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EVALUATION OF THE EFFICACY OF TREATMENT OF 3RD DEGREE BURNS WITH HLDF6 PEPTIDE AND SILVER NANOPARTICLES IN CARBOPOL 2020 GEL *IN VIVO* EXPERIMENT

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Abstract. ***Introduction.*** Between 250 and 280 thousand victims of deep thermal burns of the skin are registered annually in the territory of the Russian Federation; in every 6 cases the victims are underage patients. The lethality rate in case of thermal trauma is 7.2%, but in case of extensive deep burns it reaches 13–14%. Early surgical treatment of patients with severe thermal burns is an accepted standard and therefore the search for wound healing agents reducing the period of treatment and the risk of infectious complications is essential. ***Objective.*** To evaluate the efficacy of carbopol hydrogel with injected silver nanoparticles and HLDF6 peptide in the treatment of thermal burns of grade III skin in vivo. ***Materials and methods.*** The structure of the work is represented by an experimental study. The work was performed on 50 male Wistar rats, with an average weight of 230–250 g. The animals were divided into 5 groups depending on the applied concentration of HLDF6 peptide in Carbopol 2020 gel. Carbopol ETD 2020 hydrogel samples (0.5%) containing 0,00015% nano-silver and HLDF6 peptide with concentrations of 0%, 0,01%, 0,001%, 0,0001% and 0,00001% were used to evaluate efficacy. A planimetric method was used to assess the dynamics of wound healing. The obtained data were subjected to statistical analysis using the Mann–Whitney U-parameter. ***Results.*** Application of 0,0001 and 0,00001% doses of the peptide HLDF6 demonstrated activation of the healing processes on the 14th day of the experiment by 45,8% and 31,7% correspondingly ($p < 0,01$), and also reduced the incidence of purulent complications by 62,5% ($p < 0,05$). The peptide concentration of 0,01% shows an increase in the duration of treatment, and 0,001%, no significant differences in comparison with the control and experimental groups. ***Conclusion.*** The use of low doses of the HLDF6 peptide (volume concentration in the range of 10^{-4}–10^{-5}%) in gel preparations in the treatment of deep thermal burns of the skin shows high efficacy. Small concentrations of HLDF6 peptide allow significant activation of wound healing processes.

Key words: skin burn; human leukemia differentiation factor-6; silver nanoparticles; combustiology; reparative regeneration; experimental study; traumatology-orthopedics; skin repair.

ОЦЕНКА ЭФФЕКТИВНОСТИ ЛЕЧЕНИЯ ОЖОГОВ III СТЕПЕНИ ПЕПТИДОМ HLDF6 И НАНОЧАСТИЦАМИ СЕРЕБРА В ГЕЛЕ CARBOPOL 2020 В ЭКСПЕРИМЕНТЕ *IN VIVO*

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Резюме. ***Введение.*** На территории Российской Федерации ежегодно регистрируется от 250 до 280 тысяч пострадавших с глубокими термическими ожогами кожи, в каждом шестом случае травмированными являются несовершеннолетние пациенты. Летальность при термическом поражении составляет 7,2%, но при обширных глубоких ожогах может достигать значения 13–14%. Признанным стандартом лечения является раннее начало хирургического вмешательства у пациентов с глубокими термическими ожогами, что делает актуальным поиск ранозаживляющих средств, позволяющих сократить сроки стационарного лечения и снизить риски развития инфекционных осложнений. ***Цель*** — оценить эффективность гидрогеля Карбопола с введенными наночастицами серебра и пептида HLDF6 в лечении термических ожогов кожи III степени *in vivo.* ***Материалы и методы.*** Структура работы представлена экспериментальным исследованием. Работа выполнена на 50 самцах крыс линии Wistar, средней массой 230–250 г. Животные были разделены на 5 групп в зависимости от применяемой концентрации пептида HLDF6 в геле Carbopol 2020. Для оценки эффективности применяли образцы гидрогеля Carbopol ETD 2020 (0,5%), содержащие наносеребро 0,00015% и пептид HLDF6 с концентрациями 0%, 0,01%, 0,001%, 0,0001% и 0,00001%. В процессе работы применяли планиметрический метод оценки динамики заживления ран. Полученные данные подвергали статистическому анализу с применением U-параметра Манна–Уитни. ***Результаты.*** В ходе исследования установлено, что применение геля с содержанием 0,0001 и 0,00001% доз пептида HLDF6 демонстрирует активизацию процессов заживления на 14-е сутки на 45,8% и 31,7% соответственно ($p < 0,01$), а также снижает частоту развития гнойных осложнений на 62,5% ($p < 0,05$). Концентрация пептида 0,01% демонстрирует увеличение сроков лечения, а 0,001% — отсутствие достоверных различий относительно контрольной и экспериментальных групп исследования. ***Заключение.*** Применение малых доз пептида HLDF6 (объемной концентрацией в пределах 10^{-4}–10^{-5}%) в составе гелевых препаратов при лечении глубоких термических ожогов кожи показывает высокую эффективность. Малые концентрации пептида HLDF6 позволяют существенно активизировать процессы ранозаживления и снизить частоту инфекционных осложнений.

Ключевые слова: ожог кожи; человеческий лейкозный фактор дифференцировки-6; наночастицы серебра; комбустиология; репаративная регенерация; экспериментальное исследование; травматология-ортопедия; восстановление кожного покрова.

INTRODUCTION

Skin injuries caused by thermal and chemical burns remain an important and topical issue of modern medicine, and in particular of combustiology and traumatology [1, 2]. Between 250 and 280 thousand victims of deep thermal burns of the skin are registered annually in the territory of the Russian Federation; in every 6 cases the victims are underage patients [14]. The lethality rate in case of thermal trauma is 7.2%, but in case of extensive deep burns it reaches 13–14% [1]. In the emerging socio-political situation, associated with an increase in the number and scale of armed conflicts [3], it is possible to assume an increase in the number of different wound healing agents [21], which are convenient to use both inside and outside the hospital [7]. Modern tactics of treatment of patients with burn wounds is a multidisciplinary task and is carried out taking into account the features of the pathogenesis of burn and its complications [11, 12, 17]. Thanks to the progress of medical science, pathogenetically substantiated methods of antibacterial therapy [9], immunocorrection [8, 19, 20] and local treatment of wounds [18] have been introduced. The accepted standard of early necrectomy of deep thermal skin burns makes it necessary to search for new means that can activate wound healing

processes and reduce their overall treatment time [1, 13]. The most promising new methods of treating superficial and deep burns are biotechnological [10], including stem cell use [24], complex tissue-engineered constructs based on biopolymer matrices [23], populated with allogeneic and autologous cell cultures [13].

One of the promising ways to improve the effectiveness of treatment of patients with extensive deep skin burns involves the use of growth stimulants and regeneration factors [4, 22]. In particular, this refers to epidermal, fibroblast, platelet-derived, and vascular endothelial growth factors [15, 16]. This principle is also true for the development of tissue-engineered constructs [1, 13]. Growth factors and bioactive molecules are introduced into the polymer matrix and onto its surface in these constructs [4, 12].

One possible biologically active substance to be used may be a peptide — human leukemia differentiation factor (HLDF) [2, 4]. It was isolated from the culture medium of the HL-60 promyelocytic leukemia cell line in 1994 [5, 6]. It was found that the HLDF factor induces differentiation along the granulocytic pathway [6]. As a result of this factor, a six-membered peptide fragment human leukemia differentiation factor-6 (HLDF6) was discovered. HLDF6 peptide provides the ability of the full-length factor to differentiate and inhibit cell proliferation, including HL-60 [4, 5]. HLDF6 is also able to interact with membrane lipids, enhancing the activity of cytokines, which participate in the cell proliferation and differentiation [2]. One study showed that HLDF6 also increases the activity of oxidation-reduction processes and enhances the metabolic activity of macrophages [4–6].

For effective delivery and control of the localization of the HLDF6 peptide on the wound surface, it is proposed to use a hydrogel of sparsely cross-linked acrylic polymers (carbopols), in particular, easy-to-disperse (ETD) Carbopol 2020 [2]. They form stable hydrogels that are thermally and chemically stable. The work studied the use of a gel with various concentrations of the target peptide [2]. High efficiency of wound healing was revealed, which was expressed in the improvement of planimetric and histological parameters. However, despite this, a fairly high number of purulent complications in the wound defect zone was also noted in all the studied groups [2, 4]. In the study we plan to carry out, the samples used were additionally modified with antibacterial agents, namely nanodispersed silver, in order to create antibacterial properties in them.

AIM

The aim of the study is to evaluate the efficacy of carbopol hydrogel with injected silver nanoparticles and HLDF6 peptide in the treatment of third-degree thermal burns *in vivo.*

MATERIALS AND METHODS

The structure of the work is represented by a prospective experimental study. The work was performed on 50 male Wistar rats, with an average weight of 230–250 g. Laboratory animals were divided into 5 groups, 10 animals respectively to study samples in each group.

Carbopol ETD 2020 hydrogel samples (0.5%) containing 0,00015% nano-silver and HLDF6 peptide with concentrations of 0%, 0,01%, 0,001%, 0,0001% and 0,00001% were obtained by reducing dissolved $AgNO_3$ in Carbopol ETD 2020 hydrogel solution containing HLDF6 peptide at a temperature of 70 °C. Glucose was used as a reducing agent.

Description of the manipulations performed

Sevoflurane inhalation anesthesia was used in the study. The animal was anesthetized by putting it in a special induction chamber with sevoflurane vaporized at concentrations of 4%. The surgical anesthesia stage developed over 5–10 minutes. After the animal was removed from the induction chamber, anesthesia was maintained by inhalation of concentration of 3% sevoflurane.

The animal was fixed to the operating table with ligatures to simulate the defect. Surgical field preparation included: depilation of the back area and marking a square in this area measuring 4x4 cm. The area of the intervention zone was 16 cm^2. After preparation, the surgical field was treated three times with an alcohol-based antiseptic solutions. Then, the temperature of the skin and the metal plate heated through a resistive heating element were determined using an electrothermocouple sensor of the Electroline multimeter (China). Exposure time was 10 seconds at a skin surface temperature of 95–97 °C. Next, radical necrectomy to the fascia was performed under aseptic conditions. An abdominal surgical scalpel blade was used to make an incision 1.5–2 mm deep. Then, using surgical tweezers and curved surgical scissors, the dermis with a small thickness of the subcutaneous fat was separated from the thoracolumbar fascia adjacent to it. Large-diameter bleeding vessels were coagulated using a coagulator. The resulting defect was washed with 0.9% sodium chloride solution at room temperature. After that, surgical sutures that involve the skin and muscle were applied to fix the wound edges. This was done in order to preserve the lesion area, as well as to prevent premature closure of the wound due to primary intension due to the anatomical and physiological features of the structure of the skin and subcutaneous fat of rats. Suturing was performed using atraumatic suture material Monocryl 3–0 (Bbraun). A needle holder and surgical tweezers were used for suturing. Sutures were applied at a distance of 1 cm from each other.

After suturing, the affected area on the back of the experimental animal was treated with the target agent. 1 ml of gel

was applied to the wound as standard. Repeated application of the gel was performed on the 7th, 14th and 21st days.

Maintenance and withdrawal of animals from the experiment

The maintenance of experimental animals was carried out on the basis of the vivarium of the National Medical Research Center for Pediatric Traumatology and Orthopedics named after G.I. Turner, and it fully complied with GOST 33215-2014 and GOST 33216-2014.

High demands were placed on the cleanliness of the conditions of maintenance, caused by the presence of massive skin injuries. Cleaning, washing and treatment of the cages of experimental animals with disinfectant solutions were carried out daily.

The animals were removed from the experiment on the 28th day after surgery. The withdrawal procedure was developed in accordance with paragraph 6.11 of GOST 33215-2014 and the Recommendations for euthanasia of experimental animals of the European Commission. It was an intravenous injection of 1 ml of lidocaine solution, carried out under deep anesthesia, which led to sudden cardiac arrest.

Disposal of laboratory animals and vivarium waste was carried out within the framework of standard procedures for disposal of Class B waste.

Evaluating treatment effectiveness

The effectiveness of the proposed treatment methods and the general appearance of wounds were assessed by photographing them once every 7 days. Visual examination of wounds was performed daily. The nature of the exudate, the presence and type of granulation, the time of scab rejection and healing of wound surfaces were recorded. The wound area was determined using planimetric method of L.N. Popov. This method involved applying a special film material to the wound surface, outlining the wound edges and then calculating the area either by transferring it to graph paper or using technical means.

In addition, the wound healing index was calculated using the following formula (Fenchin K.I., 1979):

$$\frac{(S-S_n)\cdot 100}{S\cdot T},$$

where S is the wound area at the previous measurement, mm^2; S_n is the wound area at the current measurement, mm^2; T is the interval between measurements, days.

This index allowed us to quantitatively assess the dynamics of the wound healing process based on the planimetric evaluation data.

The reliability of the differences in the obtained results was assessed using nonparametric analysis, namely the Mann–Whitney U-parameter. On its basis, the value of the reliability parameter p was determined. This method was used because of the impossibility of applying a normal distribution and Student's t-distribution due to the small number of groups, caused by requirements of GOST ISO 10993-2014 Part 2 and ethical standards.

Statistical data processing and its visualization were performed using the MS Excel, OriginR 2016 and Wolfram Mathematica 11.0 software packages.

RESULTS

During the experimental work, the survival rate of animals was 100% in all groups studied. The number of purulent complications during the entire treatment period was 4 cases in the control group, 1 observation in the group of gel-carrier with the addition of silver nanoparticles. No significant changes in body weight in experimental animals were detected throughout whole period of the experiment.

The results of the planimetric assessment of the wound surface area are represented in Table 1.

Based on the results obtained, a reliable difference was established between the groups of target gels (with the presence of the peptide in the range of 0.001 and 0.0001%) on the 14th day compared to the control group. In addition, the study revealed a reliable difference between the groups with the minimum peptide content (0.0001 and 0.00001%) and the gel group with 0.01% peptide content on the 14th day ($p < 0.05$). The best treatment effect from the standpoint of planimetry was shown by the gel with silver particles and a peptide content of 0.00001%, both in comparison to control group and other gels ($p < 0.05$).

It should be noted that the moment of increasing the efficiency of the gel with a decrease in the peptide concentration was identified. These changes were most pronounced by day 14, amounting to 84.3% of the wound area reduction

Table 1

Median values and interquartile ranges for the obtained samples

Group	Value	7th day	14th day	21th day	28th day
Gel + HLDF6 0,01%	Median, cm^2	11,39	6,2	3,26	1,32
	IQR, cm^2	4,59	3,59	2,97	2,17
Gel + HLDF6 0,001%	Median, cm^2	9,36	3,46	1,93	1,33
	IQR, cm^2	1,58	1,61	1,09	1,26
Gel + HLDF6 0,0001%	Median, cm^2	9,86	3,16	1,68	0,92
	IQR, cm^2	2,57	1,12	1,76	0,76
Gel + HLDF6 Peptide 0,00001%	Median, cm^2	8,28	2,51	1,61	1,19
	IQR, cm^2	1,41	1,33	1,03	0,89
Gel (without HLDF6)	Median, cm^2	10,5	4,63	1,9	1,985
	IQR, cm^2	3,075	3,12	1,48	1,49

over 14 days in the group with the gel containing 0.00001% peptide. In the control group, the wound area decreased by 58.7%, in the group with the gel containing 0.01% peptide — by 61.3%, and in the group with the gel containing 0.0001% peptide — by 78.4%, over the same period ($p < 0.05$) (Fig. 1).

There was no significant difference between the two groups with the lowest peptide content. Both groups showed a significant improvement in the wound healing dynamics on the 14th day, both when compared with the control group without the addition of the peptide and in the group with its maximum content.

At the same time, it is necessary to note the effect of increasing the wound surface area on 28th day in the group with a peptide content of 0.01% This is especially clearly observed in the graph of the dynamics of the wound healing indices (Fig. 2).

It is also possible to noted extremely high values of this indicator for the period between the 7th and 14th days for the groups with the lowest peptide content in the graph of the dynamics of the wound healing indices. It should be emphasized that the group with the highest peptide content showed the worst wound healing index values among all the groups studied and had a peak only on the 21st day. At the same time, the groups with a lower peptide content demonstrated this peak on the 14th day of the study.

FINDINGS

1. The use of low doses of the HLDF6 peptide tested proved to be the most effective for activating healing processes on the 14th day. Gels containing 0.0001 and 0.00001% of the peptide studied had the most reliable ($p < 0.05$ relative to the control gel group without the peptide) and pronounced differences on the 14th day of treatment.

2. Application of a gel with the highest peptide content (0.01%) led to an increase in the treatment period and a significant deterioration in the final results of the therapy. This suggests a high degree of immunogenicity of such concentrations of the peptide tested. The gel containing 0.001% HLDF6 peptide did not show reliable differences relative to either the control group or other gels with the studied substance.

CONCLUSION

According to the results of the study, it is possible to state the prospects of using low doses of the HLDF6 peptide (volume concentration in the range of 10^{-4}–10^{-5}%) in gel preparations in the treatment of full-layer wounds. Small concentrations of HLDF6 peptide allow significant activating of wound healing processes in the early period and reducing the incidence of infectious complications.

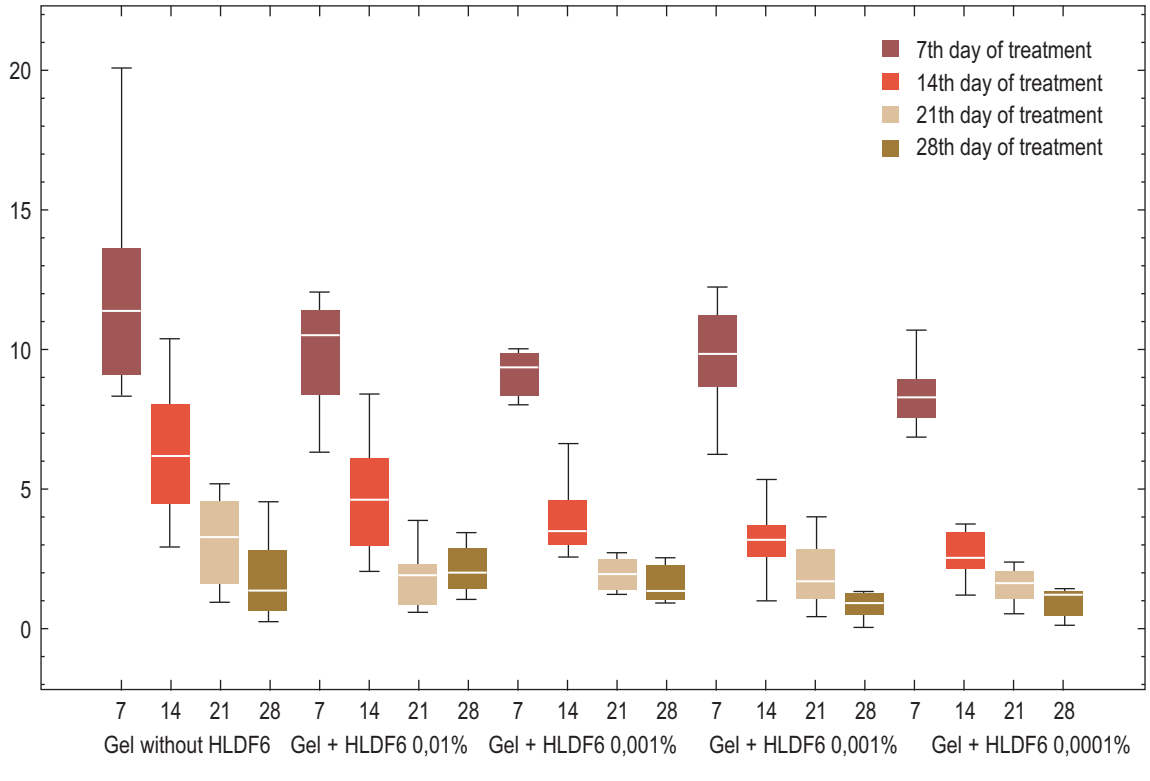

Fig. 1. Diagram comparing the areas of wound surfaces in all studied groups

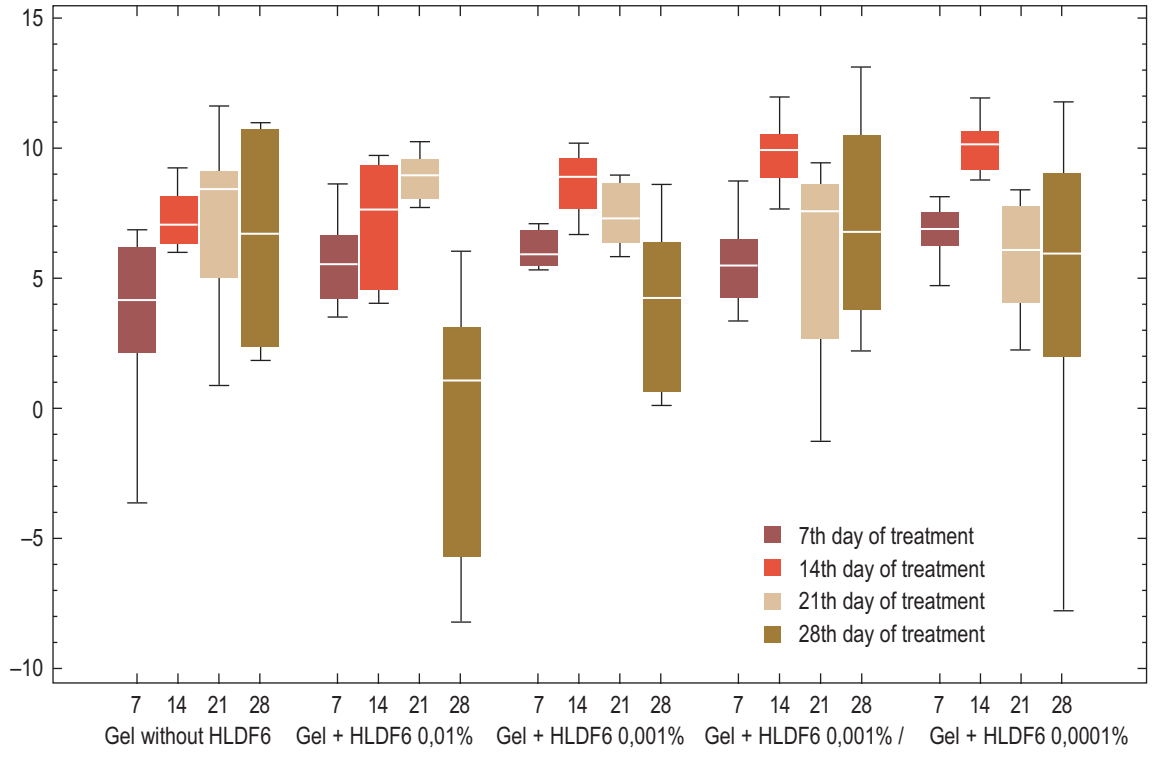

Fig. 2. Graph of the dynamics of wound healing indices in experimental groups

ADDITIONAL INFORMATION

Author contribution. Shabunin A.S. — formulation of the goal and development of the design of the study, writing all sections of the article, statistical processing of the data obtained; Zinoviev E.V. — stage editing of the text of the article; Vissarionov S.V. — final editing of the text of the article; Asadulaev M.S. — writing the "Introduction" section, step-by-step editing of the text of the article; Makarov A.Yu. — conducting experimental studies, collecting and analyzing the data obtained; Fedyuk A.M. — conducting experimental studies, studying histological preparations; Rybinskikh T.S., Kostyakov D.V., Semiglazov A.V., Pyatakov S.N. — conducting experimental studies, analysis of the obtained data; Pershina P.A. — step-by-step editing of the text of the article, translation of the text into English.

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REFERENCES

1. Alekseev A.A. Kompleksnoye lecheniye glubokikh ozhogov na osnove primeneniya khirurgicheskoy nekrektomii I sovremennykh biotekhnologicheskikh metodov. [Comprehensive treatment of deep burns based on the use of surgical necrectomy and modern biotechnological methods]. Annaly khirurgii. 2012; 6: 41–5. (in Russian).
2. Zinoviev E.V., Tsygan V.N., Artsimovich I.V. i dr. Eksperimental'naya otsenka effektivnosti mestnogo lecheniya ozhogov kozhi gidrogelem legkodispergiruyemogo karbopola 2020 s peptidom chelovecheskogo leykoznogo faktora differentsirovki-6. [Experimental evaluation of the effectiveness of local treatment of skin burns with easily dispersed carbopol 2020 hydrogel with human leukemic differentiation factor-6 peptide]. Vestnik rossiyskoy voyenno-meditsinskoy akademii. 2020; 3(63): 48–152. (in Russian).
3. Kopichev O.A., Nikolaev A.E. Sovremennyye voyny: analiz tendentsiy razvitiya mezhgosudarstvennogo protivoborstva, klassifikatsiya form i sposobov bor'by, formirovaniye priznakov I kriteriyev voyennogo konflikta. [Modern wars: analysis of trends in the development of interstate confrontation, classification of forms and methods of struggle, formation of signs and criteria of a military conflict]. Sistemy upravleniya, svyazi i bezopasnosti. 2021; 32(1): 1–32. (in Russian).
4. Lagvilava T.O., Zinoviev E.V., Ivakhnyuk G.K. i dr. Ranozazhivlyayushchiye sredstva na osnove karbopolov. [Wound healing agents based on carbopols] Izvestiya Sankt-Peterburgskogo Gosudarstvennogo Tekhnologicheskogo Instituta (Tekhnicheskogo Universiteta). 2013; 18(44): 47–52. (in Russian).
5. Sosnina A.V., Mikhailova E.S., Autenshlyus A.I. i dr. Klassy I subklassy antitel k faktoru dif-ferentsirovki HLDF I peptidam gaponina, vzaimosvyaz' ikh urovnya s patogistologicheskimi parametrami adenokartsinom tolstoy kishki. [Classes and subclasses of antibodies to the differentiation factor HLDF and gaponin peptides, the relationship of their level with pathohistological parameters of colon adenocarcinomas]. Immunologiya. 2012; 2: 92–3. (in Russian).
6. Sysoeva G.M., Danilenko E.D., Masycheva V.I. i dr. Vliyaniye peptida HLDF-6 na proliferativnuyu aktivnost' splenotsitov v kul'ture kletok na fone vvedeniya agonistov opiatnykh retseptorov. [The effect of HLDF-6 peptide on the proliferative activity of splenocytes in cell culture against the background of the administration of opiate receptor agonists]. Sibirskiy meditsinskiy zhurnal. 2009; 4: 55–9. (in Russian).
7. Uskov V.M., Uskov M.V. Osnovnyye zadachi sluzhby meditsiny katastrof v usloviyakh chrezvychaynykh situatsiy mirnogo I voyennogo vremeni. [The main tasks of the disaster medicine service in emergency situations of peacetime and wartime]. Vestnik Voronezhskogo gosudarstvennogo tekhnicheskogo universiteta. 2010. Available at: https://cyberleninka.ru/article/n/osnovnye-zadachi-sluzhby-meditsiny-katastrof-v-usloviyah-chrezvychaynyh-situatsiy-mirnogo-i-voennogo-vremeni (accessed 06/07/2023). (in Russian).
8. Ali Y., Ali T. Nandrolone decanoate safely combats catabolismin burned patients: A new potential indication after recall. Burns. 2022; 48(1): 59–68.
9. Bakadia B.M., Lamboni L., Abeer A.Q. Antibacterial silk sericin/poly (vinyl alcohol) hydrogel with antifungal property for potential infected large burn wound healing: Systemic evaluation. Smart Mater. Med. 2023; 4: 37–58.
10. Behshood P., Rezaei M. A glimpse into the use of silver-nanoparticles as a promising treatment for burn wounds Burns. 2023; 49(1): 241–3.
11. Cao Y.L., Liu Z.C., Chen X.L. Efficacy of hydrosurgical excision combined with skin grafting in the treatment of deep partial-thickness and full-thickness burns: A two-year retrospective study. Burns. 2022. Available at: https://www.researchgate.net/publication/362350344_Efficacy_of_hydrosurgical_excision_combined_with_skin_grafting_in_the_treatment_of_deep_partial-thickness_and_full-thickness_burns_a_two-year_retrospective_study (accessed 07.06.2023).
12. Cenkey A., Hargitai E., Pakai E. et al. Effectiveness of four topical treatment methods in a rat model of superficial partial-thickness burn injury: the advantages of combining zinc-hyaluronan gel with silver foam dressing. Injury. 2022; 53(12): 3912–9.
13. Dobrovolskaya I.P., Yudin V.E., Popryadukhin P.V., Lebedeva I.O. In vivo study of the nanofiber-based composite wound dressing intended for treatment of deep skin wounds. J. Appl. Cosmetol. 2016; 34(1): 1–8.
14. Evdokimov V.I., Kourov A.S. Genesis of research on burn injury (analysis of domestic articles in 2005–2017). Medico-Biological Socio-Psychological Issues Saf. Emerg. Situations. 2019; 6(4): 108–20.
15. Baassiri M., Dosh L., Haidar H. et al. Nerve growth factor and burn wound healing: Update of molecular interactions with skin cells. Burns. 2022. Available at: https://www.sciencedirect.com/science/article/abs/pii/S0305417922002820?via%3Dihub (accessed 07.06.2023).
16. Gragnani A., Tonarelli E., Chomiski V. et al. Fibroblast growth factor in the treatment of burns: A systematic review. Burns. 2022; 48(1): 104–10.
17. Haik J., Segalivich M., Visentin D. et al. Comparison of stationary and dynamic fractional CO2 laser modalities of large burns treatment: Experimental laboratory model. Burns. 2021; 49(1):162–8.
18. Issler-Fisher A.C. The importance of biomechanics and the kinetic chains of human movement in the development and treatment of burn scars — A narrative review with illustrative cases. Burns. 2022; 49(3): 707–15.
19. Keyloun J.W. Assessing Factor V Antigen and Degradation Products in Burn and Trauma Patients. J. Surg. Res. 2022; 274: 169–77.
20. Muthukumar V., Dash S., Danish A. F. et al. Fibrin sealant for split-thickness skin graft fixation in burn wounds — An ancillary postulated role in scar modulation. Wound Med. 2020; 31: 00197.
21. Ozturk S., Karagoz H. Experimental stem cell therapies on burn wound: Do source, dose, timing and method matter? Burns. 2015; 41(6): 1133–9.
22. Sun T.C., Yan B.Y., Ning X.C. et al. Cool and hot chitosan/platelet-derived growth factor nanofibers for outdoors burns. Int. J. Biol. Macromol. 2022; 218: 409–19.
23. Sun T.C. Icy core–shell composite nanofibers with cooling, antibacterial and healing properties for outdoor burns. J. Colloid Interface Sci. 2023; 629: 206–16.
24. Zinovyev E.V. Experience of stem cell use in treatment of skin burns. Pediatr. 2018; 9(4): 12–27.

ЛИТЕРАТУРА

1. Алексеев А.А. Комплексное лечение глубоких ожогов на основе применения хирургической некрэктомии и современных биотехнологических методов. Анналы хирургии. 2012; 6: 41–5.
2. Зиновьев Е.В., Цыган В.Н., Арцимович И.В. и др. Экспериментальная оценка эффективности местного лечения ожогов кожи гидрогелем легкодиспергируемого карбопола 2020 с пептидом человеческого лейкозного фактора дифференцировки-6. Вестник Российской военно-медицинской академии. 2020; 3(63): 48–152.
3. Копичев О.А., Николаев А.Е. Современные войны: анализ тенденций развития межгосударственного противоборства, классификация форм и способов борьбы, формирование признаков и критериев военного конфликта. Системы управления, связи и безопасности. 2021; 32(1): 1–32.
4. Лагвилава Т.О., Зиновьев Е.В., Ивахнюк Г.К. и др. Ранозаживляющие средства на основе карбополов. Известия Санкт-Петербургского государственного технологического института (Технического Университета). 2013; 18(44): 47–52.
5. Соснина А.В., Михайлова Е.С., Аутеншлюс А.И. и др. Классы и субклассы антител к фактору диф-ференцировки HLDF и пептидам гапонина, взаимосвязь их уровня с патогистологическими параметрами аденокарцином толстой кишки. Иммунология. 2012; 2: 92–3.
6. Сысоева Г.М., Даниленко Е.Д., Масычева В.И. и др. Влияние пептида HLDF-6 на пролиферативную активность спленоцитов в культуре клеток на фоне введения агонистов опиатных рецепторов. Сибирский медицинский журнал. 2009; 4: 55–9.
7. Усков В.М., Усков М.В. Основные задачи службы медицины катастроф в условиях чрезвычайных ситуаций мирного и военного времени. Вестник Воронежского государственного технического университета. 2010. Доступен по: https://cyberleninka.ru/article/n/osnovnye-zadachi-sluzhby-meditsiny-katastrof-v-usloviyah-chrezvychaynyh-situatsiy-mirnogo-i-voennogo-vremeni (дата обращения: 07.06.2023).
8. Ali Y., Ali T. Nandrolone decanoate safely combats catabolismin burned patients: A new potential indication after recall. Burns. 2022; 48(1): 59–68.
9. Bakadia B.M., Lamboni L., Abeer A.Q. Antibacterial silk sericin/poly (vinyl alcohol) hydrogel with antifungal property for potential infected large burn wound healing: Systemic evaluation. Smart Mater. Med. 2023; 4: 37–58.
10. Behshood P., Rezaei M. A glimpse into the use of silver-nanoparticles as a promising treatment for burn wounds Burns. 2023; 49(1): 241–3.
11. Cao Y.L., Liu Z.C., Chen X.L. Efficacy of hydrosurgical excision combined with skin grafting in the treatment of deep partial-thickness and full-thickness burns: A two-year retrospective study. Burns. 2022. Available at: https://www.researchgate.net/publication/362350344_Efficacy_of_hydrosurgical_excision_combined_with_skin_grafting_in_the_treatment_of_deep_partial-thickness_and_full-thickness_burns_a_two-year_retrospective_study (accessed 07.06.2023).
12. Cenkey A., Hargitai E., Pakai E. et al. Effectiveness of four topical treatment methods in a rat model of superficial partial-thickness burn injury: the advantages of combining zinc-hyaluronan gel with silver foam dressing. Injury. 2022; 53(12): 3912–9.
13. Dobrovolskaya I.P., Yudin V.E., Popryadukhin P.V., Lebedeva I.O. In vivo study of the nanofiber-based composite wound dressing intended for treatment of deep skin wounds. J. Appl. Cosmetol. 2016; 34(1): 1–8.
14. Evdokimov V.I., Kourov A.S. Genesis of research on burn injury (analysis of domestic articles in 2005–2017). Medico-Biological Socio-Psychological Issues Saf. Emerg. Situations. 2019; 6(4): 108–20.
15. Baassiri M., Dosh L., Haidar H. et al. Nerve growth factor and burn wound healing: Update of molecular interactions with skin cells. Burns. 2022. Available at: https://www.sciencedirect.com/science/article/abs/pii/S0305417922002820?via%3Dihub (accessed 07.06.2023).
16. Gragnani A., Tonarelli E., Chomiski V. et al. Fibroblast growth factor in the treatment of burns: A systematic review. Burns. 2022; 48(1): 104–10.
17. Haik J., Segalivich M., Visentin D. et al. Comparison of stationary and dynamic fractional CO2 laser modalities of large burns treatment: Experimental laboratory model. Burns. 2021; 49(1):162–8.
18. Issler-Fisher A.C. The importance of biomechanics and the kinetic chains of human movement in the development and treatment of burn scars — A narrative review with illustrative cases. Burns. 2022; 49(3): 707–15.
19. Keyloun J.W. Assessing Factor V Antigen and Degradation Products in Burn and Trauma Patients. J. Surg. Res. 2022; 274: 169–77.
20. Muthukumar V., Dash S., Danish A. F. et al. Fibrin sealant for split-thickness skin graft fixation in burn wounds — An ancillary postulated role in scar modulation. Wound Med. 2020; 31: 00197.
21. Ozturk S., Karagoz H. Experimental stem cell therapies on burn wound: Do source, dose, timing and method matter? Burns. 2015; 41(6): 1133–9.
22. Sun T.C., Yan B.Y., Ning X.C. et al. Cool and hot chitosan/platelet-derived growth factor nanofibers for outdoors burns. Int. J. Biol. Macromol. 2022; 218: 409–19.
23. Sun T.C. Icy core–shell composite nanofibers with cooling, antibacterial and healing properties for outdoor burns. J. Colloid Interface Sci. 2023; 629: 206–16.
24. Zinovyev E.V. Experience of stem cell use in treatment of skin burns. Pediatr. 2018; 9(4): 12–27.