of 20 minutes between applications and a single application of the corresponding dosage forms after administration of carrageenan. Carrageenan was administered 10 minutes after the second prophylactic use of a cream or ointment. In the study of analgesic activity, not only the change in pain sensitivity in animals was taken into account, but also the duration and speed of the onset of the effect.

The groups of rats are shown in Table 1, which highlights the route of administration of drugs and a pathogenic agent and the duration of exposure on the plantar surface of the rat foot. The animals of the control group included rats untreated by the studied or referential preparation, that is, animals in which only a pain reaction was caused by the administration of a 1% aqueous carrageenan solution. After the introduction of carrageenan, as well as after exposure of the experimental samples of the

preparations, each animal was placed under a glass hood with an air hole (one animal under the hood). The determination of pain sensitivity was done when the infrared beam was focused on the plantar of the right foot of each animal.

**Table 1.** Characterization of the study of the analgesic effect of the combined drug Mastitnano-BelGAU.

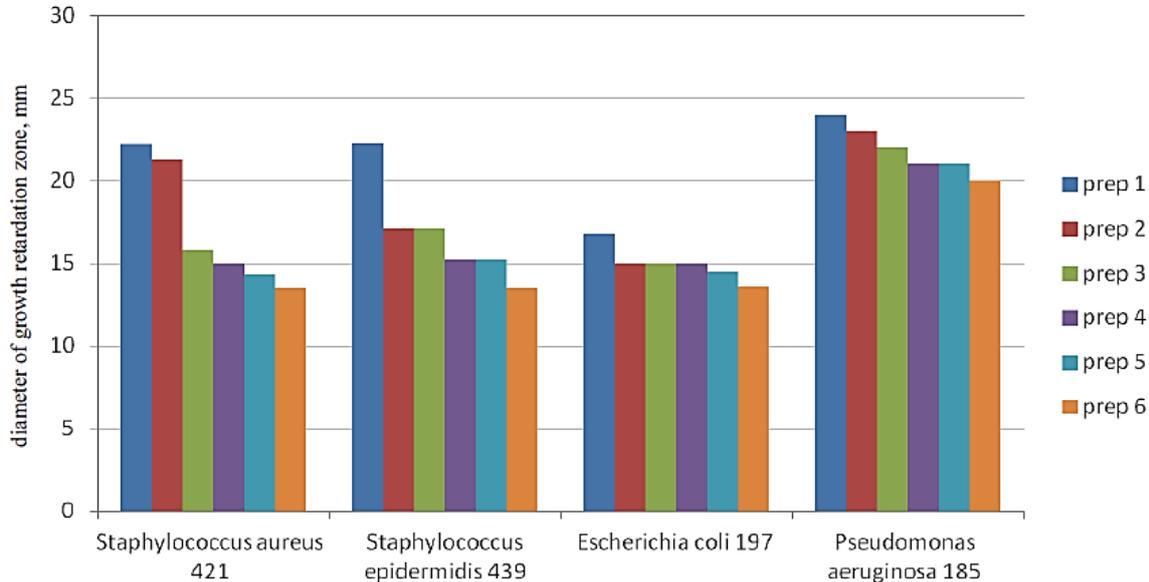
Group of animals	Agent	Administration way	Time of the drug exposition, sec
Control, 10 animals	Carrageenan, 1% aqueous solution	Subplantar, right hind paw	-
Mastitnano-BelGAU, 10 animals	Carrageenan + Mastitnano-BelGAU	An experimental preparation on the plantar surface of the affected paw	120
Dexpanthenol Ointment, 10 animals	Carrageenan + Dexpanthenol Ointment	Dexpanthenol on the plantar surface of the affected paw	120

Mastitnano-BelGAU and Dexpanthenol were applied to animals of the experimental groups three minutes after the administration of carrageenan. The actual pain response caused by carrageenan was recorded separately for animals of each group within 240 min after administration of carrageenan. That is, the analgesic effect of the drug Mastitnano-BelGAU and dexpanthenol was evaluated in fact with the development of inflammatory pain sensitivity (PS). The efficacy (analgesic effect) of the preparations was compared with analgesic activity (AA), which was calculated as a percentage as the ratio of the difference between PS in the group of control and experimental animals in PS in the group of control animals. The duration and speed of the onset of the analgesic effect of Mastitnano-BelGAU preparations, cream and Dexpanthenol, ointment was determined by dynamic measurement of warheads 30, 60, 120 and 240 minutes after the administration of carrageenan and the application of these agents. All animal manipulations were carried out in accordance with the European Convention for the Protection of Vertebrate Animals, which is used for experimental and scientific purposes (Strasbourg, 1986). Analysis of the research results was performed using the Statistica 6.0 software package. The likelihood of differences was evaluated by Student's t-test. The results were considered significant at  $P \leq 0.05$ .

## Results and Discussion

Some preliminary results of Mastitnano-BelGAU anti-microbial activity towards *Staphylococcus aureus* 421, *Staphylococcus epidermidis* 439, *Escherichia coli* 197, *Pseudomonas aeruginosa* 185 at different microbial loads are shown in Figures 1 and 2. We established that the diameters of the zones of growth inhibition of cultures around discs saturated with samples of the experimental preparation depended on the concentration of microbial suspension deposited on the surface of the Mueller-Hinton medium.

The smallest diameters of the zones of growth inhibition of *S. aureus* 421 culture were observed when applying the culture at a concentration of  $10^6$  cells/mL around the disks impregnated with sample 6 (Figures 2 and 3). The diameters of the growth inhibition zones of samples 1-6 decreased in descending order. While the largest diameters of staphylococci growth retardation zones were detected at a microbial load of  $10^4$  cells/mL around the discs with sample 1 and 2.

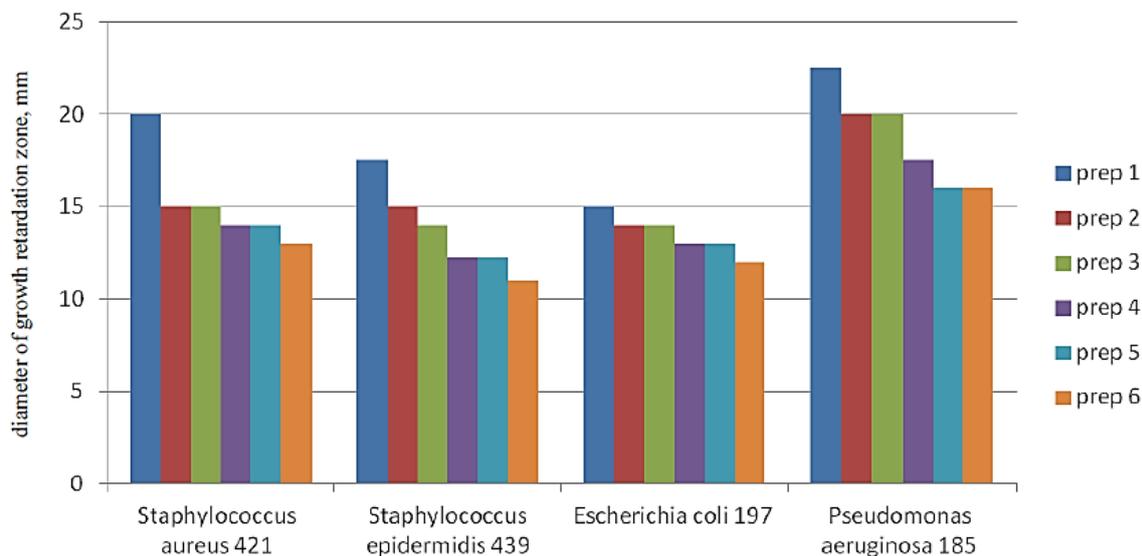


**Figure 2.** The sensitivity of clinical strains of microorganisms to samples of the drug Mastitnano-BelGAU with a microbial load of  $10^4$  cells/mL (active substance in silver nanoparticles: 1 – 0.15 mg/mL, 2 – 0.12 mg/mL, 3 – 0.1 mg/mL, 4 – 0.09 mg/mL, 5 – 0.05 mg/mL, 6 – 0.002 mg/mL).

Regarding strain *S. epidermidis* 439, the following was observed: with a microbial load of  $10^4$  cells/mL, samples 2 and 3 showed moderate activity, and sample 1 showed a fairly high anti-microbial activity. Samples 4 and 5 had growth retardation zones of 16 mm. The smallest value of the zones of growth inhibition was in sample 6 (13 mm). When applying the culture at a concentration of  $10^6$  cells/mL, samples 4 and 5 had the same growth retardation zones, and sample 1 showed moderate antimicrobial activity (19 mm). Thus, from the studied samples of the Mastitnano-BelGAU preparation, the highest anti-microbial activity against clinical multiresistant strains of the genus *Staphylococcus* at a concentration of  $10^4$  cells/mL was exhibited by samples 1 and 2.

We registered the data pattern on the antimicrobial activity of the drug in relation to clinical strains of gram-negative microorganisms *E. coli* 197 and *P. aeruginosa*. Thus, sample 1 (microbial load  $10^4$  cells/mL) inhibited the growth of *E. coli* 197 colonies (growth retardation zone 17 mm), while while samples 2, 3, and 4 had the same activity, which had 15 mm diameters of the zones of growth inhibition of *E. coli* 197 under a microbial load of  $10^6$  cells/mL. Sample 1 was characterized by antimicrobial

activity (growth inhibition zone of 15 mm). In samples 2 and growth inhibition zones did not exceed 14 mm, and in samples 4 and 5–13 mm.



**Figure 3.** The sensitivity of clinical strains of microorganisms to samples of the drug Mastitnano-BelGAU with a microbial load of  $10^6$  cells/mL (active substance in silver nanoparticles: 1 – 0.15 mg/mL, 2 – 0.12 mg/mL, 3 – 0.1 mg/mL, 4 – 0.09 mg/mL, 5 – 0.05 mg/mL, 6 – 0.002 mg/mL).

The studied samples of the Mastitnano-BelGAU preparation were characterized by higher antimicrobial properties in relation to the clinical strain *P. aeruginosa* 185, in contrast to the *E. coli* strain 197. The largest diameters of the growth inhibition zones of *Pseudomonas aeruginosa* were observed around the disks impregnated with all the studied samples of the preparation with respect to microbial concentrations of  $10^4$  and  $10^6$  cells/mL of *P. aeruginosa* 185 culture.

It was found that the diameters of the growth inhibition zones of the studied cultures of *Staphylococcus aureus* 421, *S. epidermidis* 439, *Escherichia coli* 197, and *Pseudomonas aeruginosa* 185 around the disks saturated with samples of the experimental preparation depend on the concentration of microbial suspension deposited on the surface of the Mueller-Hinton medium and on the concentration of API (active pharmaceutical ingredient).

According to the data in Table 2, in animals of the control group (administration of carrageenan), an increase in pain sensitivity was recorded 30 min, 60 min, 120 min, and 240 min after the use of the phlogogenic agent, as evidenced by a decrease in SPS by 30%, 27.2%, 22.1% and 15.1%, respectively. Obviously, this fact can be explained by the increased sensitivity of peripheral receptors through the development of an acute inflammatory process.

**Table 2.** Pain sensitivity in white rats on the background of hyperalgesia induced by carrageenan, when exposed to Mastitnano-BelGAU and dexpanthenol,  $M \pm m$ .

indicator	start	Time of registration of PS, min			
		30	60	120	240
<b>Carrageenan, 1% solution (control; n=10)</b>					
PS, sec.	13.60 ± 0.4	9.5 ± 0.9*	9.9 ± 0.9*	10.6 ± 0.7*	11.55 ± 0.8*
% towards start		-30.1	-27.2	-22.1	-15.1
<b>Dexpanthenol (n=10)</b>					
PS, sec.	13.63±1=1.1	9.9 ± 0.8*	11.2 ± 0.4	12.7 ± 0.6	12.9 ± 0.4
AA, %	-	5	13	20	11.7
<b>Mastitnano-BelGAU (n=10)</b>					
PS, sec.	13.12 ± 0.9	11.73 ± 0.8	13.82 ± 1.1	12.8 ± 0.6	12.7 ± 0.8
AA, %	-	23.5	39.6	20.8	10

\* - Significant at  $p < 0.05$ , PS – Pain Sensitivity, AA - Analgesic Activity.

Against the background of the use of dexpanthenol, an increase in warhead in rats was recorded, compared with the data observed in animals of the control group for the corresponding observation period: by 4.2% 30 minutes after administration of carrageenan, by 13.1% – after 1 h, by 19.8% – after 2 hours and by 11.7% – after 4 hours. So, the most pronounced analgesic effect was registered at 60-120 min after the administration of the drug Dexpanthenol against the background of a carrageenan-induced inflammatory reaction. At the same time, dexpanthenol has a relatively moderate analgesic effect, as evidenced by the AA of the drug, registered at the level of 11-20% at different times of the development of the pain response to the introduction of phlogogen. A more significant analgesic effect is characteristic of the Mastitnano-BelGAU preparation, as evidenced by the absence of a significant difference in the value of warheads recorded at 30, 60, 120 and 240 minutes after administration of carrageenan and application of the drug relative to the initial values of this indicator in animals of this group, and is also quite high AA, which is registered for 30-120 minutes after the induction of a pain reaction – 20.8-39.6%. By the way, similarly to the indicators recorded after the application of dexpanthenol, it was 60-120 minutes after the use of carrageenan that the highest AA was observed, which is inherent in Mastitnano-BelGAU. Obviously, this fact can be justified by synergism or potentiation of analgesic activity in the interaction of the active components of the cream.

## Conclusion

The studied samples of the drug Mastitnano-BelGAU high antimicrobial properties were characterized by samples 1 and 2. The largest diameters of staphylococci growth retardation zones were observed when applying microbial suspension at a concentration of  $10^4$  cells/mL around discs saturated with samples of preparation 1 and 2. The drug Mastitnano-BelGAU had a high antimicrobial activity in all studied concentrations relative to the culture of *P. aeruginosa* 185.

We established that the developed experimental drug Mastitnano-BelGAU exhibits bacteriostatic and bactericidal action against multiresistant clinical strains of various types of microorganisms.

Mastitnano-BelGAU exhibits a significant long-term (within 4 hours) analgesic effect on the model of the pathological process induced by carrageenan, which appears practically at the beginning of the inflammatory reaction.

The new drug Mastitnano-BelGAU showed prolonged analgesic activity on a model of carrageenan inflammation, characterized by a significant increase in pain sensitivity during four hours of observation.

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