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<https://doi.org/10.24959/cphj.19.1506>**T. I. Iermolenko, N. G. Ruda, O. I. Pautina**

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THE STUDY OF THE IMPACT OF HERBAL MEDICINAL PRODUCTS IN SOFT DOSAGE FORMS ON THE BURN WOUND PROGRESSION IN THE EXPERIMENT

The treatment of burns with topical preparations, namely ointments, which consist of herbal ingredients, becomes relevant among the population due to the fact that this dosage form is the most convenient to apply as self-medication; and biologically active substances that are part of these medicines are less toxic, and at the same time, they are not less effective than synthetic drugs against burn damages.

Aim. To study the wound-healing effect of drugs containing biologically active herbal ingredients using the model of burn wound.

Materials and methods. The study was conducted on 24 white female rats weighing 200-240 g. The experimental animals were divided into 4 groups: Group 1 – pathology (n = 6); Group 2 – animals treated with Wundahyl ointment (n = 6); Group 3 – animals treated with Spasatel Forte ointment (n = 6); Group 4 – animals treated with 2 % thiotriazoline ointment (n = 6).

Results. When treating the burn wounds with Wundahyl ointment and 2 % thiotriazoline ointment the wound-healing progression was better. The burn wound area for the following two weeks of observation (Days 14-21) decreased faster compared to the application of Spasatel Forte ointment and much faster in compared to the group of pathology. On Day 28, the burn wound was epithelized completely.

Conclusions. According to the results of the experiment, the effect of Wundahyl ointment was the most pronounced in relation to all the soft dosage forms under study.

Key words: herbal medicinal products; soft dosage form; burn wound; healing

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Дослідження впливу фітопрепаратів у м'яких лікарських формах на перебіг опікової рани в експерименті

Актуальність лікування опіків засобами для місцевого використання серед населення, тобто мазями, що мають у своєму складі рослинні компоненти, набуває певного значення тому, що ця лікарська форма є найбільш зручною для самостійного використання, а біологічно активні речовини, що входять до складу цих препаратів, є менш токсичними, але не менш ефективними, ніж синтетичні протиопікові засоби.

Мета дослідження. Вивчення лікувального ефекту препаратів, що містять біологічно активні рослинні компоненти на моделі опікової рани.

Матеріали та методи. Дослідження проведено на 24 білих щурах-самицях масою 200-240 г. Експериментальні тварини були розподілені на 4 групи: 1 група – патологія (n = 6); 2 група – тварини, яких лікували маззю Вундехіл (n = 6); 3 група – тварини, яких лікували маззю Спасатель форте (n = 6); 4 група – тварини, яких лікували маззю тіотриазоліну 2 % (n = 6).

Результати. При лікуванні опікових ран маззю Вундехіл та маззю тіотриазоліну 2 % перебіг ранового процесу відбувався краще. Площа опікової рани впродовж наступних двох тижнів спостереження (14-у-21-у добу) зменшувалася швидше, ніж при застосуванні мазі Спасатель-форте і значно швидше в порівнянні з групою патології. На 28 добу опікова рана була повністю епітелізована.

Висновки. За результатами експерименту дія мазі Вундехіл була найбільш вираженою по відношенню до всіх м'яких лікарських форм, що вивчались.

Ключові слова: фітопрепарати; м'яка лікарська форма; опікова рана; загоєння

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Исследование влияния фитопрепаратов в мягких лекарственных формах на течение ожоговой раны в эксперименте

Актуальность лечения ожогов среди населения средствами для местного применения, а именно мазями, имеющими в своем составе растительные компоненты, приобретает определенное значение. Данная лекарственная форма является наиболее удобной для самостоятельного использования, а биологически активные вещества, входящие в состав этих препаратов, менее токсичны и не менее эффективны, чем синтетические противоожоговые средства.

Цель исследования. Изучение ранозаживляющего эффекта препаратов, содержащих биологически активные растительные компоненты на модели ожоговой раны.

Материалы и методы. Исследование проведено на 24 белых крысах-самках массой 200-240 г. Экспериментальные животные были разделены на 4 группы: 1 группа – патология (n = 6); 2 группа – животные, которых лечили мазью Вундехил (n = 6); 3 группа – животные, которых лечили мазью Спасатель форте (n = 6); 4 группа – животные, которых лечили мазью тиотриазолина 2 % (n = 6).

Результаты. При применении мази Вундехил и мази тиотриазолина 2 % течение раневого процесса происходило лучше. Площадь ожоговой раны в течение следующих двух недель наблюдения (14-21-е сутки) уменьшалась быстрее, чем при применении мази Спасатель-форте и значительно быстрее по сравнению с группой патологии. На 28 сутки ожоговая рана была полностью эпителизована.

Выводы. Результаты эксперимента показали, что действие мази Вундехил наиболее выражено по отношению ко всем мягким лекарственным формам, которые изучались.

Ключевые слова: фитопрепараты; мягкая лекарственная форма; ожоговая рана; заживление

The relevance of the problem of superficial thermal lesions is determined by the high frequency of their occurrence in everyday life; they constitute up to 80 % of cases among other burns [1, 2]. Partial-thickness second-degree skin burns are able to epithelize themselves within three weeks with complete restoration of the normal skin and usually require only local conservative treatment. Therefore, victims of superficial burns quite often do not seek medical care and try to heal the wounds themselves, choosing soft dosage forms with wound healing properties [3].

Treatment of a local burn wound plays an important role in providing uncomplicated course of the wound process. Properly selected drugs for local treatment of burn wounds can reduce infections of wounds and create the optimal conditions for regeneration [4].

At present, the population more often chooses drugs containing plant biologically active substances that exhibit the multi-component effect [5].

Herbal medicinal products occupy almost one third of the world market of medicines [6]. Quite often, they are special, and it is almost impossible to replace them with synthetic drugs due to the complexity of the structure, and because the medicinal plant raw material contains a complex set of biologically active substances that collectively give the biological activity of a particular direction [7]. In this case, preference is given to herbal medicinal products that exhibit a wide spectrum of action, high therapeutic activity, and at the same time, they are less toxic and more cost effective than synthetic analogs [8, 9, 10].

The correct choice of a dosage form providing the penetration of active substances to one or another depth of the skin is also important for the success of external therapy. Local treatment of burn wounds is aimed at creating the most favorable conditions for their healing in optimal terms. Ointment is a topical dosage form that is mostly used in external burn therapy [11] and it is the most convenient treatment for burn wounds. The main advantage of soft dosage forms is the uniform distribution of the active substance and ease of use, which makes it possible to treat the affected areas individually daily. Ointments show mild effect and low toxicity against the background of high efficiency. Typically, the ointment

contains a minimum amount of water, and it is an active substance dissolved in the fatty base. In addition, the ointment base softens and moisturizes the dry skin, softens scales and peels. Due to this there is an increase in microcirculation that helps to reduce infiltrates [12].

Therefore, the effectiveness of treating superficial thermal burns depends on the correct choice of the medicinal product and its dosage form.

The aim of this work was to study the effect of soft dosage forms of herbal ingredients on the progression of a burn wound in the experiment.

Materials and methods

To study wound-healing properties, soft dosage forms containing herbal ingredients – Wundahyl ointment, Spasatel Forte ointment were used. As a reference drug 2 % thiotriazoline ointment was used. We selected this drug as a reference drug since the wound-healing properties of thiotriazoline ointment were found in the experiment [13, 14]. The therapeutic effect of 2 % thiotriazoline ointment is due to its membrane-stabilizing properties, inhibition of lipid peroxidation processes and activation of anti-radical defense enzymes in damaged tissues that are beneficial to wound-healing processes [15].

Wundahyl multi-component ointment is widely known as a stimulant for wound healing processes. When applying it pain, swelling, and necrosis are intensively removed. The ointment helps to normalize metabolic processes and to regenerate rapidly the tissues, has the anti-inflammatory, bactericidal and hemostatic effect due to the ingredients of the ointment. One of the ingredients of the ointment is caryophyllene (the extract of calendula) with the anti-inflammatory, wound-healing, bactericidal, antiseptic, capillary-aging activity. The action of the roots of northern cinquefoil (*Potentilla maculata*) is based on the rich content of tannins and causes the anti-inflammatory and hemostatic effects. The *Sophora Japonica* fruit contains a large amount of rutin, which reduces the permeability and fragility of blood vessels, has the hemostatic, bactericidal, anti-edema, anti-inflammatory effects. Vitamins, essential oils, esters, organic acids of the yarrow (*Achillea millefolium*) herb possess the anti-inflammatory, bactericidal, anti-allergic, and wound-healing effect. Propolis has a detrimental effect on

a number of bacteria and exhibits a marked local analgesic effect [16].

The valuable therapeutic properties of Spasatel Forte ointment are its ability to activate the local immunity, and initiate regenerative processes. The ointment prevents the development of infections, has the analgesic activity. The drug composition includes vegetable oils, vitamins, and natural extracts. Sea buckthorn oil helps to accelerate the process of wound healing due to a mixture of active substances: sterols, phytoncides, carotenoids, organic acids. Chamomile essential oil has the anti-inflammatory, analgesic, antiseptic effect. Lavender oil has the antiseptic, bactericidal effects, accelerates the regeneration of epidermis cells. Carotenoids, flavonoids, essential oils, organic acids of calendula have the anti-inflammatory, wound-healing effect, promotes the growth of granulation and epithelization [16].

The pharmacological activity of these medicinal products containing herbal ingredients, namely, the antipyretic and wound-healing effect, was determined on the model of thermal burn.

Modeling of burn wounds to animals was carried out under anesthesia on the depilated area of the skin of the right posterior thigh [15]. For this purpose a device with the adjusted temperature scale and an electric soldering tool with a circular metal plate of 2.5 cm in diameter attached at the end of it were used. The exposure time of the contact plate heated up to 2 °C was 5 seconds [17]. This method allowed obtaining standard burns with the area and depth of skin lesions corresponding to the degree II-A of clinical classification of burns. Experiments were conducted on 24 white female rats weighing 200-240 g. The experimental animals were divided into 4 groups: Group 1 – pathology (n = 6); Group 2 – animals treated with Wundahyl ointment (n = 6); Group 3 – animals treated with Spasatel Forte ointment (n = 6); Group 4 – animals treated with 2 % thiotriazoline ointment (n = 6), total 24, respectively. The ointments were applied with a thin layer to the wound surface immediately after the thermal action and within the experimental period. Visual monitoring of the condition of the animals and the state of the wound were performed on Days 4, 7, 14, 21, 28. The area of the wound was also measured these Days. The process of regeneration of skin wounds was assessed using planimetric indices.

The rate of healing wounds (V , mm/day) was measured on Days 1, 4, 7, 14, 21, 28 of the experiment and determined by the formula [18]:

$$V_{heal} = \frac{S_{heal}}{n},$$

where S is an area of healing in mm^2 , n is a number of the treatment days.

The experimental data obtained were processed by the methods of variation statistics, the aver-

age arithmetic value and its standard error were calculated [19]. In order to obtain statistical conclusions, mathematical calculations were applied with the use of "Statistica 6.0" analytics software package [20].

The experiments were performed on the experimental animals grown in the vivarium of the Central Research Laboratory of KhNMU equipped in accordance with the current sanitary and hygienic requirements. The experimental animals were kept on a standard diet. The animals always had free access to water. During the experiment, the animals were in the research room at $t = 18-24$ °C, humidity was not more than 55 %, light conditions of "day-night" were natural, the animals were in plastic cages, with the balanced feeding. The study was performed in compliance with the bioethics rules – humane treatment of animals in accordance with the provisions of the European Convention for the Protection of Vertebrate Animals (Strasbourg, 1986) and the National Congress of Bioethics IV (Kyiv, 2010).

Results and discussion

Observation over the healing process showed that the final formation of the burn wound in all experimental groups occurred on the second day. After the onset of the burn wound in all experimental animals a dense gray and brown scab appeared with a clearly restricted necrotic area and pronounced inflammatory changes in surrounding tissues. Starting from the third day there was a tendency to soften the central part of the thick scab; a serous-purulent exudate appeared when pressing the scab. On Day 7, the burn wound of the pathology group was a zone of necrotic nature filled with a serous-purulent exudate. The regenerative process was very slow and solely due to physiological mechanisms of the organism. Partial ecdysis occurred on Day 14, complete – on Day 21. The process of edge epithelization was slower than in the groups of animals receiving the treatment. On Day 28, the wounds in animals of the pathology group were not completely healed.

In the groups of treated animals, serous exudation was moderate, swelling and hyperemia of the wound were also less pronounced compared to the group of pathology. In animals treated with Wundahyl ointment and 2 % thiotriazoline ointment the wound process was better (Table). The area of necrotic nature in the center of the burn wound for the next two weeks of observation (Days 14-21) decreased faster (Wundahyl ointment – by 82.17 % and 96.88 %, and 2 % thiotriazoline ointment – by 78.5 % and 96.78 %, respectively) than when applying Spasatel Forte ointment (83 % – on Day 14, and 90.96 % – on Day 21) and much faster compared to the group of pathology (76.75 % – on Day 14, and 85.96 % – on Day 21). On Day 28, the burn wound

Table

Changes in the wound surface area (mm²) in the dynamics of healing after thermal burn in rats in the experiment (n=6)

| Treatment days | Experimental groups | | | |
|----------------|----------------------------|---------------------------|----------------------------|----------------------------|
| | Pathology | Pathology + Wundahyl | Pathology + Spasatel Forte | Pathology + thiotriazoline |
| Baseline | 400.0±0.0 | 400.0±0.0 | 400.0±0.0 | 400.0±0.0 |
| Day 4 | 246.33±14.43* [^] | 238.0±29.3* [^] | 225.0±21.42* [^] | 206.0±44.81* [^] |
| Day 7 | 196.33±8.84* [^] | 183.0±28.11* [^] | 183.33±23.66* [^] | 181.33±25.52* [^] |
| Day 14 | 93.0±28.9* [^] | 71.33±24.56* [^] | 68.0±11.66* [^] | 86.0±26.84* [^] |
| Day 21 | 56.17±5.53* [^] | 12.5±5.9* [^] # | 36.17±29.4* [^] | 12.83±6.77* [^] # |
| Day 28 | 22.5±17.68* [^] | - | 19.0±9.9* [^] | - |

Notes:

- 1) * – significant difference in relation to the previous values, $p < 0.05$;
 2) [^] – significant difference in relation to the baseline, $p < 0.05$;
 3) # – significant difference in relation to the group of pathology, $p < 0.05$.

was completely epithelized in the groups treated with Wundahyl ointment and 2 % thiotriazoline ointment (unlike the group of pathology – 94.38 % epithelization). In the group treated with Spasatel Forte ointment for healing of the burn wound was accompanied by a gradual decrease in the area of the wound defect up to Day 28 by 95.25 % compared to the original area of the wound.

During the whole experiment there were no deaths of animals both in experimental groups and in the group of pathology.

Thus, in the second group of experimental animals (treated with Wundahyl ointment) the wound healing progress was more pronounced compared to the group treated with Spasatel Forte ointment, and it was almost the same compared to group 4 treated with the reference drug – 2 % thiotriazoline ointment, and it had more significant indices

in relation to the group of pathology without treatment of the experimental animals.

CONCLUSIONS

As a result of the experimental studies in animals on the model of thermal burn, Wundahyl ointment revealed better burn wound-healing properties than Spasatel Forte ointment. Wundahyl ointment also exhibited better burn wound-healing properties compared to the reference drug – 2 % thiotriazoline ointment.

Thus, it can be concluded that Wundahyl multi-component ointment containing herbal biologically active ingredients has a pronounced anti-inflammatory and wound-healing effect, and it can be effectively used in the treatment of superficial burn wounds.

Conflict of interests: authors have no conflict of interests to declare.

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