# EXPERIMENTAL WORKS

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## EFFICACY OF HUMAN HEPARIN-BINDING EGF-LIKE GROWTH FACTOR IN HEALING EXPERIMENTAL CHEMICAL BURNS

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*According to the WHO, burns are the third most common cause of traumatic skin injuries. Chemical burns are characterized by a complex course and a long healing process. The use of the representatives of the epidermal growth factor family seems to be a promising direction in the treatment of chemical burns. The aim of this study was to evaluate the effectiveness of the recombinant human heparin-binding EGF-like growth factor (rhHB-EGF) in treating burn wounds in mice. The expression of a recombinant human HB-EGF analog was induced in the prokaryotic system E. coli BL21 Star, the protein was isolated, purified and its preparations in PBS or in a form of gel containing sodium hyaluronate and potassium sorbate were obtained. The burn wound was simulated in white non-inbred mice by subcutaneous injection of 10% paraformaldehyde solution, healing was observed for 17 days. The initial wound area was measured on the 7th day after the burn injury when the treatment was started. The mice with burn injury were divided into groups of 3 each - untreated mice (control), treated with different preparations: gel without rhHB-EGF; rhHB-EGF in a gel form; rhHB-EGF in PBS solution. The preparations (100 µl, 1.5 mg of rhHB-EGF) were applied to burn wounds daily for 5 days. Wound area, healing rate and histological patterns of skin samples were estimated. It was shown that groups with burn injury treated with HB-EGF protein (both in solution and gel form) demonstrated an advantage in reducing the wound area and inflammatory cells infiltration, improving healing rate, increasing the proliferative activity of epithelial cells and neovascularization as compared with the untreated group. Thus, the use of rhHB-EGF is a promising direction in the treatment of skin wounds.*

*K e y w o r d s: heparin-binding EGF-like growth factor, chemical burns, wound healing, skin regeneration, histological analysis.*

Skin injuries, particularly severe burns, are among the pressing issues in medicine, as they lead to prolonged healing processes, frequent wound infections, and scarring, which limits the function of the affected skin areas.

According to the WHO, burns are the third most common cause of traumatic skin injuries, affecting approximately 7–12 million people who require medical attention annually. Moreover, about 180,000 deaths each year are attributed to burn injuries, predominantly in low- and middle-income countries [1].

Burn injury statistics in Ukraine indicate a trend of increasing burn frequency and severity among both children and adults. Annually, over 20,000 adults and 10,000 children (60% of whom

are under 3 years old) require inpatient treatment for burn disease. This care is provided in both non-specialized medical facilities and specialized burn units. The average hospital stay for a burn patient is about two weeks; however, for severe burns, hospitalization may last a month or significantly longer. To date, the primary approach to treating severe burn wounds remains surgical: early necrotectomy followed by autologous skin grafting [2].

Burns are defined as skin damage caused by high temperatures or other intensive injuries, such as contact with hot surfaces or flames. They lead to varying degrees of vascular damage. Based on tissue depth, burns are classified as superficial, partial-thickness, and full-thickness. Superficial burns (1st degree) affect only the epidermis. Partial-thickness burns (2nd degree) extend into the dermis and are further classified into superficial and deep partial-thickness burns. Superficial partial-thickness burns involve the papillary (upper) dermis and typically heal within 1–2 weeks with minimal scarring. Deep partial-thickness burns affect deeper dermal layers, take ≥2 weeks to heal, and are often accompanied by scarring and potential functional loss. Full-thickness burns (3rd degree) extend through the entire dermis and into the subcutaneous fat. Healing occurs only from the periphery, and these burns, if extensive, require excision and skin grafting [3, 4].

Chemical burns, caused by exposure to aggressive chemical agents, can result in severe skin damage and require prolonged and complex treatment. In this context, the use of recombinant forms of epidermal growth factor, particularly recombinant human heparin-binding epidermal growth factor (rhHB-EGF), has shown promising results in accelerating the healing process.

One of the main challenges in treating burn disease is managing and healing large and deep tissue injuries, which carry a high risk of infection. These injuries often require costly treatment, including skin grafting, particularly autologous grafting. When the wound area exceeds 30–40% of the body surface, even perforated autografts cannot completely cover the wound in one procedure, necessitating multiple surgeries over an extended period.

Various members of the epidermal growth factor (EGF) family have demonstrated effectiveness in wound healing [5-8], including heparin-binding epidermal growth factor (HB-EGF) [9]. An important aspect of applying recombinant human HB-EGF (rhHB-EGF) is its ability to enhance wound healing and promote faster skin regeneration while reducing the risk of scarring, which significantly improves the quality of life for burn patients.

To evaluate the impact of rhHB-EGF on the healing process of chemical burns, a series of experimental studies is required [10-13]. These studies should include both *in vitro* and *in vivo* models to analyze the mechanisms of action of this compound and its clinical efficacy.

## Materials and Methods

*Laboratory animals.* The study used non-inbred (non-breeding) mice aged 5-6 weeks and weighing 20-25 g (SI "L.V. Gromashevskyi Institute of Epidemiology and Infectious Diseases of the NAMS of Ukraine", Kyiv, Ukraine). All work with animals was performed in accordance with bioethical standards, in particular, the European Convention for the Protection of Vertebrate Animals used for Experimental and Other Scientific Purposes (Strasbourg, 1986). Permission to conduct animal experiments was granted by the Ethics Committee of the SI "L.V. Gromashevskyi Institute of Epidemiology and Infectious Diseases of the NAMS of Ukraine" and Interfaculty Commission on Bioethics National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" (protocol No. 3 of 10.12.2024).

At the end of the experiment, animals were humanely euthanized to minimize physical and psychological suffering. The method of euthanasia was cervical dislocation. All animals selected for the experiment underwent a veterinary examination and a 5-day acclimatization period, after which they were randomized into groups, numbered, and marked accordingly.

The animal housing conditions were maintained as follows: temperature of 20–24°C, humidity of 30–60%, and an 18-hour light cycle. The mice were fed standard laboratory animal chow [14, 15].

*rhHB-EGF-based preparations.* Preparations based on rhHB-EGF were manufactured by the National Technical University of Ukraine "Igor Sikorsky Kyiv Polytechnic Institute" based on rhHB-EGF samples provided by the Palladin Kyiv Institute of Biochemistry of the NAS of Ukraine. The technology for obtaining the protein used in gel production involves the induction of expression of a recombinant human HB-EGF analog in the prokaryotic expression system *E. coli* BL21 Star (DE3). The isolation and purification of rhHB-EGF were performed using metal-affinity chromatography on $Co^{2+}$-containing HisPur Superflow agarose.

Sodium hyaluronate was added to the gel as an excipient, which is widely used in medical devices for various skin injuries [16].

The biologically active protein, which promotes tissue regeneration and wound healing, is supplied by the manufacturer in a dissolved form in phosphate-buffered saline (PBS) at concentrations ranging from 1 to 5 mg/ml. The solution is clear, colorless, and odorless, and it is stored at -20°C.

For the study, the following samples were used: protein-free gel with the following composition: sodium hyaluronate – 250 mg, potassium sorbate – 20 mg, phosphate-buffered saline 0.1 M, pH 7.2; Gel with HB-EGF with the following composition: rhHB-EGF – 1.5 mg, sodium hyaluronate – 250 mg, potassium sorbate – 20 mg, phosphate-buffered saline 0.1 M, pH 7.2; HB-EGF protein solution in 0.015% PBS.

*Modeling the formation of burn wounds.* In the initial stage, thermal burns of varying degrees were used as a model of traumatic skin injuries in experiments on laboratory animals. Burn disease in mice was modeled as follows:

Mice aged 3–4 weeks were premedicated with an intramuscular injection of 0.2 mg/kg of a 2% solution of xylazine hydrochloride. After administering the drug and observing its sedative effects, the animals were given an intraperitoneal injection of a 1% sodium thiopental solution at a dose of 60 mg/kg body weight.

Once full anesthesia was achieved, the hair on the caudal part of the back was shaved and removed using a cosmetic depilatory agent. In the center of the prepared field, 100 µl of a buffered 10% paraformaldehyde solution (pH 7.4) was injected subcutaneously, with the needle positioned at a 45° angle to the sagittal axis of the body.

A few days after the procedure, tissue induration and the formation of small superficial ulcers were observed on the skin surface around the injection site. Over the next 2–3 days, these ulcers expanded, deepened, and merged, resulting in a burn injury with a diameter of 10–15 mm.

*Wound treatment.* The preparations were applied to burn wounds daily in an amount of 100 µl for 5 days, except for the control group. Each experimental group included 3 animals. Daily photofixation of the wound surface was carried out.

*Measurement of the area of chemical burns.* After digitization, the wound area was analyzed using ImageJ 1.49v software (National Institutes of Health, Bethesda, Maryland, USA). The wound healing rate was expressed as a percentage change in the initial wound area according to the following formula:

$$WHR = \frac{IWA - WASD}{IWA} \times 100,$$

where *WHR* – wound healing rate; *IWA* – initial wound area; *WASD* – wound area on a specific day.

The initial wound area was measured on the 7$^{th}$ day after the burn injury, prior to the start of treatment. The specific daily wound area was the wound area measured on that particular day.

*Wound healing assessment.* Wound healing was evaluated using a scale developed based on the principles described in works [17-19] using the following criteria: wound area (wound healing rate), edema, skin texture, crusting, skin color, and presence of epidermis/reepithelialization. Results were interpreted by summing scores across all criteria, with a maximum score of 27 (complete healing across all parameters): 0-6 points: little or no healing; 7-13 points: initial healing; 14-20 points: significant healing; 21-27 points: complete healing. In the burn wound healing study, the healing period was defined as the period when the wound healing score was 21 points or more. According to the scale, where 21-27 points corresponded to complete wound healing.

*Histological analysis.* Skin samples were fixed in a 10% formalin solution and embedded in paraffin. For histological analysis, skin sections were stained with hematoxylin and eosin, allowing for a detailed examination of the epidermis and dermis structures under a microscope [20, 21]. Histological slides were studied using a Leica BX 51 microscope, a Leica MC 190 digital camera, and Leica LAS software at magnifications of 100x–200x.

## Results and Discussion

For the study, mice were divided into groups, each containing 3 mice with different degrees of burns. The distribution of animals was balanced, proportional to the degree of burn lesions, which ensured an even representation of mice with different degrees of lesions in each of 4 groups: control (mice with burns and without treatment); treatment with gel without protein; treatment with gel with HB-EGF protein; treatment with a solution of HB-EGF protein in PBS 0.015%.

In the process of further observations, photofixation of the results was carried out. The results

of photofixation were stored in JPEG format. Upon completion of the experiment, all images were brought to the same scale using ImageJ 1.54g software, and the wound area was measured using this program. Mathematical processing of the results was carried out using Origin 8.1 software.

The post-burn wounds were rounded, which is explained by the local introduction of the substance into a certain area of the skin. The edges between the wound areas and normal skin were clearly demarcated. On the 1st day after the burn, there were almost no external changes. From the 3rd day, the area of the affected skin began to change color. On the 7th day after the burn, burns were formed with a change in the color and texture of the skin. Treatment with the studied drugs began on the 7th day.

*Clinical evaluation.* Healing was observed for 17 days. Clinical evaluation parameters, including duration of edema, days required for crusting, and wound area, were recorded. Crusting was defined as the time from the day of burn lesion induction to the day the crust was detached from the wound. The end point of complete reepithelialization was considered to be crusting. In the reepithelialization phase of wound healing, epithelial cells migrate to the wound site, cover the granulation tissue, and then meet in the middle, at this point contact inhibition causes them to stop migrating, completing the reepithelialization [22]. The time from burn induction to the day of complete epidermal healing was considered the reepithelialization period. Fig. 1 shows the healing rate of burn wounds by day.

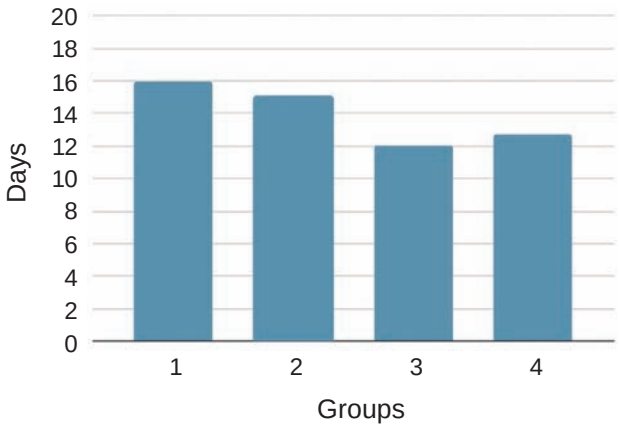


*Fig. 1. The healing rate of burn wounds of experimental animals by day in different groups: 1 – control (mice with burn and no treatment); 2 – protein-free gel treatment; 3 – treatment with gel with HB-EGF protein; 4 – treatment with a solution of HB-EGF protein in PBS 0.015%*

On the 5th-7th day after the burn, the skin became pearly white or red with edema. After the edema was removed, the wound was covered with a layer of brown hard crust. Then, the crust dried up and peeled off from the wound. Detachment of the crust for the control group was 16.0 ± 0.72 days, slightly longer than for the other groups, which were: for the protein-free gel group – 15.0 ± 0.68; for the gel with HB-EGF protein – 12.0 ± 0.54 and for the HB-EGF protein solution 12.7 ± 0.57 days. After the crust peeled off from the wound, a second new crust was formed, which then peeled off from the wound.

The rate of wound reduction in all experimental groups increased depending on time. The assessment was carried out for each mouse separately at the time of healing, and then, the average value of the wound area in % for each group was taken. The results of measuring the area of the chemical burn are shown in Fig. 2.

The comparative evaluation showed that the HB-EGF group had faster wound healing: the wound area was reduced by 73% compared to 60% in the control group. Clinical evaluation showed improved skin color, reduced swelling, and faster crusting in the groups treated with HB-EGF gel.

*Histological analysis. Control group (burned and untreated mice).* Representative histological images of the skin of untreated mice are shown in Fig. 3.

There are no ridges and furrows on the skin surface, stratum corneum is exfoliated. All layers of the skin are well visualized, the epidermis consists of a small number of epithelial layers. The basal epithelium is separated from the dermis, located on the basement membrane.

The dermis forms small papillae that protrude into the epidermis. The dermis cells are diffusely scattered and, in places, form small clusters. Hair follicles are unevenly located in the fields of view; their clusters are noticeable in some areas.

The epidermis has a slightly thickened structure, and proliferative activity of basal layer cells is observed. In some areas of the dermis, clusters of hair follicles are visible.

*Protein-free gel treatment.* Representative histological images of the skin of mice treated with the gel base are presented in Fig. 4.

In Fig. 4 (*A*), it is observed increased proliferative activity of the basal layers of the epidermal epi-

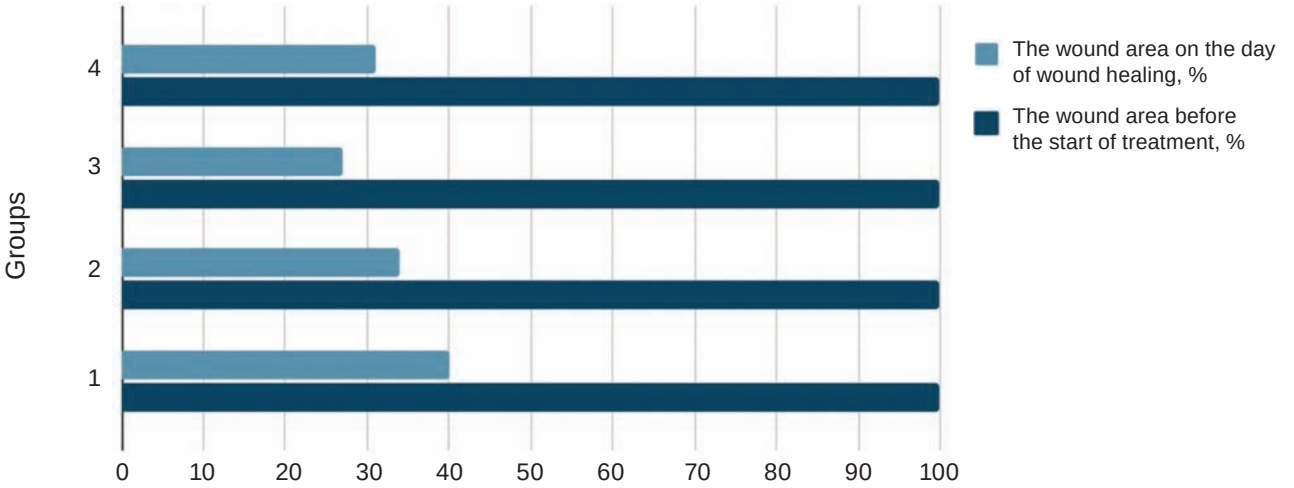


*Fig. 2. Change in the surface area of a chemical burn in control animals and animals after treatment with drugs during the healing process of a burn wound: 1 – control (mice with burn and no treatment); 2 – protein-free gel treatment; 3 – treatment with gel with HB-EGF protein; 4 – treatment with a solution of HB-EGF protein in PBS 0.015%*

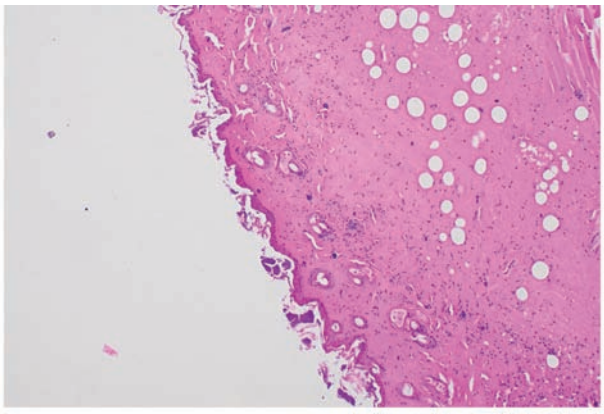

*Fig. 3. Image of a histological section of mouse skin from the control group (histological preparation of thin skin)*

thelium, which causes thickening of the granular layer. Collagen-forming processes in the dermis are not sufficiently expressed, significant accumulations of lymphoid infiltrates are noticeable. Fig. 4 (*B*) shows that the epidermis is somewhat thinned, and large accumulations of lymphoid infiltrates are present in the dermis.

*HB-EGF gel treatment.* Representative histological images of the skin of mice treated with HB-EGF gel are shown in Fig. 5–7.

The main structural components of the regeneration of the connective tissue of the skin are fibroblasts and capillaries, but the main source of their supply is not the dermis, but the subcutaneous tissue.

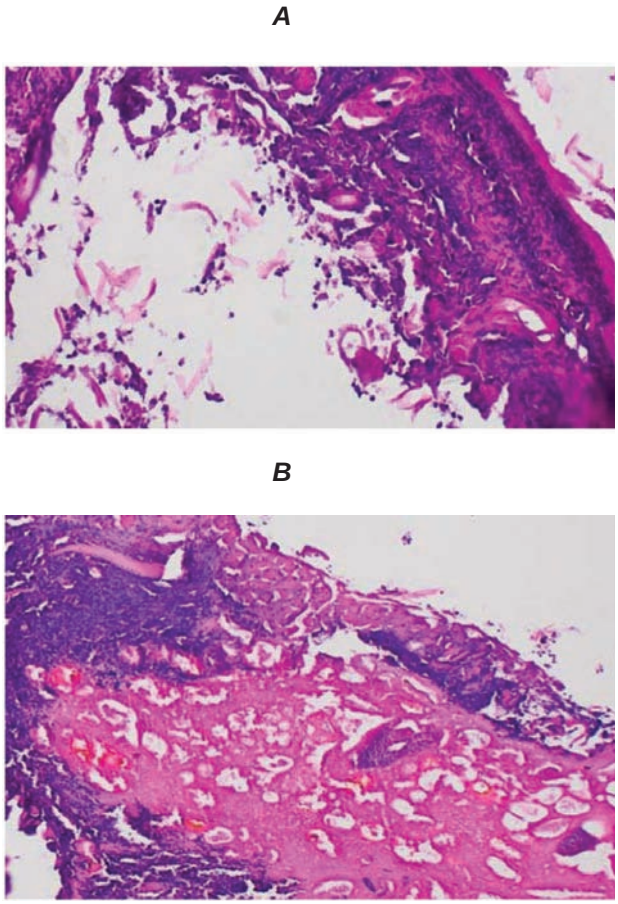


*Fig. 4. Image of a histological section of mouse skin from the "Protein-free gel treatment" group.* ***A*** *– basal layers of the epidermal epithelium;* ***B*** *– epidermis*

Such features of the structural and functional support of the restoration of skin components when it is damaged are because the dermis has a small number of blood vessels and cells. Therefore, when hair follicles move into the subcutaneous tissue, this is a positive indicator of a full and stable restoration of the skin parenchyma and stroma.

In histological samples obtained from a group of animals treated with HB-EGF protein gel (Fig. 5), in some areas of the epidermis, increased proliferative activity of the basal layers of the epithelium is observed. In some places, the papillary layer of the dermis is thinned, but its eosinophilicity is quite saturated, which may indicate active metabolic processes in the connective tissue. There is a small amount of collagen fibers in the reticular layer of the dermis. Hypertrophy of hair follicles is noted, some of which are displaced to the muscle layer. Intensive proliferation of epithelial cells of hair follicles is observed. Hair bulbs are significantly thickened, epithelial cells are basophilic. Pronounced angiogenesis processes develop around the hair follicles, which creates favorable conditions for improving metabolism in the dermis, as one of the main factors in restoring the structural organization of the skin.

Langerhans cells, like most immune cells, have a limited ability to self-replicate. That is, they do not divide as actively as, for example, epithelial skin cells, which are constantly renewed. The processes of proliferation and differentiation of Langerhans cells are complex and not fully understood.

Regulation of the number of these cells is an important mechanism for maintaining the immune homeostasis of the skin. Langerhans cells are dendritic cells located in the epidermis of the skin. Although their primary function is associated with the immune response, they also play an important role in wound healing. After skin damage, Langerhans cells capture antigens (particles of foreign substances or infectious agents) and present them to T lymphocytes. This triggers an immune response that helps fight infection and prevents the development of inflammation [23].

Langerhans cells secrete a variety of cytokines that regulate the intensity of the inflammatory reaction. Too weak an inflammatory response can lead to chronic wound healing and excessive – to scar formation. Langerhans cells secrete growth factors that stimulate the proliferation of keratinocytes – cells of the epidermis. This contributes to faster wound healing [24].

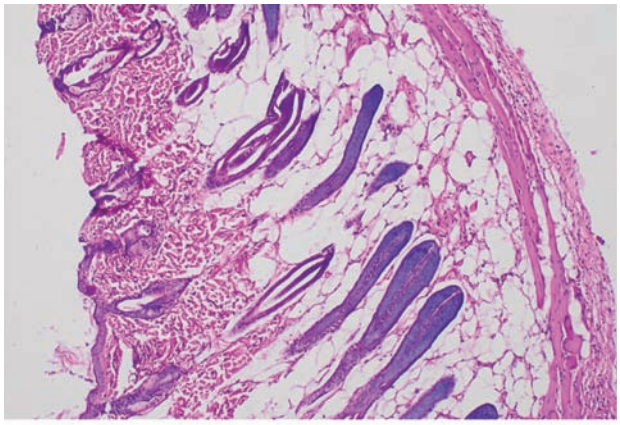

*Fig. 5. Histological image of mouse skin from the group "Treatment with HB-EGF protein gel"*

Langerhans cells interact with fibroblasts – cells that synthesize collagen and other components of the extracellular matrix. This interaction is important for scar formation.

Langerhans cells participate in the process of angiogenesis – the formation of new blood vessels in the microcirculatory bed, which is necessary to provide nutrition to the wound.

Thus, Langerhans cells are important regulators of the wound-healing process. They not only provide an immune response, but also take an active part in tissue regeneration processes. Understanding the role of these cells allows us to develop new methods of wound treatment and accelerate the healing process.

HB-EGF can influence Langerhans cell maturation and migration. It may enhance their ability to present antigens to T cells, altering adaptive immune responses. HB-EGF is known to have cytoprotective properties, which may protect Langerhans cells from apoptosis during inflammatory responses. It may also reduce excessive immune activation, helping to maintain immune homeostasis in the skin.

Hair follicles, whose function is associated with hair growth, also play an important role in the wound healing process. They are not just passive structures, but active participants in skin regeneration. Hair follicles contain stem cells that have the ability to self-renew and differentiate into different types of skin cells. When the skin is damaged, these stem cells are activated and migrate to the wound area, where they participate in the regeneration of the epidermis and dermis. Hair and hair follicles provide a certain structure to the skin, serving as a kind of framework for newly formed tissues. This

is especially important in the healing of deep skin wounds. The blood vessels that nourish the hair follicles also ensure the supply of oxygen and nutrients to the wound area, which contributes to the healing process. Hair follicle cells produce various growth factors that stimulate cell proliferation and migration, as well as the synthesis of extracellular matrix. Hair and hair follicles can create a barrier that prevents bacteria and other pathogens from entering the wound [25-27].

Thus, hair follicles play an important role in the wound healing process, ensuring rapid skin regeneration and reducing the risk of scarring.

Fibroblasts and capillaries are the main structural components of connective tissue regeneration, but the main source of their supply is not the dermis, but the subcutaneous tissue. Such features of the structural and functional support of the restoration of skin components when it is damaged are because the dermis has a small number of blood vessels and cells. Therefore, when hair follicles move into the subcutaneous tissue, this is a positive indicator of a full and stable restoration of the skin parenchyma and stroma [28].

In addition, in histological samples of the group that received treatment with HB-EGF protein gel (Fig. 6) there is a pronounced lymphocytic infiltration in the dermis, in places, there are foci of destruction. The foci of thickening of the epidermis of the skin occur due to the spinous and granular layers.

Treatment with HB-EGF protein solution in PBS 0.015%. Representative histological images of the skin of mice treated with HB-EGF protein solution are shown in Fig. 7.

The number of epithelial layers in the epidermis is reduced in places (Fig. 7, *A*). Hair follicles are

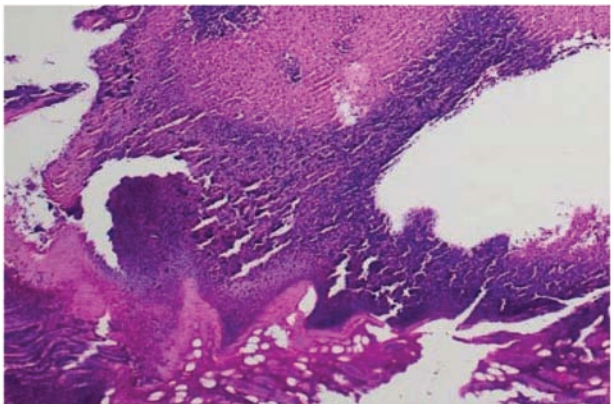

*Fig. 6. Histological image of mouse skin from the group "Treatment with HB-EGF protein gel"*

located both in the superficial and deep parts of the dermis. There is proliferation of hair follicle cells with signs of hypertrophy and delamination of fibrous structures of the dermis.

Fragment of the dermis from Fig. 7, *B*, where hypertrophy and hyperplasia of hair follicles are visible. Some follicles are located in adipose tissue.

The epidermis is thickened; active cell proliferation is noted in the basal layers of the epithelium (Fig. 7, *C*). The number of fibrous structures of the dermis is reduced in places.

Histological analysis showed that the groups treated with HB-EGF protein (both in solution and gel form) demonstrated an advantage in reducing the wound area and more pronounced cell proliferation. However, proliferative activity of epithelial cells was observed in all groups, including the control groups ("Protein-free gel treatment" group and "No treatment" group).

These histological changes collectively contribute to improved healing rates by promoting a fa-

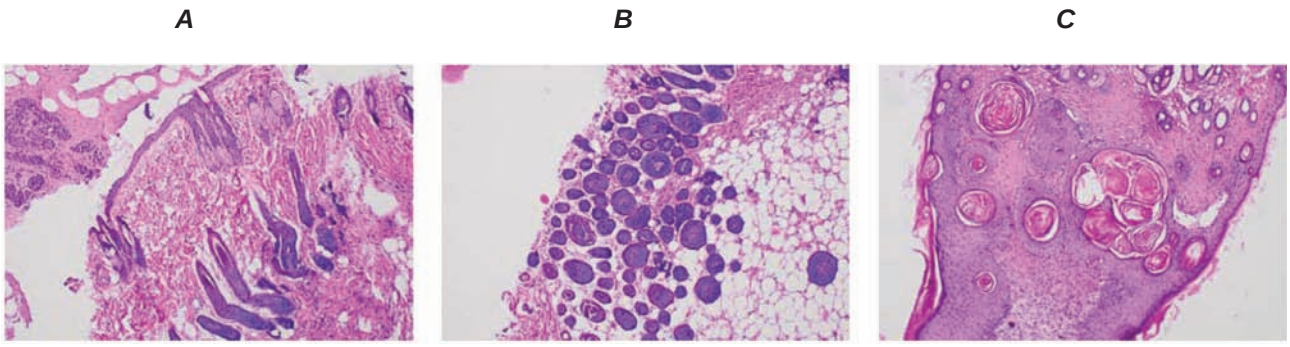


*Fig. 7. Image of a histological section of mouse skin from the group "Treatment with HB-EGF protein solution in PBS 0.015%". **A** – the number of epithelial layers in the epidermis, **B** – fragment of the dermis, **C** – basal layers of the epithelium*

vorable microenvironment for tissue repair. The ability of HB-EGF to modulate inflammation, stimulate fibroblast proliferation, and enhance neovascularization aligns with its known role in accelerating wound healing and tissue regeneration [29-31].

Further studies with larger groups of animals and testing different protein concentrations are needed to clarify the efficacy and safety of HB-EGF, which will allow determining the optimal dose and assessing the long-term effects of treatment.

*Conclusion*. The results of these studies show the effect of heparin-binding epidermal growth factor on tissue regeneration. The obtained data confirm the importance of using recombinant HB-EGF as a potential therapeutic agent for the treatment of chemical burns since this growth factor stimulates cell proliferation and accelerates the restoration of the epidermal barrier. This opens up opportunities for the creation of special dosage forms of the drug based on HB-EGF.

Histological analysis demonstrated that experimental animals treated with HB-EGF showed signs of significant healing much faster: a decrease in the volume of skin lesions, active proliferation of epidermal cells, and a decrease in infiltration by inflammatory cells. In the control group without treatment, burn lesions recovered much more slowly, and regeneration processes occurred by the 14$^{th}$ day.

Further studies may be aimed at determining the optimal doses of HB-EGF and developing protocols for its use in the treatment of chemical injuries in patients with impaired regeneration, as well as optimizing the concentration of HB-EGF to determine the most effective and safe dosage for therapeutic use. Additionally, future research should include testing on larger and more diverse animal models to better understand the translational potential of our findings. Specifically, we propose conducting dose-response studies to identify the optimal concentration range of HB-EGF and evaluating its effects in different skin conditions. Furthermore, expanding the study to include various species and genetic backgrounds will provide deeper insights into its immunomodulatory properties.

*Conflict of interest.* The authors have completed the Unified Conflicts of Interest form at http://ukrbiochemjournal.org/wp-content/uploads/2018/12/coi_disclosure.pdf and declare no conflict of interest.

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## ЕФЕКТИВНІСТЬ ГЕПАРИН-ЗВ'ЯЗУВАЛЬНОГО EGF-ПОДІБНОГО ФАКТОРА РОСТУ ЛЮДИНИ У ЗАГОЄННІ ЕКСПЕРИМЕНТАЛЬНИХ ХІМІЧНИХ ОПІКІВ

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За даними ВООЗ, опіки є третьою за поширеністю причиною травматичних ушкоджень шкіри. Для хімічних опіків характерний складний перебіг і тривалий процес загоєння. Перспективним напрямом у лікуванні хімічних опіків є застосування представників родини епідермальних факторів росту. Метою цього дослідження було оцінити ефективність рекомбінантного людського гепарин-зв'язувального EGF-подібного фактора росту (rhHB-EGF) у лікуванні опікових ран у мишей. Експресію рекомбінантного аналога HB-EGF людини індукували в прокаріотичній системі *E. coli* BL21 Star, протеїн виділяли, очищали та отримували його препарати в фосфатно-буферному (ФБ) розчині або у формі гелю, що містить гіалуронат натрію та сорбат калію. Опікову рану моделювали у білих неінбредних мишей шляхом підшкірної ін'єкції 10% розчину параформальдегіду, загоєння спостерігалося

протягом 17 днів. Початкову площу рани вимірювали на 7-й день після опікової травми, коли починали лікування. Мишей з опіковою травмою розділили на групи по 3 особини у кожній – неліковані миші (контроль), та групи які отримували різні препарати: гель без rhHB-EGF; rhHB-EGF у формі гелю; rhHB-EGF у ФБ розчині. Препарати (100 мкл, 1,5 мг rhHB-EGF) наносили на опікові рани щоденно протягом 5 днів. Оцінювали площу рани, швидкість загоєння та дані гістологічного дослідження зразків шкіри. Показано, що групи з опіковою травмою, які отримували протеїн HB-EGF (як у формі розчину, так і у формі гелю), продемонстрували зменшення площі рани та інфільтрації запальних клітин, покращення швидкості загоєння, підвищення проліферативної активності епітеліальних клітин і неоваскуляризації порівняно з групою, яка не отримувала лікування. Отже, застосування rhHB-EGF є перспективним у лікуванні опікових ран шкіри.

Ключові слова: гепарин-зв'язувальний EGF-подібний фактор росту, загоєння ран, хімічні опіки, регенерація шкіри, гістологічне дослідження.

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