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Treatment of pets with the active substance dexpanthenol in wound processes

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Abstract. Animal skin is a complex organ that directly perceives the influence of the external environment and performs a barrier-protective function, helps maintain the balance of the internal environment of the body. Disruption of each of the levels of the protective system leads to the development of inflammatory skin diseases. Treatment of wounds remains one of the most pressing scientific and practical problems of modern veterinary medicine. A number of researchers are searching for and developing new veterinary drugs for the treatment of wounds of various etiologies in small pets, but the use of drugs often causes adverse skin reactions. The purpose of this study was to evaluate the effectiveness of using a veterinary drug (ointment) in the treatment of wounds in

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domestic animals (dogs, cats, rabbits). The paper uses standard clinical, haematological, and biochemical research methods. The studies used a drug with the active substance dexpanthenol and excipients decamethoxine, Vaseline oil, emulsifier, glycerin, methylparaben, propylparaben, and purified water. The drug under study effectively reduced the wound surface area at all observation periods. It is proved that when using dexpanthenol-based ointment (10%), a complete wound-healing effect was observed in experimental animals on the 14th day of treatment: the area of wound surfaces decreased by 93.1±1.51%. The examined indicators were statistically substantially different from those in the group of untreated animals with skin wounds. The general clinical condition of domestic animals was examined, haematological and biochemical studies of animal blood were conducted under the conditions of applying an experimental drug to damaged skin areas. In animals with skin damage without treatment, the dynamic development of an acute inflammatory process in the body, the development of endogenous intoxication syndrome, signs of wound infection, pronounced exudation and slowing of contraction were observed. The developed veterinary drug with the active substance dexpanthenol simultaneously shows a pronounced anti-inflammatory and wound-healing effect and provides a rapid therapeutic effect in wound processes in small pets

Keywords: dogs; cats; rabbits; wounds; dexpanthenol; morpho-physiological parameters of blood; blood serum

INTRODUCTION

Every year, the number of small pets in the private homes of urban citizens is constantly growing. The most common pathology among animal diseases is mechanical damage to the skin – wounds that require urgent care. Veterinarians are provided with a large number of treatment tools, but the search and development of environmentally friendly and safe veterinary drugs for the treatment of skin pathologies in small pets remain an urgent issue.

All wounds, without exception, heal through inflammation, and in the absence of antiseptic treatment – through suppuration. Many aspects of wound healing in small animals have not yet been fully clarified: mechanisms of inhibition of granulation tissue growth and maturation, differentiation of connective tissue cells, and the relationship between inflammation, regeneration, and fibrosis in complicated wounds (Mauldin & Peters-Kennedy, 2016; Fernandes *et al.,* 2018; Somjorn *et al.,* 2021). Conservative means and methods of treating complicated wounds are often ineffective. There is a need to further search for new and improve registered drugs and treatment methods that stimulate reparative processes in wounds of various etiologies, and an in-depth investigation of their pharmacognosy.

Darwin & Tomic-Canic (2018) proved that the wound process is a dynamic self-regulating system, as each of its phases prepares and starts the next. The success of the wound process (Davidson, 2015; Gonzalez *et al.,* 2016; Cañedo-Dorantes & Cañedo-Ayala, 2019) depends on the type, size, location of the wound, granulation features, nature and amount of wound exudate, invasiveness and virulence of microorganisms, the immune status of the patient's body, the presence of concomitant diseases, and the rational choice of wound treatment tactics. The main condition for the normal course of the wound healing process is the synchronisation of the epithelialisation process, on the one hand, and the maturation of granulation tissue, on the other. Thus, in the dynamics of wound healing, three main periods are noted: cleaning of the wound defect from necrotic masses due to inflammation; proliferation of connective tissue elements with the formation of granulation tissue filling the wound; scar formation, its remodelling, and epithelialisation of tissues (Stettler *et al.,* 2017; Lux, 2022).

Basov *et al.* (2021) developed and tested the use in surgical practice of a device for visual monitoring of the wound during its treatment with pharmacological solutions (including antiseptic, antiseptic oxidizer, and osmotically active agent). This method accelerates the therapeutic effect by 43.8% compared to wound treatment with a 0.02% aqueous chlorhexidine solution and a local ointment with an antibiotic.

Negative Pressure Wound Therapy (NPWT) has been used in Europe and the United States for about 15 years. Studies by Nolff (2021) on cats have shown that the device effectively copes with infected wounds, increases granulation and neovascularisation, and promotes wound narrowing through active macrocontrtaction.

The group of researchers (Bekeschus *et al.,* 2021) tested gas plasma technology and recommended it for use in veterinary practice. Reactive oxygen and nitrogen forms have been shown to promote wound healing at various stages, have a negative effect on various types of microorganisms that complicate the inflammatory process, and lead to rapid hemostasis in the wounds of experimental animals (rodents and pigs). Enciso *et al.* (2020) recommend the use of allogeneic ASC therapy to improve the healing of acute and chronic wounds in dogs. They proved that treatment of wounds with fat mesenchymal stem cells from an adult animal already on the 90th day contributes to re-epithelialisation (more than 97%).

Alshehabat *et al.* (2020), based on experimental studies, suggest using the following methods for treating wounds in dogs: wet burn ointment (contains B-sitosterol, baicalin, and berberine as active ingredients based on beeswax and sesame oil). They note that this method

of treatment helps to accelerate epithelialisation, quickly reduces the wound area, and does not cause allergic reactions in animals with weakened immune systems.

In recent years, the attention of researchers has been attracted to therapeutic drugs for wound healing, especially with signs of bacterial infection, based on pantothenic acid. Researchers (Ebner *et al.,* 2002; Li-Mei *et al.,* 2016; Ogden *et al.,* 2019) prove that it is necessary for the normal function of the epithelium. It is a component of coenzyme A, which serves as a co-factor for various enzyme-catalysed reactions that are important in the metabolism of carbohydrates, fatty acids, proteins, gluconeogenesis, sterols, steroid hormones, and porphyrins. A stable alcoholic analogue of pantothenic acid is dexpanthenol, the local application of which is based on good penetration into the skin and rapid local concentration. During the treatment of superficial, postoperative wounds, and scars at the stage of formation, its effectiveness increases if dexpanthenol is introduced into the emulsion or ointments. It provides support for anti-inflammatory and antioxidant activity, which play an important role in cellular defence and recovery systems against oxidative stress and inflammatory response (Marquardt *et al.,* 2015; Nahirniy, 2022). Proksch *et al.* (2017) identified that the mode of action of dexpanthenol at the molecular level increases the mobility of molecular components of the stratum corneum of the skin, which are important for ensuring its barrier function, and modulates the expression of genes important for wound healing.

The purpose of this study was to determine the therapeutic effectiveness of dexpanthenol-based ointment in wound processes in small domestic animals.

MATERIALS AND METHODS

The study was conducted in 2020-2021 based on the laboratory of Veterinary Hygiene and Parasitology of the National scientific centre "Institute of Experimental and Clinical Veterinary Medicine", and in an animal shelter (Balakliya, Kharkiv region). The study programme was reviewed and approved in accordance with the current procedure by the bioethics commission of the National scientific centre "Institute of Experimental and Clinical Veterinary Medicine".

A drug with the active substance dexpanthenol was used to evaluate the effectiveness of the ointment in the treatment of wounds in domestic animals. Composition of the product (1 ml): dexpanthenol – 10 mg; excipients: decamethoxine, Vaseline oil, emulsifier, glycerin, methylparaben, propylparaben, purified water.

The following groups of animals were formed to conduct research:

Group I (intact animals) – clinically healthy animals. No clinical signs of skin damage were identified. The skin was smooth, elastic, moderately hydrated.

Group II (control pathology) – animals with skin damage, whose owners sought help within the first five days after the occurrence of wound damage. By origin, wounds are accidental, by the nature of the damage – stab and torn, by the depth of the damage – surface, by the degree of tissue destruction – with a large area of damage, by the degree of infection – contaminated. The animals were not treated with chemotherapeutic agents.

Group III (experiment) – animals with skin damage, whose owners sought help within the first four hours after the occurrence of wound damage (fresh wounds). By origin, wounds are accidental, by the nature of the damage – stab and torn, by the depth of the damage – surface, by the degree of tissue destruction – with a large area of damage, by the degree of infection – contaminated. The animals were treated with the drug under study.

In the first stage of the study, the wound-healing effectiveness of a veterinary drug was examined on mongrel cats of different ages and sexes. The following groups of animals were formed to conduct research:

Group I (intact control) – clinically healthy mongrel cats (n=15) aged 1 to 4 years with body weight from 2.1 to 3.9 kg. The animals were kept in a vivarium, but they did not have skin pathology, and the drug was not applied to them.

Group II (positive control, control pathology) – animals (n=9) with skin damage without treatment.

Group III (experiment) – animals (n=15) that were treated with the drug under study on damaged skin areas.

The animals were kept in aviaries on a standard balanced diet with free access to water, according to physiological needs. During the experiment, cats were examined, which included visual, palpation, thermometry, respiratory and heart rate examinations. Clinical examination of cats in the study groups included a detailed medical history and examination of the condition of the skin and mucous membranes (Stein, 1981; Vojtkovská *et al.,* 2020). Dynamic monitoring of animals was performed and changes in the wound surface area were determined 3, 7, and 14 days after the onset of the pathological process. In cats of the experimental groups, the affected skin areas were treated with preparations by applying a thin layer to the skin 3 times a day. Before applying the drug, hygienic treatment of the affected area was performed. Evaluation of the wound-healing effect of the drug was performed by analysing the activity of wound surface contraction in dynamics on the 3rd, 5th, 7th, 9th, and 14th days, determining the area of the wound surface in animals. The intensity of skin damage was established: slight erythema, clear erythema, clear erythema with compaction, erythema with hemorrhagic phenomena, and ulcers with severe infiltration (Elzayat *et al.*, 2018; Sofrona *et al.,* 2020). During the study period, blood samples were taken from cats for haematological and biochemical evaluation: before the drug was used, on the 3rd, 5th, 7th, and 14th days of the experiment.

In the second stage of experimental studies, the effectiveness of the veterinary drug was examined on

mongrel dogs of different ages and sexes. The following groups of animals were formed to conduct research:

Group I (intact animals) – clinically healthy mongrel dogs (n=17) aged from 1 to 9 years with body weight from 3.8 to 9.7 kg. No clinical signs of skin damage were identified.

Group II (control pathology) – dogs (n=10) with skin damage without correction and treatment.

Group III (experiment) – dogs (n=17) that were treated with the drug under study on damaged skin areas.

Animals of the control and experimental groups were kept in aviaries on a standard balanced diet with free access to water, according to physiological needs. Clinical examination of dogs of the experimental groups included a detailed medical history and evaluation of the coat condition, namely, the determination of thickness, elasticity, and dryness of the skin (Hardy, 1981). Dynamic monitoring of dogs was performed and changes in the wound surface area were determined 3, 5, 7, 9, and 14 days after the onset of the pathological process. In dogs of experimental groups, the affected skin areas were treated with the drug by applying a thin layer 3 times a day. Before applying the drug, hygienic treatment of the affected area was performed (Frees, 2018).

When assessing the influence of the adverse factor, substantial deviations in relation to the indicators of animals of the intact group and control pathology were determined ($p<0.05$). The criteria for the wound-healing effect of the drug under study were only substantially positive changes in the examined indicators in relation to the control pathology group.

During the study period, blood samples were taken from dogs for haematological and biochemical studies: before the drug was administered, on the 3rd, 7th, and 14th days of the experiment.

In the third stage of the experiment, the wound-healing effectiveness of the drug under study was examined on decorative rabbits. The following groups of animals were formed to conduct research:

Group I (intact animals) – clinically healthy decorative rabbits (n=5) without skin damage.

Group II (control pathology) – rabbits (n=5) with skin damage without correction and treatment.

Group III (experiment) – rabbits (n=5), that were treated with the drug under study on damaged skin areas.

Animals of the control and experimental groups were kept in cages on a standard diet with free access to water, according to physiological needs. Clinical examination of rabbits of the research groups included determining the condition of the coat. In rabbits of the experimental groups, the affected skin areas were treated with the drug by applying a thin layer 3 times a day. Before applying the drug, hygienic treatment of the affected area was performed.

Assessment of the wound-healing effect of the drug under study was conducted by determining the area of the wound surface in animals in dynamics on the 3rd, 5th, 7th, 9th, and 14th days. When assessing the influence of the adverse factor, substantial deviations in relation to the indicators of animals of the intact group and control pathology were determined ($p<0.05$).

The blood samples were kept in test tubes in a thermostat for 15 minutes to obtain serum from animals. A stainless metal stick was applied along the inner wall of the test tube to separate the serum from the clot. The samples were centrifuged at 3000 rpm for 15 minutes. Blood serum was taken using a pipette dispenser in sterile Eppendorf-type tubes.

Haematological examinations included: the determination of total haemoglobin (HGB), hematocrit (HCT), red blood cell count (RBC), and white blood cell count (WBC) (Bauer & Moritz, 2008; Becker *et al.,* 2008). The level of activity of the following enzymes was determined in the blood serum of animals: alanine aminotransferase (ALAT; EC 2.6.1.2) and aspartate aminotransferases (ASAT; EC 2.6.1.1) according to the Reitman-Frenkel method (Wilkinson *et al.,* 1972).

Examinations of the functional state of the liver of experimental animals included the determination of total protein by turbodimetric method, c-reactive protein (CRP), and urea – by the diacetylmonooxime method (Doumas *et al.,* 1981).

Statistical processing of the results was conducted using statistical methods (STATISTICA 10.0 for Windows) with the determination of the arithmetic mean (M), the statistical error of the arithmetic mean (m), the probability of difference (P) between the arithmetic mean of two variational series by the confidence coefficient for the difference of the averages (t). The difference between the two values was considered substantial at $*p\leqslant0.05$; $**p\leqslant0.01$; $***p\leqslant0.001$.

All experimental studies were conducted in accordance with modern methodological approaches and in compliance with the relevant requirements and standards, in particular, they meet the requirements of DSTU ISO/IEC 17025:2005 (2006). The keep of animals and all manipulations were conducted in accordance with the provisions of the procedure for conducting experiments and experiments on animals by scientific institutions (Law of Ukraine No. 249, 2012), the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (European convention..., 1986).

RESULTS AND DISCUSSION

In the first stage of the study, clinical examinations of mongrel cats were conducted to establish the effectiveness of the veterinary drug under study. The general clinical condition of cats was examined, haematological and biochemical examinations of cat blood were performed under the conditions of applying the drug to damaged areas of the skin. The clinical condition of cats in the control and experimental groups was determined daily throughout the entire study period.

Thermometry was performed, the condition of visible mucous membranes, skin and coat was examined.

According to the results of clinical observations at the beginning of the experiment, it was established that cats of Group I (intact animals) were clinically healthy, had visible mucous membranes of pale pink colour, moderately shiny, without damage, pigmented. The skin was smooth, medium thickness, elastic, without damage. The coat was thick, shiny, and close to the body. In cats of Group II (control pathology), a skin wound process of various etiologies was recorded: acute inflammation, skin compaction, scratches, rashes, pale skin, not elastic. Animals of this group were not treated with drugs. In cats of Group III (experiment), clinical signs of skin inflammation in the extremities and muzzle were noted: redness, peeling and itching, cracks, and bleeding. The animals were depressed and did not consume food willingly. On the damaged areas of the skin of cats, a thin layer of the drug under study was applied three times a day. Analysis of experiments on the wound-healing and anti-inflammatory properties of the experimental drug showed its high effectiveness (Table 1).

Table 1. *Dynamics of changes in the area of wound surfaces (M±m) in cats under conditions of skin damage*

Observation period, day	Wound surface area in observation groups, mm^2	
	Skin damage without correction	Application of the experimental drug
3	0.72±0.02	0.52±0.02*
5	0.59±0.02	0.28±0.01*
7	0.54±0.01	0.20±0.01*
9	0.37±0.03	0.12±0.02*
14	0.05±0.01	003±0.01*

Note: ** – this value differs statistically substantially (p<0.05) from the same value in the group of untreated animals with skin damage*
Source: *compiled by the authors*

The above indicates a tendency to heal wound processes when using the experimental drug. Cats with untreated skin damage showed signs of wound infection, severe exudation, and slowing contraction. Notably, in cats with skin damage, no wound infection was observed when using the ointment, and there was no exudation. The drug under study effectively reduced the wound surface area at all observation periods. The examined indicators were statistically substantially different from those in the group of untreated animals with skin wounds. Along with this, a number of morphological parameters of the blood of cats of the control and experimental groups were examined (Table 2).

Table 2. *Dynamics of morpho-physiological parameters of cat blood under the influence of the experimental drug (M±m)*

Experimental groups	Duration of the examination, days			
	before application	3rd day	7th day	14th day
	Haemoglobin (HGB), g/dm^3			
I	127.42±0.90	128.07±1.11	130.03±1.09	127.44±0.97
II	123.19±1.02*	123.17±1.32*	123.93±2.14*	128.15±1.58
III	119.75±1.15*	122.18±1.02*	124.17±1.2*	125.09±1.47
	Hematocrit (HCT), %			
I	36.34±1.23	37.15±1.42	38.16±1.12	37.35±1.12
II	37.13±1.12	37.08±0.25	37.24±1.15	38.19±1.83
III	45.33±1.03*	44.94±1.91*	36.22±1.26	37.12±1.54
	Red blood cells (RBC), $10^{12}/ dm^3$			
I	8.18±0.46	8.24±0.85	8.59±0.27	9.03±0.51
II	8.17±0.93	8.75±1.32	8.16±0.11	8.12±0.47

Table 2, Continued

Experimental groups	Duration of the examination, days			
	before application	3rd day	7th day	14th day
III	8.36±0.24	8.11±0.32	8.26±0.12	8.38±0.51
White blood cells (WBC), 10^9/dm^3				
I	9.51±0.43	9.57±0.26	9.87±0.24	9.54±0.15
II	13.25±0.41*	14.74±0.53*	13.74±0.43*	13.98±0.43*
III	12.85±0.63*	11.42±0.91*	10.99±1.14	9.67±0.54

Notes: ** – p<0.05; ** – p<0.01 according to the indicator in intact control*
Source: *compiled by the authors*

Analysing the obtained data (Table 2), the substantial changes in morpho-physiological parameters of the blood of cats were established, in particular, a reduced haemoglobin content in cats of groups II and III was recorded: before the start of the drug – by 3.32% and 6.02%, respectively; on Day 3 – by 3.83% and 4.60%, respectively; on Day 7 – 4.69% and 4.51%, respectively. A substantial increase in the hematocrit value was identified in cats of Group III before the start of the experiment – by 24.74%; on the 3rd day of the experiment – by 20.96%. The hematocrit values and the number of red blood cells in the cats of the experimental groups did not substantially differ from the indicators of the intact control. A substantial increase in white blood cells in groups II and III of cats with skin damage was identified before the experiment – by 39.33% and 35.12%, respectively; on Day 3 – by 54.02%, and 19.33%, respectively. On the 7th and 14th days of the experiment, leukocytosis was recorded in cats of Group II (39.21% and 46.54%, respectively). Such changes in the blood picture indicate the development of endogenous intoxication syndrome, which is caused by toxic products that are formed during the breakdown of tissues due to their destruction.

The examination of the dynamics of biochemical parameters in the blood serum of cats (Table 3) showed a substantial increase in the concentration of total protein in the blood serum of cats of groups II and III who had skin damage before use – by 7.63%, and 10.99%, respectively; on Day 3 – by 5.32% and 8.17%, respectively. On Day 7 of the experiment, total protein was higher than intact control in cats of Group III by 5.19%, and on Day 14 – by 2.08%. It was identified that the content of C-reactive protein (acute phase protein, an indicator of tissue damage during inflammation) in the blood serum of cats of groups II and III was substantially higher than the intact control: before the experiment, by 2.1 and 2.21 times; on Day 3 – by 2.04 and 2.15 times. On Day 7, the CRP content in the blood of Group III cats exceeded the control by 1.42 times. No substantial changes were recorded on Day 14.

Table 3. *Dynamics of biochemical parameters in the blood serum of cats under the influence of the experimental drug (M±m)*

Experimental groups	Duration of the examination, days			
	before application	3rd day	7th day	14th day
Total Protein, g/L				
I	77.33±0.21	78.57±0.16	77.13±1.11	78.68±1.34
II	83.23±1.12*	82.75±0.96*	80.11±1.14	79.21±1.02
III	85.83±1.32**	84.99±0.32**	81.13±1.23*	80.32±1.44*
C-reactive protein, mg/L				
I	4.23±0.08	4.25±0.08	4.59±0.24	4.65±0.31
II	8.96±0.11*	8.65±0.12*	5.52±0.36	5.12±0.36
III	9.23±0.21**	9.14±0.25**	6.54±2.54*	4.94±0.24
ALAT, IU/L				
I	12.57±0.63	12.92±0.35	12.19±0.46	13.15±0.38
II	12.46±1.24	12.73±0.17	12.88±1.13	12.56±0.43
III	12.58±1.17	11.99±0.65	12.61±0.24	12.44±1.82

Table 3, Continued

Experimental groups	Duration of the examination, days			
	before application	3rd day	7th day	14th day
		ASAT, IU/L		
I	28.17±0.96	28.14±0.46	27.84±0.54	29.14±0.36
II	28.51±1.02	28.31±1.13	28.23±0.42	27.17±1.06
III	28.33±0.42	27.97±0.41	29.11±1.24	28.31±0.94
		Urea, mmol/L		
I	5.25±0.17	5.31±0.24	5.77±0.23	5.81±0.14
II	7.36±0.75*	6.49±0.93*	5.99±0.46	5.67±0.26
III	7.14±0.17*	6.71±0.85*	6.14±0.87	5.39±0.43

Notes: ** – p<0.05; ** – p<0.01 according to the indicator in intact control*
Source: *compiled by the authors*

The activity of indicator enzymes (ALAT, ASAT) in the blood serum of cats during the experiment was within the physiological norm. The concentration of urea in the blood of cats of groups II and III exceeded the control: before the experiment – by 1.40, and 1.36 times; on Day 3 – by 1.22, and 1.26 times.

Clinical examinations were conducted on mongrel dogs to establish the effectiveness of the veterinary drug under study. The general clinical condition of dogs was examined; haematological and biochemical studies of dog blood were conducted under the conditions of applying an experimental drug to damaged skin areas. The clinical condition of the dogs of the control and experimental groups was determined daily throughout the experiment. Thermometry was performed, the condition of visible mucous membranes, skin and coat was examined. According to the results of clinical observations at the beginning of the experiment, it was established that dogs of Group I, intact animals, were clinically healthy, had visible mucous membranes of pale pink colour, moderately shiny, without damage, pigmented. The skin was smooth, medium thickness, elastic, without damage. The coat was thick, shiny, and close to the body. In dogs of Group II (control pathology), a skin wound process of various etiologies was recorded: acute inflammation, skin compaction, scratches, rashes. Dogs of this group were not treated with wound-healing drugs. In dogs of the III experimental group, clinical signs of skin inflammation in the extremities and muzzle were noted: redness, peeling and itching, cracks. The animals were depressed and did not consume food willingly. The drug under study was applied to the damaged areas of the skin of dogs in a thin layer three times a day. The results of the conducted planimetric studies are presented in Table 4.

Table 4. *Dynamics of changes in the area of wound surfaces (M±m) in dogs under conditions of skin damage*

Observation period, day	Wound surface area in observation groups, mm^2	
	Skin damage without correction	Application of the experimental drug
3	0.84±0.01	0.62±0.03*
5	0.78±0.02	0.32±0.02*
7	0.63±0.02	0.28±0.02*
9	0.45±0.03	0.19±0.01*
14	0.07±0.01	0.06±0.01*

Note: ** – this value differs statistically substantially (p<0.05) from the same value in the group of dogs with skin damage that were not treated*
Source: *compiled by the authors*

Dogs with skin damage that were not treated with a wound-healing ointment showed a slowdown in the wound-healing process. Notably, in dogs with skin damage, no wound infection was observed when using the ointment, and there was no exudation. The drug under study effectively reduced the wound surface area at all observation periods. The examined indicators were statistically substantially different from those in the group of dogs with skin wounds that were not treated. The results of the examination of a number of morphological parameters of the blood of dogs of control and experimental groups are given in Table 5.

Table 5. *Dynamics of morpho-physiological parameters of dog blood under the influence of the experimental drug (M±m)*

Experimental groups	Duration of the examination, days			
	Before application	3rd day	7th day	14th day
		Haemoglobin (HGB), g/dm^3		
I	126.44±1.08	127.52±1.17	126.47±1.25	127.84±1.25
II	124.51±1.12	125.218±1.11	125.96±1.12	126.11±1.21
III	123.15±1.47*	123.94±1.05*	124.11±1.45*	125.087±1.36
		Hematocrit (HCT), %		
I	36.99±1.24	37.16±1.12	37.87±1.15	37.28±1.16
II	37.54±1.19	38.11±0.15	37.18±1.19	36.83±1.11
III	41.23±1.55*	39.91±0.55*	37.84±1.23	36.28±1.09
		Red blood cells (RBC), 10^{12}/ dm^3		
I	8.21±0.24	8.54±0.16	8.54±0.83	9.18±0.65
II	8.32±0.78	9.01±0.32	8.37±0.12	8.15±0.32
III	8.53±0.63	9.13±0.47	8.28±0.19	8.37±0.96
		White blood cells (WBC), 10^9/dm^3		
I	9.87±0.32	9.56±0.34	9.57±0.37	9.67±0.95
II	12.47±0.92*	12.58±0.14*	10.85±0.89	9.99±0.57
III	14.26±0.53*	12.39±0.72*	11.81±1.17*	10.77±0.86

Notes: ** – p<0.05; ** – p<0.01 according to the indicator in intact control*
Source: *compiled by the authors*

The data provided in Table 5 shows that the haemoglobin concentration in dogs of Group III was substantially lower than the control: before the experiment – by 2.60%; on Day 3 – by 2.81%; on Day 7 – by 1.87%, respectively. In dogs of the III experimental group, a substantial (p<0.05) increase in the hematocrit value was established: before the start of the experiment – by 11.46%; on the 3rd day of the experiment – by 7.40%. The content of red blood cells in dogs of the experimental groups did not substantially differ from the indicators of the intact control group. Leukocytosis was established in dogs of groups II and III. Thus, before the start of the experiment, an increase in the number of white blood cells was recorded by 26.34% and 44.47%, respectively; on Day 3 – by 31.59% and 29.60%. On Day 7, an increased white blood cell count was established in dogs of Group III – by 23.41%. The results of the study of biochemical parameters in the blood serum of dogs are given in Table 6.

Table 6. *Dynamics of biochemical parameters in the blood serum of dogs under the influence of an experimental drug (M±m)*

Experimental groups	Duration of the examination, days			
	Before application	3rd day	7th day	14th day
		Total Protein, g/L		
I	78.22±0.32	77.67±0.52	77.23±1.16	79.58±1.53
II	82.69±1.24*	81.98±0.49*	79.46±0.55	78.54±1.11
III	83.64±0.51*	82.13±0.61*	81.35±0.82*	79.86±1.39
		C-reactive protein, mg/L		
I	3.98±0.67	4.23±0.16	4.46±0.21	4.51±0.25
II	4.79±0.24	5.09±0.32	4.97±0.37	4.36±0.51
III	5.42±0.36*	4.86±0.27	5.02±0.85	4.75±0.26
		ALAT, IU/L		
I	11.79±1.55	12.21±1.16	12.11±1.12	12.23±1.53

Table 6, Continued

Experimental groups	Duration of the examination, days			
	Before application	3rd day	7th day	14th day
II	11.46±1.81	11.93±1.37	12.19±1.71	11.17±1.26
III	12.03±1.25	11.05±1.52	11.51±1.32	12.04±1.45
ASAT, IU/L				
I	23.11±1.27	23.56±1.21	23.24±1.24	21.03±1.42
II	22.97±1.08	22.86±1.22	23.59±1.21	23.78±1.32
III	23.34±1.37	23.17±1.34	22.32±1.54	23.33±1.51
Urea, mmol/L				
I	5.53±0.56	5.86±0.42	5.94±0.22	5.67±0.26
II	6.87±0.81	6.19±0.51	5.63±0.21	5.48±0.26
III	7.73±0.17*	6.72±0.29*	6.59±0.43	6.58±0.15

Notes: ** – p<0.05; ** – p<0.01 according to the indicator in intact control*
Source: *compiled by the authors*

The results of the assessment presented in Table 6 indicate the dynamic development of an acute inflammatory process in the body of dogs that have had skin damage. Thus, the concentration of total protein in the blood serum of dogs was substantially higher than the control in dogs of groups II and III: before the experiment – by 5.71% and 6.93%, respectively; on Day 3 – by 5.54% and 5.74%; on Day 7 in dogs III – by 5.33%. The concentration of C-reactive protein in the blood was substantially higher (P<0.05) for intact control in dogs of Group III before the experiment – by 36.18%. The activity of the ALAT and ASAT enzymes in the blood of dogs of the experimental group did not substantially differ from the control.

A substantial increase in the urea content in the blood of dogs of Group III was established: before the experiment – by 39.78%; on Day 3 – by 14.68%. On Day 14 of the experiment, no substantial changes were recorded.

Clinical examinations were conducted on decorative rabbits to assess the effectiveness of the veterinary drug. The general clinical characteristics of rabbits were examined; haematological and biochemical examinations of rabbit blood were performed under the conditions of applying an experimental drug to damaged skin areas. The clinical condition of rabbits in the control and experimental groups was determined daily throughout the entire study period. Thermometry was performed, the condition of visible mucous membranes and skin was examined.

According to the results of clinical observations at the beginning of the experiment, it was identified that intact rabbits of Group I were clinically healthy, had visible mucous membranes of pale pink colour, moderately shiny, without damage, pigmented. The skin was smooth, thin, elastic, without damage. The coat was thick, shiny, and close to the body. In rabbits of Group II with control pathology, the wound process of the skin of various etiologies was recorded: acute inflammation, skin compaction, scratches, rashes. Rabbits of this group were not treated with wound-healing drugs. In rabbits of the III experimental group, clinical signs of skin inflammation in the muzzle and ears were noted: redness, peeling and itching, cracks. An experimental drug was applied to the damaged areas of the skin of rabbits in a thin layer three times a day. The results of the conducted planimetric studies are shown in Table 7.

Table 7. *Dynamics of changes in the area of wound surfaces (M±m) in decorative rabbits under conditions of skin damage*

Observation period, day	Wound surface area in observation groups, mm^2	
	Skin damage without correction	Application of the experimental drug
3	0.32±0.01	0.29±0.01*
5	0.29±0.01	0.21±0.01*
7	0.27±0.01	0.17±0.01*
9	0.15±0.02	0.12±0.005*
14	0.06±0.005	0.03±0.005*

Note: ** – this value differs statistically substantially (p<0.05) from the same value in the group of rabbits with skin damage that was not treated*
Source: *compiled by the authors*

On the 14th day of observation, the area of wound surfaces in rabbits that were treated with the drug under study decreased by 5.33 times. Decorative rabbits with skin damage that were not treated with the drug showed signs of wound infection. In rabbits with skin damage, no wound infection was observed when applying the ointment, and there was no exudation. The drug effectively reduced the area of the wound surface at all stages of the study. The indicators were statistically substantially different from those in the group of rabbits with skin wounds that were not treated. The results of the study of a number of morphological parameters of blood in rabbits of control and experimental groups are given in Table 8.

Table 8. *Dynamics of morpho-physiological parameters of rabbit blood under the influence of an experimental drug (M±m)*

Experimental groups	Duration of the examination, days			
	Before application	3rd day	7th day	14th day
		Haemoglobin (HGB), g/dm^3		
I	114.23±1.12	114.73±1.16	116.06±1.42	114.33±1.54
II	116.18±1.23	114.26±1.43	117.21±1.15	116.15±1.10
III	114.41±1.37	115.14±1.09	118.69±1.24	117.36±1.55
		Hematocrit (HCT), %		
I	35.18±1.11	35.23±1.32	34.59±1.22	35.12±1.11
II	36.42±1.06	34.99±1.29	35.11±1.36	34.99±1.08
III	35.76±1.43	36.05±1.44	34.57±1.20	35.45±1.33
		Red blood cells (RBC), 10^{12}/ dm^3		
I	7.16±0.98	7.97±0.67	7.62±0.93	7.27±0.68
II	7.52±0.63	7.83±0.55	7.35±0.38	7.66±0.85
III	7.97±0.46	8.12±0.74	7.68±0.54	7.16±0.63
		White blood cells (WBC), 10^9/dm^3		
I	7.38±0.84	7.64±0.51	7.82±1.43	7.21±1.53
II	8.35±0.60	8.17±0.43	7.94±0.31	7.72±0.96
III	9.17±0.54*	9.34±0.60*	8.76±1.12	8.22±0.90

Notes: ** – p<0.05; ** – p<0.01 according to the indicator in intact control*
Source: *compiled by the authors*

Analysis of the obtained data presented in Table 8 showed a substantial increase in the level of white blood cells in the blood of ornamental rabbits with a wound skin process (Group III). Thus, before the start of the experiment, the content of white blood cells exceeded the control by 1.24 times; on Day 3 – by 1.22 times. Notably, other morpho-physiological blood parameters in rabbits were within the physiological norm. The results of the examination of biochemical parameters in the blood serum of rabbits are given in Table 9.

Table 9. *Dynamics of biochemical parameters in the blood serum of rabbits under the influence of the experimental drug (M±m)*

Experimental groups	Duration of the examination, days			
	Before application	3rd day	7th day	14th day
		Total Protein, g/L		
I	64.62±1.48	65.78±1.97	65.23±1.13	66.63±1.58
II	72.54±1.21**	72.38±1.46**	71.42±0.93**	69.18±1.10
III	71.89±0.98**	71.73±1.32**	70.61±1.34**	69.36±1.17
		C-reactive protein, mg/L		
I	3.78±0.57	3.99±0.26	3.78±0.14	3.54±0.96
II	4.98±0.26*	5.12±0.21*	3.97±0.17	4.56±1.44

Table 9, Continued

Experimental groups	Duration of the examination, days			
	Before application	3rd day	7th day	14th day
III	5.34±0.38*	4.84±0.37*	4.23±0.56	4.16±1.20
		ALAT, IU/L		
I	32.21±1.56	31.74±1.85	30.59±1.15	31.15±1.21
II	31.51±1.24	30.27±1.12	31.75±1.32	30.52±1.14
III	32.96±1.68	31.89±1.36	32.51±1.10	32.87±1.04
		ASAT, IU/L		
I	43.14±1.55	44.52±1.44	42.24±1.69	43.26±1.38
II	42.46±1.48	43.85±1.26	43.22±1.27	42.32±1.85
III	43.14±1.37	44.26±1.48	42.97±1.51	43.17±1.37
		Urea, mmol/L		
I	3.11±0.21	3.26±0.15	3.14±0.15	3.47±0.19
II	4.52±0.26*	4.38±0.19*	4.20±0.18	4.11±0.21
III	4.78±0.16*	4.64±0.23*	4.55±0.16	3.99±0.15

Notes: ** – p<0.05; ** – p<0.01 according to the indicator in intact control*
Source: *compiled by the authors*

Analysis of the obtained data (Table 9) showed a statistically substantial increase in the total protein content (at the level of p<0.01) in the blood serum of rabbits of groups II and III: before the experiment – by 12.26%, and 11.25%, respectively; on Day 3 – by 10.03% and 9.04%, respectively; on Day 7 – by 9.49% and 8.25%, respectively. On the 14th day of the experiment, no substantial deviations were established.

A substantial (p<0.05) increase in the concentration of CRP in the blood of rabbits of groups II and III was established: before the start of the experiment – by 31.75% and 41.27%, respectively; on the 3rd day of the experiment – by 28.32% and 21.30%, respectively. The activity of the ALAR and ASAT enzymes in the blood of rabbits of the experimental group did not substantially differ from the control. The urea content in the blood serum of rabbits of groups II and III was substantially (p<0.05) higher than the control: before the experiment – by 45.34% and 53.69%; on Day 3 – by 48.16% and 42.33%, respectively. On days 7 and 14, deviations of this indicator were within the physiological norm.

As a result of the research on the effectiveness of the veterinary drug with the active substance dexpanthenol, an optimal pharmacological effect was achieved by the authors, namely, a pronounced anti-inflammatory and wound-healing effect of the drug: it promotes healing, activation of reparative processes (granulation and epithelialisation) of the skin and mucous membranes, and prevents bacterial complications. The drug effectively reduced the area of the wound surface at all stages of the study.

Saliy *et al.* (2022), based on a marketing analysis of the pharmaceutical market of Ukraine of medicines under pressure for veterinary practice, identified that the largest segment belongs to the D03 group "Products for the treatment of wounds and ulcerative lesions" – 13.79%, including 12.07% of dexpanthenol-based drugs.

Researchers (Motatabzadeh & Abtahi Froushani, 2020; Barrionuevo-Gonzalez *et al.,* 2021; Karahan *et al.,* 2021) agreed that dexpanthenol-based preparations, used to achieve an effective therapeutic effect on skin pathologies, in particular, wounds, deserve special attention. Being absorbed into the cells of the stratum corneum of the skin, dexpanthenol is rapidly converted to pantothenic acid, thereby contributing to the restoration and regeneration of damaged skin layers. Its effect is enhanced in combination with decamethoxin, which has a bactericidal effect. Rodin (2019), based on clinical studies, proved a high therapeutic effect of decamethoxin for skin wounds with bacterial complications. Bororova (2021) notes its antimicrobial effect against Gram-positive (*Staphylococci, Streptococci, Pneumococci*) and Gram-negative (meningococci, gonococci) cocci, *Corynebacteria, Enterobacteria, Pseudomonas*, protozoa, dermatophytes, yeast-like fungi of the *Candida* genus, chlamydia, and viruses.

The obtained data correlate with the data of other researchers. Boehm *et al.* (2021) prove that a local approach (the use of ointment) is the best treatment option for focal surface bacterial infections to prevent the development of acquired resistance to microbial strains. Ogden *et al.* (2021) proved the therapeutic effect of dexpanthenol on sciatic nerve compression injury in an experiment on Wistar albino rats. They noted that administration of 50 mg/kg dexpanthenol intraperitoneally in combination with 10 mg/kg thymoquinone intraperitoneally once a day for a week.

Data obtained by Sezgin *et al.* (2019) confirms the hypothesis that the use of dexpanthenol contributes to

the reduction of wound surface during treatment. In experiments on rats, the researchers proved that the local use containing a combination of dexpanthenol, silbiol, undecylenic acid, and lidocaine decreased the wound surface area on the 7th day of treatment from 5.07 to 1.42 mm^2 in the test group. As in this experiment, the full therapeutic effect was observed on the 14th day of treatment. The data obtained is also consistent with the results of the group of researchers (Küba *et al.,* 2021). During an experimental assessment of dexpanthenol (5% ointment) efficacy on rats, the greatest reduction in wound size in the late postoperative phase was noted: from day 10 to day 14. Ulger *et al.* (2014), comparing the effectiveness of 5% dexpanthenol ointment and 5% nebivolol ointment for wound healing, based on experimental modelling of the wound process in rats, concluded that no substantial changes in the healing process were recorded between the examined ointments. However, a therapeutic effect was observed only on the 21st day, which is 6 days longer compared to this experiment. This may be due to a 2-fold lower concentration of the active substance compared to the experimental sample of the ointment in this study.

Therewith, Gültekin *et al.* (2020) do not recognise the therapeutic effect of dexpanthenol. During the experiment on a monkey, they did not observe any changes in wound size and epithelialisation when using a 4-component ointment made from a mixture of dexpanthenol (5% ointment), nitrofurazone ointment (0.2%), zinc oxide (20%), and Centella asiatica (1%) twice a day for local treatment. However, unlike this experiment, the authors additionally used intramuscular administration of 5% diluted dexpanthenol (500 mg/2 ml ampoule) 1 time for 10 days. The lack of therapeutic effect may be due to the antagonistic effect of the simultaneous use of dexpanthenol and zinc oxide. Ultimately, the latter in the experimental 20% concentration shows an astringent effect, due to which the rate and level of dexpanthenol adsorption are disrupted.

CONCLUSIONS

Skin inflammations in small pets of various origins are characterised by intense itching of the skin and are complicated by bacterial microflora. In the absence of treatment with a wound-healing ointment, the wound-healing process slows down.

Changes in morpho-physiological parameters of blood (reduced haemoglobin content, increased hematocrit value, urea content, leukocytosis) in experimental animals with signs of a wound process before the start of the experiment indicate the development of endogenous intoxication syndrome. Analysing biochemical parameters in the blood serum of animals with skin damage, a substantial increase in the concentration of total and C-reactive protein was noted.

In experimental animals with skin damage, when using a dexpanthenol-based ointment (10 mg per 1 ml), no signs of infection of wounds with microflora and exudation were observed. The drug under study effectively reduced the wound surface area in experimental animals during the course of treatment: in cats – by 95.83%, in dogs – by 92.86%, and in decorative rabbits – by 90.63%.

On the 14th day of treatment, the number of white blood cells and C-reactive protein in experimental animals were within the physiological norm – in cats – (9.67±0.54) x $10^9/dm^3$ 4.94±0.24 mg/L, in dogs – (10.77±0.86) x $10^9/dm^3$ and 4.75±0.26 mg/L, in rabbits – (8.22±0.90) x $10^9/dm^3$ and 4.16±1.20 mg/L, respectively. There is no substantial difference between experimental and intact animals.

It was identified that the examined drug is well tolerated by sick animals, does not cause adverse reactions, does not have a negative effect on healthy tissues, and has a positive effect on the dynamics of haematological and biochemical parameters of the blood of experimental animals. The experimental drug can be recommended for use in clinical veterinary practice as an anti-inflammatory and wound-healing agent for small pets.

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CONFLICT OF INTEREST

The authors declare no conflict of interest.

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Лікування домашніх тварин препаратом з діючою речовиною декспантенол при ранових процесах

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Abstract. Шкіра тварин є комплексним органом, який безпосередньо сприймає вплив зовнішнього середовища і виконує бар'єрно-захисну функцію, а також допомагає підтримувати рівновагу внутрішнього середовища організму. Порушення кожного з рівнів захисної системи призводить до розвитку запальних захворювань шкіри. Лікування рани залишаються однією з найактуальніших наукових та практичних проблем сучасної ветеринарної медицини. Ряд науковців проводить пошук та розробку нових ветеринарних препаратів для лікування ран різної етіології у дрібних домашніх тварин, однак застосування лікарських засобів часто викликає побічні реакції з боку шкіри. Метою цієї роботи була оцінка ефективності застосування ветеринарного препарату (мазь) при лікуванні ран у домашніх тварин (собаки, коти, кролі). В роботі використано стандартні клінічні, гематологічні та біохімічні методи дослідження. У дослідженнях застосовували препарат з діючою речовиною декспантенол та допоміжними речовинами декаметоксин, масло вазелінове, емульгатор, гліцерин, метилпарабен, пропілпарабен, вода очищена. Досліджуваний препарат ефективно зменшував площу ранової поверхні на усіх термінах спостереження. Доведено, що за використання мазі на основі декспантенолу (10 %) повний ранозагоювальний ефект у дослідних тварин спостерігався на 14-ту добу лікування: площа ранових поверхонь зменшувалась на 93,1±1,51 %. Досліджувані показники статистично достовірно відрізнялися від аналогічних у групі нелікованих тварин із ранами шкіри. Вивчено загальний клінічний стан домашніх тварин, проведено гематологічні та біохімічні дослідження крові тварин за умов нанесення на пошкоджені ділянки шкіри дослідного препарату. У тварин із пошкодженням шкіри без лікування спостерігали динамічний розвиток гострого запального процесу в організмі, розвиток синдрому ендогенної інтоксикації, ознаки інфікування ран, виражену ексудацію та сповільнення контракції. Розроблений ветеринарний препарат з діючою речовиною декспантенол одночасно проявляє виражену протизапальну і ранозагоювальну дію та забезпечує швидкий лікувальний ефект при раньових процесах у дрібних домашніх тварин

Keywords: собаки; коти; кролі; рани; декспантенол; морфо-фізіологічні показники крові; сироватка крові