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Experimental substantiation of in vitro anti-radical and immunomodulating properties of injection form of drugs containing hyaluronic acid

Abstract. An in vitro experimental study was conducted to evaluate the antiradical and immunomodulatory properties of injectable formulations containing 1% and 1.4% hyaluronic acid (HA) for the prevention and correction of conditions associated with excessive free radical activity, as well as the regulation of imbalances in oxidative-reduction processes and energy metabolism. **Materials and methods.** The experiment utilized model systems generating reactive oxygen species (ROS). To assess immunomodulatory effects, oxygen-dependent metabolism and ROS generation by phagocytes were simulated. Parameters of oxygen-dependent metabolism in blood were analyzed after adding 1% and 1.4% HA preparations, both in unstimulated and zymosan-stimulated conditions. **Results.** Both HA-containing formulations significantly reduced ROS generation, indicating their ability to neutralize free radicals and protect cells from oxidative stress. The antioxidant and antiradical properties of HA correlated with decreased ROS production, suggesting utility in mitigating oxidative damage. Additionally, the 1.0% and 1.4% HA preparations enhanced immune response efficiency by elevating basal and stimulated phagocyte activity and improving their functional reserve. **Conclusion.** The findings demonstrate the high efficacy of injectable hyaluronic acid formulations (1% and 1.4%) in preventing and correcting conditions linked to excessive free radical activity and imbalances in redox processes and energy metabolism.

Key words: hyaluronic acid, phagocytic cells, neutrophils, oxidative processes, chemiluminescence, periodontal tissue

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Экспериментальное обоснование in vitro антирадикальных и иммуномодулирующих свойств инъекционной формы препаратов, содержащих гиалуроновую кислоту

Реферат. Проведено экспериментальное исследование in vitro антирадикальных и иммуномодулирующих свойств инъекционной формы препаратов, содержащих 1- и 1,4%-ную гиалуроновую кислоту, для профилактики и коррекции состояний, связанных с избыточной активностью свободных радикалов, и для регуляции состояний, связанных с дисбалансом окислительно-восстановительных процессов и энергетического метаболизма. **Материалы и методы.** Эксперимент проводился в модельных системах с генерацией активных форм кислорода (АФК). Для оценки иммуномодулирующих свойств препаратов, содержащих

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в своем составе 1,0 и 1,4% гиалуроновой кислоты, моделировали усиление кислородозависимого метаболизма фагоцитов и их генерацию АФК, параметры кислородозависимого метаболизма в крови изучали при добавлении препаратов, содержащих в своем составе 1 и 1,4% гиалуроновой кислоты, не стимулированных и стимулированных зимозаном. **Результаты.** Оба материала, содержащих гиалуроновую кислоту, приводят к значительному снижению генерации АФК, что является критерием для нейтрализации свободных радикалов и защиты клеток от повреждений, вызванных окислительным стрессом. Антиоксидантные и антирадикальные свойства препаратов, содержащих в своем составе гиалуроновую кислоту, приводят к значительному снижению генерации АФК, что может быть полезно для нейтрализации свободных радикалов и защиты клеток от повреждений, вызванных окислительным стрессом. Препараты, содержащие в своем составе 1,0 и 1,4% гиалуроновой кислоты, оказывают положительное влияние на эффективность иммунного ответа, что выражается в повышении как базальной, так и стимулированной активности, а также в увеличении функционального резерва фагоцитов. **Заключение.** Полученные данные указывают на высокую эффективность инъекционных препаратов, содержащих в своем составе 1,0 и 1,4% гиалуроновой кислоты, для профилактики и коррекции состояний, связанных с избыточной активностью свободных радикалов, и для регуляции состояний, связанных с дисбалансом окислительно-восстановительных процессов и энергетического метаболизма.

Ключевые слова: гиалуроновая кислота, фагоцитарные клетки, нейтрофилы, оксидативные процессы, хемолюминесценция, пародонт

ДЛЯ ЦИТИРОВАНИЯ:

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INTRODUCTION

Hyaluronic acid is a natural polysaccharide, an anionic sulfate-free glycosaminoglycan, and is the main component of the extracellular matrix and gingival fluid [1, 2], has the ability to absorb water, swell in tissues [3], restore tissue loss, is a powerful anti-inflammatory agent [4, 5], modulates wound healing due to its ability to destroy reactive oxygen species formed as a result of the activity of inflammatory cells [2, 6, 7]. It is capable of stimulating the generation of active forms of oxygen by phagocytes, which ensures the effective implementation of the immune response, since oxidative processes are an important link in the biocidal apparatus of the cellular link of the immune system [8]. Hyaluronic acid can regulate the inflammatory response by acting as an antioxidant, neutralizing excess amounts of reactive oxygen species [9].

Currently, non-surgical methods of treating periodontal tissues are particularly relevant, including the application of gel or spray to the mucous membrane [4], injections into the transitional fold or into the interdental papillae [5, 9], and local treatment of chronic periodontitis [10].

In a systematic review by S.B. Alsharif and B. Aljahdali (2024) provide convincing data on the effectiveness of various methods, assess their safety, and provide data on the results of injections of different concentrations of hyaluronic acid in the treatment of black triangles and restoration of lost interdental papilla in the anterior teeth [9], V. Mehta, et al. (2019) provided data on the effectiveness of hyaluronic acid in the treatment of patients with gingival recession [11]. When forming an experimental model of periimplantitis, the introduction of calcium hydroxyapatite and β-tricalcium phosphate modified with hyaluronic acid into the peri-implant area contributed to the rapid regeneration of the postoperative jaw defect [12]. When introducing hyaluronic acid fillers for the reconstruction of multiple papillae losses, Z. Turgut Çankaya and E. Tamam (2020) provided convincing evidence of their effectiveness in the dynamics of clinical observation [13]. A randomized clinical trial conducted by R. Kumar, et al. (2014) provides data on the effectiveness of 0.2% hyaluronic acid gel in a complex consisting of root coverage and the use of a coronally advanced flap [14]. Various randomized controlled clinical trials have shown convincing results of the use of hyaluronic acid in the coronally advanced flap procedure in the treatment of gingival recession of Miller class I recession [15—17].

Samanta S., et al. (2022) created a hydrogel for use in regenerative medicine based on hyaluronic acid, crosslinked with hydrazone and functionalized with gallol, which has pronounced viscoelastic and immunomodulatory, antioxidant properties, protects encapsulated fibroblasts from peroxide exposure, and gives them antioxidant properties to suppress oxidative stress [18]. Based on the above, it becomes obvious that the task of reducing the inflammatory process in the gum, closing the black triangles of the gum, preventing and treating peri-implantitis is complex, i.e. it consists in achieving an antiradical and immunomodulatory effect in the gum tissues due to the influence of 1% or 14% injectable hyaluronic acid. According to the available data on the characteristics and properties of hyaluronic acid, the antiradical and immunomodulatory characteristics remain poorly understood, in this regard, their study in vitro may be of particular interest, which determined the relevance and purpose of our study.

The aim of the study is to evaluate in model systems the antiradical and immunomodulatory properties of the injectable form of drugs containing 1.0% and 1.4% hyaluronic acid for the prevention and correction of conditions associated with excessive activity of free radicals and for the regulation of conditions associated with an imbalance of oxidation-reduction processes and energy metabolism.

MATERIALS AND METHODS

The study used in vitro methods aimed at assessing the antiradical and immunomodulatory properties of drugs containing 1% and 1.4% hyaluronic acid.

To evaluate the immunomodulatory and antiradical properties of the studied preparations containing 1% and 1.4% hyaluronic acid, a chemiluminescent method (CL) was used on the CL-003 device (Ufa, Russia). The device measures radiation with a wavelength of 300—600 nm, the sensitivity is 10^4—10^7 photon/s. ZhS-19 (uranium yellow glass) emitting light in the visible region of the spectrum and calibrated in absolute units (quantum/s·4p·mg) using a standard radioluminescent source was used as a standard for assessing the CL intensity. The standard is made in the form of a parallelepiped measuring 5×8×8 mm and weighing within 581—614 mg. The glow intensity of the standard is $5.1 \cdot 10^5$ quantum/s, which was taken as one conventional unit.

Antiradical activity was studied in model systems with generation of reactive oxygen species (ROS). The system included a phosphate buffer (20 mmol KH_2PO_4, 105 mmol KCl, pH 7.45), 50 mmol sodium citrate and luminol (10^{-4} M solution in DMSO, added in an amount of 0.2 ml per 1 liter of the system). 0.1 ml of the preparation (1% and 1.4% hyaluronic acid) was added to a sample of the model system (20 ml), and ROS hyperproduction was initiated by adding 1 ml of a 50 mmol $FeSO_4 \cdot 7H_2O$ solution.

Chemiluminescence kinetics is recorded using a computer interface. A special program processes signals received from the device in a time interval determined by the researcher. The entire process of chemiluminescence measurement and results processing is carried out automatically, which allows for increased accuracy and objectivity of the information obtained. The program determines the following chemiluminescence parameters: light sum, spontaneous luminosity, flash, maximum luminosity, and curve slope. The light sum (S) and maximum amplitude of the slow flash (I_{max}) were taken as the most informative chemiluminescence parameters. During the study, the sample temperature was maintained at 37°C by an ultrathermostat.

To evaluate the immunomodulatory properties of preparations containing 1% and 1.4% hyaluronic acid, we modeled the enhancement of oxygen-dependent metabolism of phagocytes and their generation of ROS. For this purpose, we used whole heparinized blood collected in the morning from the cubital veins of patients using a standard technique. Blood with heparin (50 units/ml) was placed in the wells of a 96-well plastic plate. Spontaneous (basal) and induced levels of metabolism of phagocytic cells were assessed. To induce oxygen-dependent metabolism, 0.01 ml of zymosan suspension (a biopolymer from yeast cell membranes based on glucan) in physiological saline was added to the wells and incubated at 37°C for 15 minutes.

Oxygen-dependent metabolism, which characterizes the accumulation of reactive oxygen species (ROS), was determined using luminol-dependent chemiluminescence (LDCL). 0.1 ml of whole blood was added to 2 ml of physiological solution (0.9% NaCl, pH 7.2) with the addition of 10^{-5} M luminol, after which CL was measured for 3 minutes. LDCL mainly reflects the generation of ROS by neutrophils. As a result, six preparations were studied: blood with 1% hyaluronic acid (with and without the addition of zymosan), blood with 1.4% hyaluronic acid (with and without the addition of zymosan), whole blood, and blood with zymosan. The study continued according to the BLOOD program on the CL-003 device, with the following parameters: “Thermostat on”, “Stirrer off”, “Measurement time 10 min.”

Two CL parameters were analyzed: the light sum (S), reflecting the integral luminescence intensity, and the slow flash amplitude (I), characterizing the luminosity maximum. These indicators evaluate the absolute parameters of oxygen-dependent metabolism. To evaluate the potential of the phagocytic link, reserve capabilities were additionally calculated. This indicator (X) was determined as the difference between the maximum intensity of induced luminescence and spontaneous luminescence, evaluating their ratio:

$$X = \frac{I_{ind} - I_{sp}}{I_{sp}},$$

where I_{ind} is the maximum intensity of induced blood glow, I_{sp} is the maximum intensity of spontaneous blood glow.

The results of the experiments were expressed in conventional units (1 c.u.=$5.1 \cdot 10^5$ quantum/s) and recalculated as percentages relative to the control group.

In statistical processing the Student—Welch test was used to compare the means.

RESULTS

The preparation containing 1% and 1.4% hyaluronic acid was tested on a model system for measuring chemiluminescence, which allows assessing the level of generation of active oxygen species (ROS). During the experiment, two key parameters were studied: light sum (S) and slow flash amplitude (I), which characterize the intensity and peak activity of oxidative processes, respectively (table 1).

Table 1. Chemiluminescence parameters of the model system for generating active forms of oxygen with the addition of preparations containing 1% and 1.4% hyaluronic acid

	Blood control	Hyaluronic acid 1%	p	Hyaluronic acid 1.4%	p	p_1
Light sum	18.44±1.54	15.01±0.71	0.044	13.33±0.66	0.003	0.085
Slow flash amplitude	13.23±0.80	11.46±0.39	0.048	11.20±0.24	0.016	0.571

Remark. p — p-level of comparison with control samples, p_1 — p-level of comparison between the studied samples of the preparation.

The control sample was phosphate buffer without the addition of the studied preparations. The experiment was carried out on 96 samples (using the appropriate palettes) for hyaluronic acid preparations and for phosphate buffer, which served as a control.

In the control samples (n=96), the chemiluminescence parameters of the model ROS generation system were as follows: the luminescence light sum was 18.44 (fig. 1, an area under the black curve), and the slow flash amplitude was 13.23. These parameters reflect the baseline level of generation of active oxygen forms in the studied system. After adding the preparation containing 1% hyaluronic acid, the luminescence parameter values significantly decreased: the light sum dropped to 15.01 (p<0.05; fig. 1, an area under the blue curve), and the amplitude to 11.46 (p<0.05). When adding a preparation containing 1.4% hyaluronic acid, a significant decrease in the luminescence parameters was noted: the light sum dropped to 13.33 (p<0.01; fig. 1, an area under the green curve), and the amplitude to 11.20 (p<0.05). These changes were statistically significant, indicating a pronounced antioxidant effect of the preparation, while no significant differences were found between samples of 1 and 1.4% hyaluronic acid

A decrease in the light sum indicates a decrease in the total number of generated free radicals, which indicates the ability of preparations containing hyaluronic acid to suppress oxidative processes. At the same time, a decrease in the amplitude of the slow flash reflects the suppression of intense peaks of free radical generation. Both effects indicate that the preparations actively reduce the level of radical processes in the model system. Thus, the study confirms the antioxidant and antiradical properties of preparations containing hyaluronic acid. Their use leads to a significant decrease in the generation of active oxygen species, which can be useful for neutralizing free radicals and protecting cells from damage caused by oxidative stress.

According to R.J. Waddington, et al. (2000), hyaluronic acid can regulate the inflammatory response by acting as an antioxidant, burning active forms of oxygen, and has pronounced free-radical and antioxidant activity [19], which substantiates the results of our experimental study.

The key factor in the influence of injectable preparations containing 1% and 1.4% hyaluronic acid is the induction of reactive oxygen species and other free radicals [2, 20], which is consistent with the data of our study.

The study of the immunomodulatory activity of a blood preparation containing 1% and 1.4% hyaluronic acid revealed the following patterns, which were reflected in the parameters of oxygen-dependent blood metabolism in the form

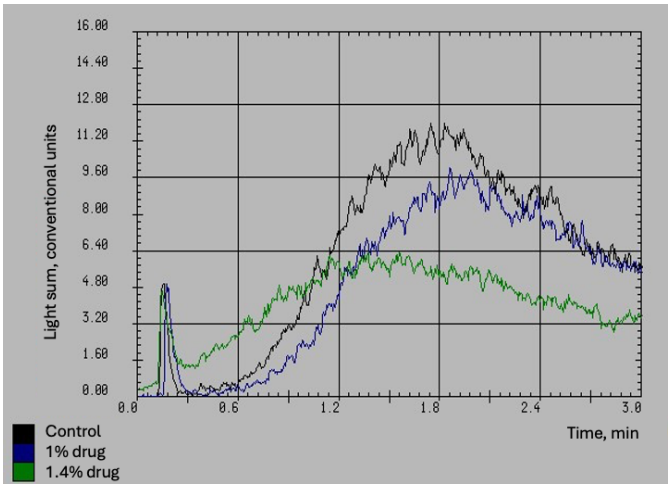

Fig. 1. Chemiluminescence indices of the model system for generating active forms of oxygen with the addition of 1 and 1.4% hyaluronic acid for one sample (the light sum index (area under the curve) is analyzed)

of changes in the spontaneous chemiluminescence light sum (S_{sp}). The parameters describing the ability of cells to activate and generate reactive oxygen species (ROS) are presented in the form of zymosan-stimulated light sum (S_{ind}) for preparations containing 1 and 1.4% hyaluronic acid (table 2).

Addition of the preparation containing 1% hyaluronic acid to blood samples has a significant effect on the parameters of oxygen-dependent metabolism of phagocytes, which is confirmed by changes in the spontaneous (S_{sp}) and stimulated (S_{ind}) chemiluminescence light sum indices (table 2). The basal level of oxidative metabolism (S_{sp}), which reflects the overall functional and metabolic activity of phagocytes, increased from 0.45 in control samples to 0.71 (p<0.05). This increase demonstrates the ability of the preparation to activate phagocytes even under resting conditions. Stimulated light sum (S_{ind}), which describes the ability of cells to become activated and generate reactive oxygen species (ROS) in response to stimulation, also increased under the influence of the drug: from 0.85 in control samples to 0.93 (p=0.089).

When adding the preparation containing 1.4% hyaluronic acid to blood samples, the basal level of oxidative metabolism (S_{sp}) increased from 0.45 in the control samples to 0.74 (p<0.05), and the stimulated light sum (S_{ind}) also increased under the influence of the preparation: from 0.85 in the control samples to 0.94 (p<0.05).

In addition, the statistically significant difference between S_{sp} and S_{ind} when adding the preparation containing

Table 2. Parameters of oxygen-dependent metabolism in the blood with the addition of preparations containing 1% and 1.4% hyaluronic acid, unstimulated and stimulated by zymosan

	Blood control	Hyaluronic acid 1%	p	Hyaluronic acid 1.4%	p	p_1
S_{sp}, without stimulation	0,45±0,11	0,71±0,07	0,048	0,74±0,09	0,043	0,793
S_{ind}, zymosan stimulation	0,85±0,04	0,93±0,03	0,089	0,94±0,03	0,049	0,808
p_2	<0,001	0,036		0,004		

Remark. p — p-level of comparison with control samples, p_1 — p-level of comparison between the studied samples of the preparation; p_2 — p-level of difference in the light sum, unstimulated and stimulated by zymosan.

Table 3. Functional reserve of phagocytes in the blood

	Blood control	Hyaluronic acid 1%	*p*	Hyaluronic acid 1.4%	*p*	p_1
S_{sp}, without stimulation	1,01±0,02	1,05±0,03	0,269	1,24±0,05	<0,001	0,001
S_{ind}, zymosan stimulation	1,22±0,05	1,35±0,06	0,091	1,60±0,16	0,025	0,145
p_2	<0,001	<0,001		0,033		

Remark. p — p-level of comparison with control samples, p_1 — p-level of comparison between the studied samples of the preparation; p_2 — p-level of difference in the light sum, unstimulated and stimulated by zymosan.

1% and 1.4% hyaluronic acid ($p<0.05$) indicates an increase in the reserve capacity of phagocytes, which indicates the development of more pronounced functional activity of cells. No significant differences in the spontaneous or stimulated light sum were found between the preparations with 1% and 1.4% hyaluronic acid ($p>0.2$).

Based on the data obtained by B. Safrankova, et al. (2010), the production of active forms of oxygen by phagocytes is associated with the so-called "oxidative burst", which is a key process in the fight against invading pathogens [8], according to H. Yamawaki, et al. (2009), hyaluronic acid exhibits a stimulating effect on blood phagocytes, as well as on other types of cells [21], which is consistent with the data obtained in our study.

Thus, the data we obtained through an in vitro experiment, the drug containing 1.0% and 1.4% hyaluronic acid in its composition has immunomodulatory properties, their action enhances both basal and activated oxidative metabolism of phagocytes, which is associated with the ability to stimulate the functional state of cells of the phagocytic system, which is consistent with the data of I. Niemietz, et al. (2020) that hyaluronic acid stimulates an oxidative burst in human neutrophils [22]. To reveal this trend, a subsequent analysis of the chemiluminescence parameters was carried out, namely the amplitude of the slow flash, on the basis of which the functional reserve of phagocytes is calculated (table 3).

Based on the presented data, it is possible to estimate the effect of preparations containing 1.0% and 1.4% hyaluronic acid on the functional reserve of blood phagocytes, an indicator characterizing the ability of phagocytes to pass from a resting state to an activated state. The functional reserve is calculated as the difference between the amplitude of the slow flash under stimulated (I_{ind}) and spontaneous (I_{sp}) conditions. The functional reserve of phagocytes, defined as the percentage increase in phagocyte activity after stimulation, increases on average from 21% in the control group to 35% with the addition of a preparation containing 1.0% hyaluronic acid, and to 60% with the addition of a preparation containing 1.4% hyaluronic acid (fig. 2). The effect of preparations containing 1 and 1.4% hyaluronic acid on oxygen-dependent blood metabolism, an increase in Ssp and Sind indicates its regulatory effect (table 3), which may be useful for stimulating antioxidant mechanisms.

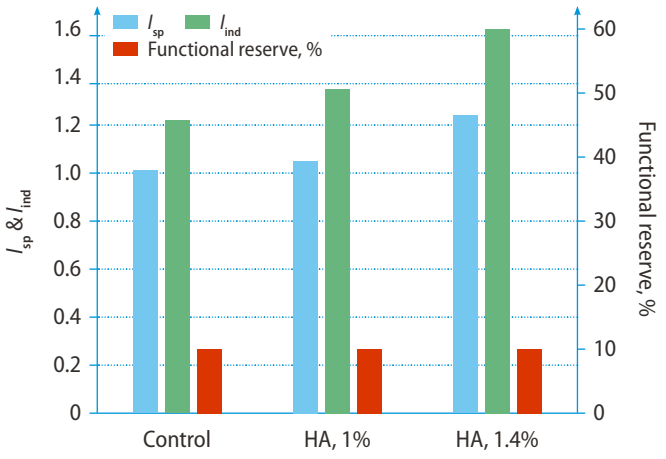

Fig. 2. Comparative characteristics of the average functional reserve of phagocytes in the blood with the addition of injectable preparations containing 1 and 1.4% hyaluronic acid

The growth of the functional reserve indicates an increase in the ability of the phagocytic system to activate in response to stimuli, which indicates a potential immunomodulatory effect of the drug. Thus, the obtained results show that drugs containing 1.0% and 1.4% hyaluronic acid have a positive effect on the effectiveness of the immune response, which is expressed in an increase in both basal and stimulated activity, as well as an increase in the functional reserve of phagocytes. This suggests that the use of the studied drugs can help enhance the protective functions of the body. Drugs containing hyaluronic acid in their composition, in given concentrations, affect the oxygen-dependent metabolism of the blood, which demonstrates a significant increase in the luminescence indices of blood cells during their stimulation and indicates their regulatory effect, which can be useful for activating antioxidant mechanisms and maintaining cellular energy.

CONCLUSION

The obtained experimental data in model systems open up possibilities for the use of injectable preparations containing 1 and 1.4% hyaluronic acid for the prevention and correction of conditions associated with excessive activity of free radicals and for the regulation of conditions associated with an imbalance of oxidation-reduction processes and energy metabolism.

As a result of the studies, it was found that preparations containing 1.0 and 1.4% hyaluronic acid in the specified concentrations do not reduce the functional capacity of phagocytes.

Thus, preparations containing hyaluronic acid in a concentration of 1.0 and 1.4% have antioxidant properties, while not inhibiting the formation of active oxygen forms in phagocytic blood cells, which allows them to be used in inflammatory processes without causing the risk of inhibition of oxygen-dependent mechanisms of phagocytosis.

Based on the presented data, it can be concluded that preparations containing 1.0 and 1.4% hyaluronic acid have a positive effect on the functional activity of phagocytes, primarily neutrophils, which play a key role in the implementation of physiological mechanisms of the immune response

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REFERENCES:

1. **Dahiya P., Kamal R.** Hyaluronic acid: a boon in periodontal therapy. *N Am J Med Sci*. 2013; 5 (5): 309—15. PMID: 23814761
2. **Berdiaki A., Neagu M., Spyridaki I., Kuskov A., Perez S., Nikitovic D.** Hyaluronan and reactive oxygen species signaling novel cues from the matrix?*Antioxidants (Basel)*. 2023; 12 (4): 824. PMID: 37107200
3. **Attenello N.H., Maas C.S.** Injectable fillers: review of material and properties. *Facial Plast Surg*. 2015; 31 (1): 29—34. PMID: 25763894
4. **Efimovich O.I.** Using hyaluronic acid preparations in complex treatment of inflammatory diseases of the parodont. Literature review. *Clinical Dentistry (Russia)*. 2018; 1 (85): 28—33 (In Russian). DOI: 10.37988/1811—153X_2018_1_28
5. **Orekhova L.Yu., Loboda E.S., Yamanidze N.A., Galeeva A.R.** The use (application) of hyaluronic acid in complex treatment of periodontal diseases. *Parodontologiya*. 2018; 3 (88): 25—30 (In Russian). DOI: 10.25636/PMP.1.2018.3.4
6. **Moseley R., Waddington R.J., Embery G.** Hyaluronan and its potential role in periodontal healing. *Dent Update*. 2002; 29 (3): 144—8. PMID: 11989392
7. **Lee J.H., Lee K.E., Kang S.W., Park S.H., Chae Y.K., Lee M.H., Kweon D.K., Choi S.C., Nam O.H.** Effect of orodispersible hyaluronic acid film on palatal mucosa wound healing. *Oral Dis*. 2024; 30 (2): 518—527. PMID: 36691707
8. **Safrankova B., Gajdova S., Kubala L.** The potency of hyaluronan of different molecular weights in the stimulation of blood phagocytes. *Mediators Inflamm*. 2010; 2010: 380948. PMID: 21403830
9. **Alsharif S.B., Aljahdali B.** The use of hyaluronic acid injection for treatment of black triangle and reconstruction of lost interdental papilla in anterior teeth: a systematic review. *Acta Odontol Scand*. 2024; 83: 371—391. PMID: 38864684
10. **Al-Shammari N.M., Shafshak S.M., Ali M.S.** Effect of 0.8% hyaluronic acid in conventional treatment of moderate to severe chronic periodontitis. *J Contemp Dent Pract*. 2018; 19 (5): 527—534. PMID: 29807962
11. **Mehta V., Kaçani G., Moaleem M.M.A., Almohammadi A.A., Alwafi M.M., Mulla A.K., Alharbi S.O., Aljayyar A.W., Qeli E., Toti Ç., Meto A., Fiorillo L.** Hyaluronic acid: A new approach for the treatment of gingival recession – A systematic review. *Int J Environ Res Public Health*. 2022; 19 (21): 14330. PMID: 36361208
12. **Sirak S.V., Rubnikovich S.P., Grigor'yanc L.A., Garunov M.M., Didenko M.O., Kochkarova Z.M., Andreev A.A.** The influence of calcium hydroxyapatite and tricalcium phosphate, modified hyaluronic acid on the regeneration of bone tissue of the alveolar process of the jaw in experimental periimplantitis. *Clinical Dentistry (Russia)*. 2019; 4 (92): 61—65 (In Russian). DOI: 10.37988/1811-153X_2019_4_61
13. **Turgut Çankaya Z., Tamam E.** An examination of the 2-year results obtained from hyaluronic acid filler injection for interdental papilla losses. *Quintessence Int*. 2020; 51 (4): 274—284. PMID: 32020128
14. **Kumar R., Srinivas M., Pai J., Suragimath G., Prasad K., Polepalle T.** Efficacy of hyaluronic acid (hyaluronan) in root coverage procedures as an adjunct to coronally advanced flap in Millers Class I recession: A clinical study. *J Indian Soc Periodontol*. 2014; 18 (6): 746—50. PMID: 25624632
15. **Pilloni A., Schmidlin P.R., Sahrmann P., Sculean A., Rojas M.A.** Effectiveness of adjunctive hyaluronic acid application in coronally advanced flap in Miller class I single gingival recession sites: a randomized controlled clinical trial. *Clin Oral Investig*. 2019; 23 (3): 1133—1141. PMID: 29961138
16. **Nandanwar J., Bhongade M.L., Puri S., Dhadse P., Datir M., Kasatwar A.** Comparison of effectiveness of hyaluronic acid in combination with polylactic acid/polyglycolic acid membrane and subepithelial connective tissue graft for the treatment of multiple gingival recession defects in human: A clinical study. *Journal of Datta Meghe Institute of Medical Sciences University*. 2018; 13: 48—53.
17. **Brignardello-Petersen R.** Hyaluronic acid used as an adjunct to coronally advanced flap probably results in an increase in recession reduction and root coverage in patients with single Miller class I gingival recessions. *J Am Dent Assoc*. 2019; 150 (1): e12. PMID: 30193902
18. **Samanta S., Rangasami V.K., Sarlus H., Samal J.R.K., Evans A.D., Parihar V.S., Varghese O.P., Harris R.A., Oommen O.P.** Interpenetrating gallol functionalized tissue adhesive hyaluronic acid hydrogel polarizes macrophages to an immunosuppressive phenotype. *Acta Biomater*. 2022; 142: 36—48. PMID: 35085799
19. **Ke C., Sun L., Qiao D., Wang D., Zeng X.** Antioxidant acitivity of low molecular weight hyaluronic acid. *Food Chem Toxicol*. 2011; 49 (10): 2670—5. PMID: 21787831
20. **Zeichner J., Bussmann T., Weise J.M., Maass E., Krüger A., Schade A.K., Lain E., Mariwalla K., Kirchner F., Draelos Z.D.** Evaluation of Antioxidants› Ability to Enhance Hyaluronic-acid Based Topical Moisturizers. *J Clin Aesthet Dermatol*. 2024; 17 (3): 48—51. PMID: 38495545
21. **Yamawaki H., Hirohata S., Miyoshi T., Takahashi K., Ogawa H., Shinohata R., Demircan K., Kusachi S., Yamamoto K., Ninomiya Y.** Hyaluronan receptors involved in cytokine induction in monocytes. *Glycobiology*. 2009; 19 (1): 83—92. PMID: 18854367
22. **Niemietz I., Moraes A.T., Sundqvist M., Brown K.L.** Hyaluronan primes the oxidative burst in human neutrophils. *J Leukoc Biol*. 2020; 108 (2): 705—713. PMID: 32421905