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WOUND HEALING EFFECT OF “PROLIDOXID” AND “DEXPANTHENOL WITH CERAMIDES”: A COMPARATIVE STUDY BASED ON THE MODEL OF CHEMICAL BURNS WITH EXPRESSED ALTERATIVE SKIN PROCESSES

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Pharmacotherapy of chemical skin injuries remains an urgent issue today due to its serious health consequences and possible development of complications. Topical treatment is one of the most effective methods of wound treatment using hydrophilic ointments and creams. For now, range of hydrophilic medicinal products with a broad spectrum of action is limited. That is why a search and development of new hydrophilic ointments and creams remains an urgent challenge.

The aim. *The aim of this research was to study effectiveness of ointment “Prolidoxid” and cream “Dexpanthenol with ceramides” on the experimental chemical burn model in rats.*

Materials and methods. *Wound healing effect of ointment “Prolidoxid” and cream “Dexpanthenol with ceramides” was proved by the study of planimetric and hematological parameters on the model of acetic acid burns in rats.*

Results. *Using animal model of chemical burns it was found that ointment “Prolidoxid” and cream “Dexpanthenol with ceramides” accelerate wound healing on Day 5 and Day 6, consequently, compared to untreated control animals, but in comparison with the action of reference medicine wounds were healed two days faster. Hematological parameters showed that studied medicines inhibit inflammation and reactivate blood rheological properties.*

Conclusions. *The results suggest that effectiveness of cream “Dexpanthenol with ceramides” is higher than for one-component cream “Dexpanthenol”, but ointment “Prolidoxid” exceeds therapeutic action of ointment “Wundahyl” as reported by hematological and planimetric parameters*

Keywords: *chemical wounds, dexpanthenol, ceramides, propolis, lidocaine, wound-healing effect, anti-inflammatory effect, healing area, cream, ointment*

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1. Introduction

Wound healing process is an urgent problem of modern medicine. Alteration of epithelium and connective tissues is relevant to impaired ability of human body to provide protection from different damaging external factors [1].

According to the WHO data, burns are a serious public health problem. An estimated 180 000 deaths occur each year from fires alone [2, 3].

These injuries to the skin or other organic tissue primarily caused by heat or due to radiation, radioactivity, electricity, friction or contact with chemicals [4, 5].

Chemical burn is a skin lesion caused by the contact with an irritant, such as an acid or a base [6]. Chemical burns represent 3–5 % of all skin burns [7]. Despite the relatively small number of chemical burns, they have caused 30 % of death associated with burns [8, 9]. More than 25 000 chemicals are commonly used in industrial and domestic conditions [10]. Variety of chemical substances results in a wide range of clinical consequences [11].

Treatment of chemical burn is focused on the fast wound healing process [12, 13]. For this reason, in chemical inflammatory-necrotic skin lesions, along with general aggressive approaches, it would make sense to apply topical medications that repair skin barrier function and stimulate reparation [14, 15].

The aim of this study was to study wound healing effect of ointment “Prolidoxid” and cream “Dexpanthenol with ceramides” on the *experimental model* for chemical burns in rats.

2. Planning (methodology) of research

New combinations of topical medications (ointment “Prolidoxid” and cream “Dexpanthenol with ceramides”) has been the subject of the research.

It is well known from literature [16–18] that wound healing effect caused by a set of different criteria. One of the most important criteria in wound healing is an inhibition of inflammation and normalization of blood rheological properties. In this context it is worthwhile investigating of therapeutic action of ointment “Prolidox-

id” and cream “Dexpanthenol with ceramides” on the model of chemical burn with expressed alterative skin processes. This model was chosen on the following criteria: repeatability, adequacy of experimental pathology of chemical injuries in rats that are comparable with similar processes in humans. This lets us to extrapolate outcomes obtained in the animal experiment to the clinical practice.

3. Materials and methods

Preclinical studies of drugs were carried out at the Central research laboratory of the National University of Pharmacy in 2016.

3. 1. Study subjects

The technology, the composition of the active ingredients and the ointment base of the new drugs “Prolidoxid” and “Dexpanthenol with ceramides” were developed by scientists from the National University of Pharmacy [19–21].

Ointment “Prolidoxid” contains biologically-active substance propolis that has antimicrobial, anti-inflammatory, reparative action; and local anesthetic – lidocaine. High margin of activity of active substances and hydrophilic PEO base (PEO-400 and PEO-1500 at the ratio 4:1) with evident osmotic activity (340 %) comply the requirements for topical treatment of wounds and partial-thickness skin burns [19].

Ointment “Wundahyl”, produced by “AIM” (Kharkiv), was chosen as reference medicine. This ointment has anti-inflammatory, reparative action, speeds up regenerative process of epidermis; stimulates growth and maturation of granulation tissue in the region of traumatic defect. It is assigned for the treatment of non-healing wounds (inflamed, infected, postoperative). Ointment “Wundahyl” contains: Tinctura Sophorae japonicae – 3.0 g, Tinctura Potentillae – 2.0 g, Tinctura Millefolii – 2.0 g, Tinctura Propolisi – 5.0 g, Carophyllum – 3.0 g per 100 g. The base of medicinal product is pork fat (interior) and anhydrous lanolin. Disadvantage of this medicine is only its hydrophobic base.

Cream “Dexpanthenol with ceramides” contains dexpanthenol 5 g, that has wound healing, anti-inflammatory and immunomodulatory effect; ceramides LS 0.2 g and emulsion base of I type with hydrophilic properties up to 100 g. Ceramides have specific biological action in the top levels of epidermis improving its proliferation and barrier function, and normalizing skin moisture balance. “*Dexpanthenol 5 %*” (“*Bayer Consumer Care AG*”, Switzerland) was chosen as reference medicine [20, 21].

It should be noted, that one-component wound-healing preparations on a hydrophobic ointment base predominate on the Ukrainian pharmaceutical market. Such ointments are methyluracil, gentamicin, decamethoxin, calendula, tetracyclin and others. One-component topical preparations have a narrow spectrum of pharmacological activity that is insufficient for effective wound healing. Healing of wounds by mono-preparations needs simultaneous use of several medicinal products that creates a nuisance and comes at a price.

It has to be said that hydrophobic base has disadvantages such as: inhibition of diffusion, drug release as well as it interferes with skin function (breath, emission).

Vaseline-lanolin or pork fat as an ingredient in ointment base inhibits mixing of active ingredients with wound exudate and its adsorption. In addition, hydrophobic ointment base is an essential barrier for releasing of active ingredients from medicinal product and their penetration into the injury (bioavailability). This causes deterioration in condition of the wound and increases the period of its healing [22].

In comparison with cream “Dexpanthenol”, developed cream “Dexpanthenol with ceramides” has advantage that includes broadening of pharmacological action because of addition of ceramides and administration of hydrophilic base. Ceramides show proliferative and moisturizing action as well as repair protective properties of skin. Hydrophilic base promotes releasing of active ingredients from dosage form and its distribution on the skin surface. Therefore, such base stimulates reparative processes in the wound.

Reference medicine “Dexpanthenol” is a multi-component medicinal product on a hydrophobic base that decreases bioavailability of active ingredient and increases healing times.

Compared to ointment “Wundahyl”, ointment “Prolidoxid” exhibits antimicrobial, anti-inflammatory, reparative and analgesic activity due to the presence of two components and hydrophilic base with evident osmotic effect. The active ingredients of the ointment are phenolic hydrophobic drug propolis (FGPP) and local anesthetic lidocaine. The main components of propolis are: phenolcarboxylic acids, hydroxy coumarins, flavones, flavonols (81.33 % of total mass), that exhibit antioxidant properties and are able to maintain stability of cellular membranes affected by increased lipid peroxidation in the course of wound healing.

“Prolidoxid” is a composition of two polyethylene oxides (PEO) – PEO-400 and PEO-1500 at the ratio 8:2 that complies the requirements for topical treatment of wounds and superficial skin burns in the first phase of WP and in transition to the second phase when there are rests of purulonecrotic fragments and reparation process begins.

High bioavailability of active ingredients and a wide spectrum of pharmacological activity of “Prolidoxid” stimulate reparative processes in the wound significantly. Although reference drug “Wundahyl” contains 5 active ingredients it was created on fat base with hydrophobic properties that decreases bioavailability of active components and rises time of wound healing.

3. 2. Research methods

During the study of therapeutic action of investigated medicinal products chemical wounds with expressed alterative processes of skin and subcutaneous tissue were imitated by the subcutaneous introduction of 0.5 mL of 9 % acetic acid solution that caused inflammation at the injection site. Dextran solution in the dose of 300 mg per kg of animal body weight was abdominally injected to increase rats' responsiveness [22].

The *effectiveness* of ointment “Prolidoxid” on healing of wounds has been studied on the chemical burn model in 27 rats. The body weights of rats ranged from 150 to 170 g (I set of experiments). Treatment was started on *Day 8* after chemical injury, when skin ulcers with

maximal surface appeared. Animals were divided on 3 groups (n=9): group of control pathology (group 1 – untreated animals), group 2 – “Prolidoxid”-treated animals and group 3 – “Wundahyl”-treated animals. Second set of experiments was performed in 18 rats *weighed* an average of 180–210 g. Animals were divided also on 3 groups (n=6): group 1 – control pathology (untreated animals); group 2 – animals were treated by the cream “Dexpanthenol with ceramides”, group 3 – animals were treated by the cream “Dexpanthenol”. Topical medications were applied with sterile spatulas on the surface of aseptic ulcer bis in day at the *conditionally therapeutic dose* 20 mg/cm². Treatment was continued till complete cicatrization (27 days in I set of experiments, 21 days in the II set of experiments). Skin healing area (S) and percentage of rats with healed wounds were main characteristics of wound-healing effect of medicinal products. Area of healing (S, mm²) was calculated according to a formula:

$$S = S_{in} - S_{exp.}$$

where S_{in} – initial area of wound (before treatment), mm²; S_{exp} – area of wound at the day of measurement, mm².

Intensity of irritation was estimated according the values of peripheral blood in rats: level of hemoglobin, leucocytes and erythrocytes, clotting time, leukogram [19]. Hematological parameters were registered 3 times: before experiment (raw data), on Day 4 and Day 15 of treatment.

Research was conducted in the central research laboratory of National University of Pharmacy (NUPh). This laboratory was certified by the State expert center MOH of Ukraine in accordance with generally accepted bioethical norms and in compliance of corresponding international regulations relating to the conducting of experimental research, that is also certified by the findings of NUPh bioethics commission (protocol No. 2 of 19.02.2016). All painful procedures were performed under the *thiopental anaesthesia* (40 mg/kg).

3. 3. Statistical analysis

All research results were processed statistically. *Statistics were calculated* with the help of *standard computer programs*: «Statistica 4.3» and «Statistica 6.0». The obtained results were treated based on one-way ANOVA using the Mann-Whitney and Wilcoxon criteria at a significance level of $p < 0.05$.

4. Results

Open ulcerous skin defects with apparent inflammatory process of adjacent tissues and rejection of secondary crustlike surface of a healing skin lesion were produced in *rats* on the place of injection of phlogogen after subcutaneous injection of acetic acid. Ulcers were clean without secondary infection and purulonecrotic processes. A surface area of skin ulcers ranged from 204.78 mm² to 307.0 mm² (Table 1).

Table 1

Effect of studied medicinal products on planimetric parameters on the model of chemical skin burn in rats, ($\bar{X} \pm S_{\bar{x}}$)

Healing area, days of treatment, mm ²	Study groups		
	I set of experiments, n=9		
	Control pathology	Ointment “Prolidoxid”	Ointment “Wundahyl”
S ₄	69.56±2.55	84.92±4.36*	118.8±5.80*
S ₇	99.50±9.43	127.1±9.79	145.33±13.25
S ₉	122.81±10.87	149.28±10.63	188.72±18.01
S ₁₃	145.60±12.55	170.45±11.87	193.55±19.67
S ₁₅	158.40±8.87	186.78±7.05*	198.33±12.36*
S ₁₉	178.80±7.95	201.27±6.30*	206.5±11.95
S ₂₂	206.5±14.43	204.78±36.81 Complete healing	223.5±13.60
S ₂₄	255.83±30.99	–	227.22±19.67 Complete healing
S ₂₇	307.0±43.35 Complete healing	–	–
Parameter	II set of experiments, n = 6		
	Control pathology	Cream “Dexpanthenol with ceramides”	Cream “Dexpanthenol”
S ₄	43.50±6.34	72.17±9.21*	55.33±2.65
S ₇	76.00±6.47	110.83±9.25*	100.67±7.27*
S ₉	94.83±5.97	181.50±4.77*/**	129.33±5.73*
S ₁₃	167.83±10.98	271.50±9.93*	260.00±6.56*
S ₁₅	217.17±14.91	289.17±8.21* Complete healing	280.00±7.33*
S ₁₇	233.83±13.03	–	287.17±8.43* Complete healing
S ₂₁	263.83±14.94 Complete healing	–	–

Note: * – differences are likely in relation to the control group, $p < 0.05$; ** – differences are likely in relation to reference medicine; n – number of animals

Further studies of wound healing process have demonstrated that in four days after the initiation of treatment the *formation of granulation tissue* and wound contraction was observed. Wound contraction *reduces* the surface *area* of the wound on Day 4, Day 15 and Day 19 of treatment with ointment “Prolidoxid”, but after application of reference medicine this reduction was observed on Day 4 and Day 15. Starting from Day 15 till Day 21 percentage of animals with scars after treatment with “Prolidoxid” increased from 22.2 % (2 rats) to 88.9 % (8 rats). At Day 22 all animals from this group (100 %) had scarring ulcers while in the group of control pathology healing was observed only in 55.6 % of rats, but in the group of “Wundahyl”-treated animals healing was observed in 77.8 % of rats. Complete healing of ulcers in experimental rats treated with “Wundahyl” was observed on Day 24, but in the group of control pathology it was only on Day 27.

After treatment of skin ulcers with cream “Dexpanthenol with ceramides” statistically significant healing area was observed on Day 4, Day 7, Day 9, Day 13, Day 15, but after application of cream “Dexpanthenol” it was observed on Day 7, Day 9, Day 13, Day 15, Day 17.

Starting from Day 11 till Day 13 percentage of animals with scars after treatment with “Dexpanthenol with ceramides” increased from 16.6 % (1 rat) to 48.8 % (3 rats). At Day 15 all animals (100 %) had scarring ulcers while in the group of “Dexpanthenol”-treated animals healing was observed in 66.4 % of rats. Complete healing of ulcers in experimental rats treated with “Dexpanthenol” was observed on Day 17 but in the group of control pathology it was only on Day 21.

Study of hematological parameters in rats of group 1 (untreated animals) proved the development of inflammatory process, as evidenced by a statistically significant decrease in hemoglobin level (average 1.3 times), in erythrocytes level (1.4 times) and in clotting time (1.2 times), as well as a statistically significant increase in the level of white blood cells (1.7 times) on Day 4 and Day 15 (1.6 times) compared with basic data (Table 2).

The *leukogram* shows a neutropenia (decrease in the level of banded neutrophils by half), a slight increase in white blood count on Day 4 (by 1.1 times) and its decrease on Day 15 (by 1.1 times), and rise of count of monocytes on Day 4 (by 2.5 times) and on Day 15 (by 2.6 times).

Table 2

Effect of investigated medicinal products on hematological parameters on the model of chemical skin burn in rats, ($\bar{X} \pm S_x$)

Parameters	Days of treatment	Study groups		
		I set of experiments, n=9		
		Control pathology	Ointment “Prolidoxid”	Ointment “Wundahyl”
1	2	3	4	5
Clotting time, s	Initial data	204.00±10.68	193.40±11.4	207.00±3.94
	Day 4	166.67±4.29**	224.00±12.82*	209.00±26.15
	Day 15	127.67±11.68**	158.33±16.90	124.67±5.36**
Hemoglobin, g/L	Initial data	146.48±3.20	153.88±5.43	139.00±2.34
	Day 4	114.93±6.08**	127.67±1.45**	121.67±2.73**
	Day 15	135.33±2.36**	147.23±4.23	131.47±6.28
Erythrocytes, 10 ¹² /L	Initial data	6.08±0.23	5.71±0.27	5.35±0.39
	Day 4	4.27±0.22**	5.20±0.08	5.19±0.08
	Day 15	5.72±0.23	5.93±0.16	5.30±0.17
Leucocytes, 10 ⁹ /L	Initial data	10.92±0.90	12.18±0.53	12.26±0.34
	Day 4	18.13±1.56**	15.47±0.64**	15.47±0.83**
	Day 15	17.77±0.95**	13.73±0.74*	14.20±0.79*
Leukogram, %:				
Banded neutrophils	Initial data	2.00±0.32	2.00±0.32	1.80±0.37
	Day 4	1.33±0.33	2.00±0.58	1.33±0.33
	Day 15	2.67±0.33	2.67±0.33	1.67±0.33
Segmentonuclear neutrophils	Initial data	31.20±3.17	31.80±1.36	36.60±2.62
	Day 4	23.67±2.33	23.00±2.08	33.33±2.33*
	Day 15	31.67±5.81	23.67±4.33	42.67±3.48
Lymphocytes	Initial data	61.00±3.74	59.20±0.86	54.20±3.48
	Day 4	64.67±2.40	65.67±2.91	59.00±2.52
	Day 15	55.00±6.56	63.00±3.79	49.00±1.15
Monocytes	Initial data	3.80±0.73	5.40±0.81	5.60±1.03
	Day 4	9.33±1.76**	9.33±0.67	10.33±0.33**
	Day 15	9.67±2.19**	10.00±1.00**	9.00±1.15**

Continuation of Table 2

1	2	3	4	5
II set of experiments, n=6				
Parameters	Days of treatment	Control pathology	Cream "Dexpanthenol with ceramides"	Cream "Dexpanthenol"
Clotting time, s	Initial data	198.33±9.36	203.40±7.33	201.33±8.60
	Day 4	160.33±5.66**	181.00±11.67*	186.00±6.67*
	Day 15	139.16±10.80**	169.33±17.33	178.67±8.33
Hemoglobin, g/L	Initial data	153.33±5.67	146.33±4.36	149.60±2.34
	Day 4	107.67±7.16**	118.81±1.45**	112.33±3.43**
	Day 15	131.93±3.67**	142.53±2.67	135.24±5.86
Erythrocytes, 10 ¹² /L	Initial data	5.98±0.17	6.01±0.13	5.46±0.27
	Day 4	4.48±0.26**	5.63±0.16	5.06±0.12
	Day 15	5.24±0.19	5.87±0.08	5.53±0.16
Leucocytes, 10 ⁹ /L	Initial data	9.89±0.67	10.29±0.33	10.86±0.24
	Day 4	16.33±1.56**	14.73±0.64**	15.14±0.76**
	Day 15	15.76±0.69**	11.47±0.74*	13.50±0.67*
Leukogram, %:				
Banded neutrophils	Initial data	2.33±0.29	2.63±0.29	1.91±0.31
	Day 4	1.27±0.31	2.09±0.36	1.53±0.26
	Day 15	2.46±0.36	2.84±0.36	1.86±0.29
Segmentonuclear neutrophils	Initial data	32.60±2.67	34.00±1.60	35.16±2.26
	Day 4	22.97±1.83	32.00±1.93	31.13±3.10
	Day 15	30.86±4.97	28.97±3.87	28.67±2.67
Lymphocytes	Initial data	60.77±2.94	58.40±0.67	57.60±3.76
	Day 4	65.78±2.67	59.86±2.31	59.40±2.33
	Day 15	57.33±6.33	61.00±3.33	61.37±1.09
Monocytes	Initial data	4.30±0.86	4.97±0.67	5.33±0.93
	Day 4	9.98±1.53**	6.05±0.73	8.94±0.36
	Day 15	9.35±2.06**	7.19±0.33	8.01±1.15

Note: * – differences are likely in relation to the control group, $p < 0.05$; ** – differences are likely in relation to initial data, $p < 0.05$

The dynamics of hematological parameters in the groups of animals that were treated with ointments and creams was similar but it differed from the group of untreated animals. Such difference was evidence of the fact that investigated medicines have marked anti-inflammatory activity. In the group of treated animals on Day 4 the level of erythrocytes did not change and on Day 15 leukocytosis was not observed compared to the group of untreated animals. In the groups of animals that were treated with "Prolidoxid", "Dexpanthenol with ceramides" and "Dexpanthenol" statistically significant decrease in clotting time was observed on Day 4 (by 1.2 times). This fact evidences improvement of blood rheology and activation of reparative processes in contrast to group of untreated animals (control pathology).

The clotting time decrease (by 1.7 times) observed for animals treated with ointment "Wundehyl". It is can be associated with an increase in platelet count and, consequently, with some slowdown in the healing process in this group.

The analysis of differential white blood cell count showed that chemical burns display severe inflammation as evidenced by an increased number of monocytes in the blood of untreated animals (in 1.3 times) and absence of change in the number of white blood cells compared to initial data. After treatment with creams "Dexpanthenol with ceramides" and "Dexpanthenol" statistically significant deviation in a level of monocytes was not observed compared to raw data as opposed to the treatment with ointments "Prolidoxid" and "Wundehyl" where a statisti-

cally significant difference compared to the control group was reported (by 1.7 times).

5. Discussion

Dynamic processes that occur as a response on the chemical injury includes skin necrosis (ulcers) and stress reaction of blood system, development of nonspecific inflammatory response followed by structural metabolic disorders [9].

According to the results of planimetric research on the chemical wound model it was found that investigated medicinal products promote healing of skin ulcers. In order of its wound-healing effect these medications can be arranged in the following sequence: cream "Dexpanthenol with ceramides" (it decreased wound healing by 6 days), ointment "Prolidoxid" (it decreased wound healing by 5 days), cream "Dexpanthenol" (it decreased wound healing by 4 days), cream "Wundehyl" (it decreased wound healing by 3 days) compared to group of control pathology.

Hematological research showed that considerable reduction in clotting time in the group of control pathology can confirm the growth of activity of platelet system. Decrease in the level of hemoglobin and erythrocytes proved the development of anemic processes, which effect delay of the healing process of ulcers [23]. Hematological parameters were almost normalized after the treatment with investigated creams and ointments that support wound-healing effect. Leukogram data showed

that irritation process was short-term in all groups of animals and did not become chronic. Probably the development of inflammation was caused by the activation of lymphocytic-monocytic series [23], neutrophilic series did not cause inflammatory response in animals that supports high immune response in rat body. It should be noted that application of creams with dexpanthenol *promoted* inhibition of inflammation as confirmed by a *normalization of monocyte count*. Increased level of monocytes have been reported in rats on day 15 following application of ointments “Prolidoxid” and “Wundahyl”. Within this framework, we can make a conclusion about the development of moderate inflammation and absence of complete healing as it appears from planimetric study.

Reparative action of ointment “Prolidoxid” was higher than the reference drug ointment “Wundahyl” due to the presence of phenolic hydrophobic drug propolis (PHDP) that possess antioxidant properties. These antioxidants are able to intercept free radicals, form chelate complexes with reactive ions, suppress activity of radical generating enzymes and that's why protect lipids, nucleic acids and other vital cellular components from oxidation and destruction.

In addition, phenolic compounds in the composition of PHDP are able to stimulate reparative processes affecting the macrophage chain of inflammatory and reparative response. Wherein chemotaxis of macrophages intensifies, proliferation and differentiation of fibroblasts occurs. During proliferation, the wound is ‘rebuilt’ with new granulation tissue. Polyethylene oxide ointment base of “Prolidoxid” potentiates the antimicrobial activity of PHDP and boosts bioavailability of active ingredients.

Greater reparative activity of cream “Dexpanthenol with ceramides” in contrast to the activity of cream “Dexpanthenol” is caused by the addition of ceramides in its composition. Ceramides hydrate skin, prevent excessive drying of tissues and deepening of necrosis, facilitate transport of growth promoting substances (epidermal, fibroblastic), neutrophils, lymphocytes, monocytes and others cells, fastening wound healing. Maintenance of skin barrier function is vital to mitigate the skin's susceptibility to irritants, allergens, and microbes. Hydrophilic base of developed cream improves bioavailability of active ingredients.

Difference in pharmacological effects of investigated medicinal products is attributable to its different therapeutic action. When tissue is damaged the need for structural (proteins, carbohydrates, lipids, water), energetic and nutritional (vitamins, especially pantothenic acid) material will grow, because all this biologically active compounds take part in a variety of biochemical processes, promoting them and restoring damaged tissues.

Consistent with the literature data, *dexpanthenol* is well *absorbed* when *applied* topically to the *skin* and *rapidly* converted to *pantothenic acid*, that plays an important role in cellular metabolism (*synthesis* of *N-acetylglucosamines* and *mucopolysaccharides*, *phospholipid metabolism* etc.) [17]. It is known that *pantothenic acid*

accelerates cell division along with *restorative properties* due to which adds *strength* to *collagen fibers* that *restores* skin defects and it *has* also been shown to *have* an *anti-inflammatory effect* on burns [17]. Ceramides are a structurally complicated and heterogeneous group of sphingolipids that play a key function in structuring and preserving the skin water permeability barrier. It should be emphasized that *skin hydration is one of the promising approaches for optimization of regenerative processes because it prevents excessive drying* out of the wound and *deepening of necrosis averting the formation of cicatricial deformities* [1]. Additionally, hydrophilic base of cream does not affect the bioavailability of *dexpanthenol as evidenced by marked therapeutic action*.

“Prolidoxid” ointment shows a marked *reparative effect probably due to* the presence of phenolic compounds that are *capable of intercepting the free radicals*. *Phenolic antioxidants can inhibit free radical formation and/or interrupt propagation of autoxidation* [14, 15]. Phenolic compounds, that contain flavones (*apigenin, luteolin*) and *flavonols (kaempferol and quercetin)* stimulate reparative processes affecting the *anti-inflammatory macrophage response* [14]. While doing that *macrophage chemotaxis intensifies, proliferation and differentiation occur and the granulation tissue matures*.

Study results can be promising for future development of plant-based *medicines* for *wound healing*.

Study limitations. Some hematological parameters have not been investigated (for example, the erythrocyte sedimentation rate et al.). It was rational to study leukocyte indices for a detailed analysis of the mechanism of action of drugs.

Prospects for further research. The obtained results might be used in preclinical research of new wound-healing drugs.

6. Conclusion

1. This study has allowed to establish therapeutic action of “Prolidoxid” and “Dexpanthenol with ceramides” using the rat burn model. According to the data of planimetric research these medicinal products *accelerated* epithelialization and granulation of skin ulcers on 2 days compared to reference medicines.

2. The results of hematological studies confirmed the effectiveness of “Dexpanthenol cream with ceramides” and “Prolidoxid”. It has been established that studied medicinal products inhibit inflammatory processes and normalize blood rheology. Strength of these medications equals in strength of reference medicines.

3. Hence we infer that further all-sided pharmacological investigation of above-mentioned medicinal products and their introduction into clinical practice is highly prospective.

Conflict of interests

The authors declare that they have no conflicts of interest.

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