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DEVELOPMENT OF DERMATOLOGICAL MEDICINAL FILMS TECHNOLOGY OF COMPLEX ACTION

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ABSTRACT

The article presents the results of research on the development of the optimal composition and technology of dermatological films of complex action, including those containing methyluracil, which stimulates regenerative processes, the antibacterial substance chloramphenicol, and chlorhexidine, which has an antiseptic effect. The nature of the interaction that occurs in the studied films between medicinal substances and a solution of the film-forming polymer Na-CMC has been studied. Using microbiological methods, the antibacterial activity of the recommended films was studied and it was found that they exhibit pronounced antimicrobial activity **against**: St. aureus, E. coli, Ps. aeruginosa, C. Albicans. Methods have been developed for the quantitative determination of the active substances of films of complex action by the method of high-performance liquid chromatography.

Keywords: dermatological polymer films, methyluracil, chlorhexidine, chloramphenicol, film-forming polymer Na-CMC.

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本文介绍了开发具有复杂作用的皮肤病薄膜的最佳成分和技术的研究结果，其中包括含有刺激再生过程的甲基尿嘧啶、抗菌物质氯霉素和具有杀菌作用的氯己定的薄膜。已经研究了药物与成膜聚合物 Na-CMC 溶液之间在所研究的薄膜中发生的相互作用的性质。使用微生物学方法研究了推荐薄膜的抗菌活性，发现它们对以下物质表现出明显的抗菌活性： 金黄色葡萄球菌、大肠杆菌、Ps。铜绿假单胞菌，C. 白色念珠菌。已经开发了通过高效液相色谱法定量测定复合作用膜的活性物质的方法。

关键词：皮肤科聚合物薄膜，甲基尿嘧啶，氯己定，氯霉素，成膜聚合物Na-CMC。

INTRODUCTION

The most common damage to the skin is all kinds of wounds, cuts, abrasions. Successful treatment of these pathologies in the shortest possible time without purulent complications is possible with the use of not only antibacterial, antiseptic drugs, but also agents that accelerate the regenerative processes in the wound. The guarantee of the success of the therapy of wound pathology is the correct choice of the dosage form and the creation of favorable conditions for epithelialization. The solution to this issue is inextricably linked with the use of a special class of dosage forms - wound dressings. The expansion of the range of wound dressings was facilitated by the creation of fundamentally new agents based on synthetic and natural polymers. Currently, wound dressings in various forms have been developed and are widely used (films, film-forming compositions, dressings, sponges, hydrocolloids, hydrogels, foam nano-fibers, combinations of various materials, containing medicinal substances that have antimicrobial, wound healing effect [1,2,3,4,5,6,7,8]. Among them, film coatings on the wound are of particular interest. The use of medicinal films based on soluble polymers is the most promising alternative to textile-based dressings and traditional dosage forms (ointments, gels, pastes, solutions), since they ensure dosing accuracy, stability, high concentration of active substances in the pathological zone, protection of the wound from external influences. Being well fixed on the wound surface, they adhere tightly to it; provide the required vapor exchange, as a result of which they are very effective for the treatment of wounds in the stage of epithelialization, as well as for the treatment of minor traumatic injuries. In addition, film coatings provide the possibility of non-contact visual monitoring of the wound, are comfortable to wear, and easy to handle [5,7,8,9,10]. The review [11] provides a classification of modern coatings for wound healing, including films, foams, hydrogels, and hydrocolloids.

The effectiveness of wound therapy is largely associated with the use of a combination of drugs, primarily suppressing the development of microorganisms, as well as providing targeted stimulation of the process of cellular regeneration in wounds. Currently, the results of numerous studies have proven the effectiveness of such a combination in ointments, gels, wound dressings, dermatological polymer films [12,13,14]. Taking into account the prospects of using all kinds of coatings on wounds in the form of films for effective treatment of the wound process, at present, wound-healing film coatings

have been developed, containing, as a rule, a complex of medicinal substances [7, 10]. In this regard, it is urgent to create films of complex action, including antibacterial, antiseptic medicinal substances, as well as agents that promote the healing of wound surfaces.

Methyluracil is widely used in the composition of ointments, gels and other applied dosage forms that primarily have a wound healing effect, which is one of the effective medicinal substances that affect biochemical and reparative processes in the treatment of wounds, improve tissue trophism, stimulate the process of cellular regeneration in wounds, thereby contributing to the acceleration of epithelialization. Known wound healing plates "Meturakol" containing methyluracil on a collagen basis [15]. The complex use of methyluracil with antibacterial and antiseptic agents allows, with the simultaneous suppression of the growth of residual microflora in it, to provide targeted stimulation of reparative processes in the wound. Thus, the studies of T.F. Marinina et al. proved the effectiveness of polymer dental medicinal films with chloramphenicol and methyluracil [16]. Known ointments that have a wound-healing effect, containing a combination of methyluracil and chloramphenicol, "Levomekol" and "Levosin", are now successfully used for the treatment of wounds.

Antiseptic agents also have a positive effect on the course of the wound process, among which chlorhexidine is the most widely used, which is active against gram-positive, gram-negative microorganisms, yeast, aerobic and anaerobic bacteria that got on the surface of the wound as a result of contamination [17]. Currently, chlorhexidine is used in various polymer films, antimicrobial wipes [4,18,19]. For example, in order to increase the effectiveness of wound treatment, a hydrophilic film coating has been developed on the wound, containing the antiseptic chlorhexidine bigluconate and lysozyme, providing a complex effect on the wound surface [13]. The use of complex films containing chlorhexidine and the anesthetic trimecaine for the successful treatment of tissue damage in the maxillofacial region has also been shown to be promising [20]. Chlorhexidine was also used in the composition of dental films of complex action [18,21].

Considering that research aimed at the creation of domestic complex preparations in the form of polymer films for the treatment of wounds is topical, the purpose of the study was to develop the composition and technology of dermatological medicinal films of complex action containing methyluracil, which stimulates regenerative processes, the antibacterial substance chloramphenicol, and chlorhexidine, which has an antiseptic effect.

The combination of the above medicinal substances included in the composition of the films was selected based on the recommendation of pharmacologists and data from literary sources regarding the effective treatment of various wound pathologies [27,28].

MATERIALS AND METHODS

The studies used medicinal substances and excipients that meet the requirements of regulatory documentation: European Pharmacopoeia 8th Edition [22]: chlorhexidine bigluconate [07/2013:0658)], chloramphenicol (chloramphenicol) [01/2008: 0071], methylcellulose (MC) [01/2014:0345], polyvinylpyrrolidone (PVP) [07/2011:0685).] Sodium carboxymethylcellulose (Na-CMC) - European Pharmacopoeia 3rd Edition - 1997:

0472. - P.547-548, gelatin [SP X ed., Art. 331], glycerol-PAP42 Uz-29399767-2020.

In the experiments, the methods of studying the films were used: appearance, potentiometric determination of pH, weight loss on drying, determination of antimicrobial activity, dissolution time given in the regulatory documentation: State Pharmacopoeia of the Russian Federation. - 14th ed.: 2018, BPA.1.4.1.0035.18. - Films in literature sources [23-26].

To study the compatibility of the components that make up the film and study the mechanism of interaction of drugs with the polymer, UV spectrophotometry and IR spectroscopy were used. The high performance liquid chromatography (HPLC) method was used for the quantitative determination of the active substances in the films. The solution method was used to form polymer films [24, 25].

The initial stage in the creation of films was the substantiation of the concentration of active substances in them. When solving this problem, we were guided by the recommendations of pharmacologists and took into account their average therapeutic concentrations in other dosage forms (ointments, gels). We also took into account the solubility of the drugs used and their limiting content, which did not lead to crystallization after the formation of films. For this purpose, with each of the medicinal substances, experimental film masses were obtained with different contents of chloramphenicol, methyluracil and chlorhexidine. The study of the properties of the films formed from them showed that an excess of the concentration of methyluracil more than 0.08%, chloramphenicol more than 0.04% and chlorhexidane more than 0.02% led, after drying the film mass, to the appearance on the surface of the films of particles of these medicinal substances as a result of their crystallization.

In order to study the compatibility of medicinal substances included in the films, a solution was prepared containing chloramphenicol, methyluracil and chlorhexidine bigluconate. Compatibility was judged by changes in such parameters as appearance (color change, presence of sediment), pH and maximum UV absorption spectrum of the solution. The results of studying these indicators of the initial, as well as after 7 and 15 days of storage are shown in Table 1.

Table 1
The results of studying the compatibility of methyluracil, chloramphenicol and chlorhexidine in a joint solution

Studied indicators	Initial	After 7 days	After 15 days
Appearance	Transparent, Colorless solution	Transparent, Colorless solution	Transparent, Colorless solution
pH value	6.64	6.65	6.65
UV absorption maximum	261 ± 1nm	261±1nm	261±1nm

The research results found that in the solution containing the above medicinal substances, no changes were noted in the studied parameters, which gave grounds to draw a conclusion about their compatibility with each other.

Since the physicomechanical characteristics and biopharmaceutical properties of films are determined by the nature of the film-forming polymer, the next stage of research was the study of various polymers widely used in polymer film technology, such as MC, Na-CMC, gelatin, PVP

in order to choose the optimal one for the formation of films. For this, model film masses were prepared, the compositions of which are shown in Table 2.

The preparation of model film masses and the formation of films were obtained by the known solution method [24, 25]. In this case, medicinal substances were previously dissolved in water and the resulting solution was used to dissolve polymers. In all film masses, 1% glycerin was added as a plasticizer. The homogenization process was carried out for 30 min using a MS-H280-ProMagnetic Stirrer magnetic stirrer. Films were formed from a homogenized film mass by pouring onto special substrates and subsequent drying at a temperature of 25-30^{0}C to the optimal residual moisture content.

The obtained polymer films were separated from the substrates and evaluated by their appearance, homogeneity, dissolution time and pH value, and the ability to lag behind the substrate according to the methods given in the normative documentation and literature [23-26]. The research results are shown in Table 3.

Table 2

Compositions of the studied film masses containing chloramphenicol, methyluracil and chlorhexidine

Components, g / Compositions	1	2	3	4
Levomycetin	0.04	0.04	0.04	0.04
Methyluracil	0.08	0.08	0.08	0.08
Chlorhexidine	0.02	0.02	0.02	0.02
Na-CMC	2.0	-	-	-
MC	-	2.8	-	-
PVP	-	-	10.0	-
Gelatin	-	-	-	10.0
Glycerol	1.0	1.0	1.0	1.0
Purified water	Up to 100	Up to 100	Up to 100	Up to 100

Table 3

Results of studying indicators of polymer films containing methyluracil, chlorhexidine and chloramphenicol

Composition №	Studied indicators			
	Appearance	Ability to lag behind substrate surface	Dissolution time, min	pH value
1	Films, elastic, transparent	Easily lagged behind the substrate surface	20-30	6.5-7.5
2	Films, elastic, transparent	Easily lagged behind the substrate surface	35-40	6.5-6.8
3	Films are transparent, but not elastic	lagged behind the substrate surface with difficulty	10-18	5.0-6.0
4	Films are transparent, but not elastic	lagged behind the substrate surface with difficulty	20-25	6.0-6.9

RESULTS AND DICUSSION

The results of the study showed that the films formed according to the composition № 1 and № 2 had satisfactory performance, both in appearance and in the ability to lag behind the substrate surface. However, the films obtained according to the composition № 1 had the best indicators in terms of dissolution time. Films obtained according to compositions № 3 and № 4 did not have sufficient elasticity, were brittle at the edges. The dissolution time of the prepared films was in the range of 10-40 minutes, and the pH value was in the range of 5.0-7.5, depending on the polymer used. Taking into account the results obtained, the first composition of the film mass was selected for further research, containing Na-CMC as a film-forming substance. In the experiments, we used Na-CMC brand Na-CMC (BLANOZECMC 7 HOFPH).

During the formation of films between medicinal substances and the polymer, various kinds of interactions are possible. Based on this, it was of interest to study the nature of the interaction that occurs in the studied films between medicinal substances and the solution of the film-forming polymer Na-CMC. During the research, the methods of UV spectrophotometry and IR spectroscopy were used. For this purpose, solutions were prepared containing medicinal substances and Na-CMC polymer, which were studied for 30 days according to the following indicators: the appearance of the solution, the pH value, and the maximum absorption of the UV spectrum. The research results showed that there were no changes in the appearance of the solution: the solutions remained colorless and transparent during the observation period. There were also no significant changes in the pH value and the maximum absorption of the UV spectrum of the solutions (Table 4), which may indicate that no changes in the chemical nature between the components of the films were observed.

Table 4
Results of studying the properties of model solutions of medicinal substances with the polymer Na-CMC

Composition of the model solution	Indicators					
	Maximum absorption of the UV spectrum, nm			pH		
	Initial	After 7 days	After 30 days	Initial	After 7 days	After 30 days
Levomycetin with Na-CMC	279	279	279	7.12	7.12	7.10
Methyluracil with Na-CMC	261	261	261	7.10	7.13	7.19
Chlorhexidine with Na-CMC	254	254	254	7.17	7.12	7.12

It was also of interest to study the UV absorption spectrum of a polymer mass containing the above combination of drugs in a Na-CMC polymer solution. For this, the comparative spectral characteristics of an aqueous solution containing methyluracil, chloramphenicol and chlorhexidine, as well as a polymer mass containing the above combination of drugs in a Na-CMC polymer solution, were studied. The research results are shown in Figures 1 and 2.

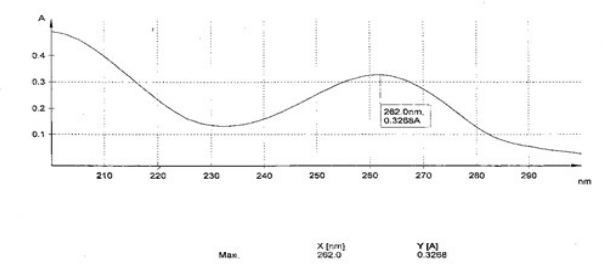

Fig.1. UV absorption spectra of a solution containing methyluracil, chloramphenicol, chlorhexidine

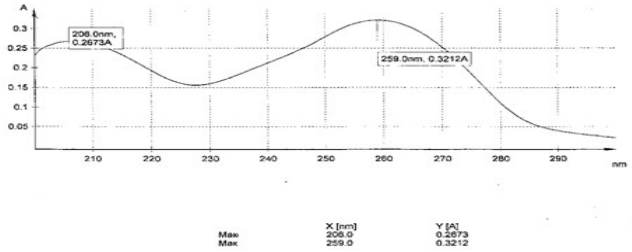

Fig.2. UV absorption spectra of a polymer mass containing the above combination of drugs in a Na-CMC polymer solution

The data presented indicate that the UV absorption spectrum of the polymer mass shows the appearance of new absorption bands in the form of maxima at 206 nm and 259 nm and a minimum at 227 nm, which are not characteristic of the UV spectra of solutions of individual substances and their solutions with the polymer. This can be explained by a complex cooperative interaction between a mixture of substances and macromolecules of the Na-CMC polymer. The presence of such a cooperative interaction between a mixture of substances and a Na-CMC solution ensures the production of transparent films and the absence of the phenomenon of salting out of substances (due to an increase in the concentration of components) during the formation of films.

To clarify the nature of the interaction of medicinal substances and the film-forming polymer, a comparative study of the IR absorption spectra of the Na-CMC polymer, as well as the IR spectra of medicinal substances in a Na-CMC solution, were also carried out, which are shown in Figures 3-6.

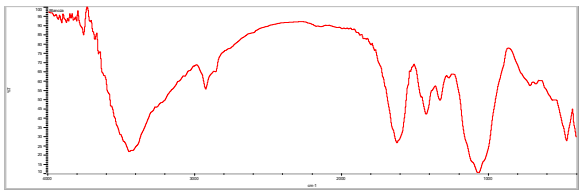

Fig.3. IR absorption spectrum obtained by casting Na-CMC films from its 1% solution

We studied the IR absorption spectra of medicinal substances included in the film in combination with a solution of the polymer Na-CMC, which are shown in Figures 4, 5 and 6.

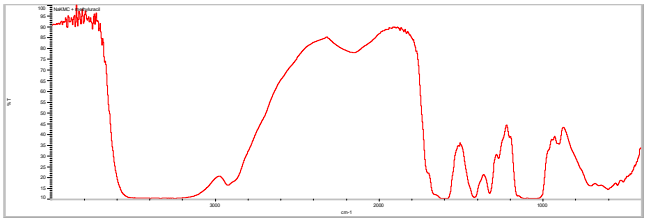

Fig.4. IR absorption spectrum of methyluracil with Na-CMC solution

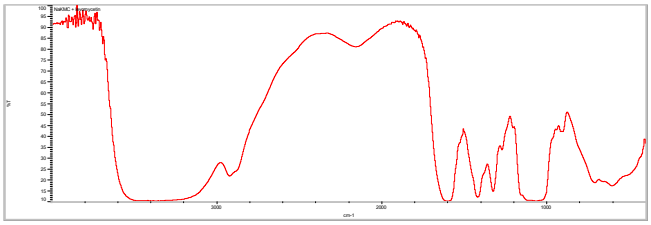

Fig.5. IR absorption spectrum of chloramphenicol with Na-CMC solution

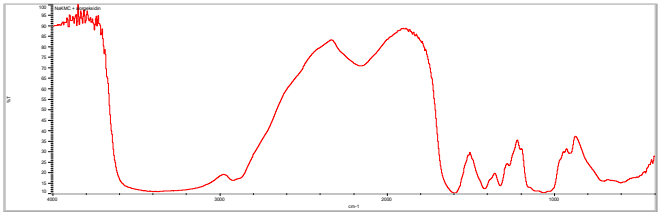

Fig.6. IR absorption spectrum of chlorhexidine with Na-CMC solution

The results of a study of the IR spectroscopy of chloramphenicol and methyluracil in combination with a solution of Na-CMC showed that the characteristic band at 1620 cm^{-1} shifts to the low-wavelength region of 1606 and 1590 cm^{-1}, which is apparently explained by the presence of interaction due to the formation of weak complex ionic bonds. A similar picture was observed in the IR absorption spectra of chlorhexidine with a solution of Na-CMC.

Since the physical and mechanical properties of the films are largely determined by the concentration of the film-forming polymer and plasticizer, these parameters were studied in further studies. For this, film masses were prepared with different contents of the Na-CMC

polymer and the properties of the formed films were studied. The results are shown in Table 4.

Table 4

Properties of films obtained from film masses with different Na-CMC polymer content

Content Na-CMC in 100g of film mass	Studied indicators		
	Appearance	Dissolution time, min	Ability to lag behind the substrate surface
1.5	The film is transparent, homogeneous, elastic	18	Films poorly fell behind the substrate surface
2.0	The film is transparent, homogeneous, elastic	20	Films easily fell behind the substrate surface
2.5	The film is transparent, elastic, but the surface is not uniform	25	Films easily fell behind the substrate surface

As can be seen from the data in the table, film compositions containing 2 and 2.5% polymer provide the best result in terms of the ability to lag behind the substrate surface. In addition, it should be noted that there are some differences in the process of homogenization and the duration of drying of polymer masses with different polymer content. So, with a polymer content in the mass of 1.5%, homogenization was carried out relatively easily, but the drying process was longer. At a Na-CMC content of 2%, the homogenization process was also easy and the drying process was shorter. The polymer mass with 2.5% Na-CMC was subjected to homogenization with difficulty, due to its high viscosity; the drying process took about 40 hours. Based on the results obtained by us, for further research, composition № 2 with 2% NaCMC was chosen as the optimal one.

The introduction of a plasticizer is aimed at ensuring the plasticity of the polymer films and protecting them from excessive drying. Considering that glycerin is often used as a plasticizer, we also used this plasticizer. To ascertain the optimal amount of glycerin, which ensures the production of high-quality films, model film masses with different glycerol content in them were prepared and the physicomechanical properties of the formed films were studied. The research results are shown in table 5.

Table 5

Effect of glycerin concentration on the properties of films containing methyluracil, chloramphenicol and chlorhexidine

Studied indicators	Glycerin content in 100 g of film mass, g			
	0.5	1.0	1.5	2.0
Appearance	Films are transparent, but brittle at the edges	Films, elastic, transparent	Films, elastic, transparent	Films, elastic, transparent
pH of the film aqueous solution	6.9-7.2	6.9- 7.25	6.9-7.0	6.8-7.0
Time dissolution, min	20	20	18	15
Ability to lag behind the substrate surface	Lagged well off the substrate	Lagged off the substrate easily	Lagged off the substrate easily	Lagged off the substrate easily

The results of studying the properties of the obtained model films, shown in Table 5, indicate that the films obtained from film masses with a

glycerol content of 0.5% (composition 1) were fragile, especially at the edges. Films formed from film masses with a glycerin content of 1; 1.5% and 2% were flexible enough and fell easily from the substrate surface. Based on the results of the study, the optimal content of glycerin in the film mass was 1%, since a further increase in the amount of glycerin is not advisable. The study of the pH value of an aqueous solution of model films showed that it is in the range of 6.8-7.25, and the dissolution time is within 15-20 minutes, depending on the concentration of glycerin.

One of the important indicators of PF is residual moisture, which largely determines the mechanical tensile strength of the films, as well as its elasticity. In order to ascertain the optimal value of this indicator, the effect of residual moisture on the physical and mechanical properties of the films was studied. The residual moisture content of the films was determined by the amount of loss in mass during drying, according to the procedure given in the State Pharmacopoeia of the Russian Federation -14th ed. [23]. The results of the research have ascertained that the value of residual moisture has a significant effect, first of all, on the elasticity of the film and on the ability to lag behind the substrate surface. At the same time, residual moisture does not have a noticeable effect on the dissolution time and the pH of the aqueous solution of the films. The research results made it possible to ascertain the optimal limits for the residual moisture content of the films, which amounted to 10-14%.

One of the informative methods for assessing the effectiveness of polymer films containing antibacterial substances is the method of diffusion of medicinal substances into an agar gel with a test culture of microorganisms, which makes it possible to assess not only the antimicrobial activity of the drug, but also the rate of release of active substances from the dosage form, according to the size of the growth retardation zones of the test-microorganisms for a given time [27, 28]. Due to the fact that the studied films include both antimicrobial and antiseptic substances for a complete assessment of their effectiveness, we studied the antimicrobial activity and estimated the release rate of active substances by diffusion into an agar gel by measuring the growth inhibition zone of test-microorganisms during incubation. The study of the antibacterial activity of the films was carried out using microbiological methods given in the State Pharmacopoeia of the Russian Federation, 14th edition [23]. The following collection test strains of microorganisms were used in the experiments: Escherichiacoli ATCC 25922; Staphylococcusaureus ATCC 25923; Pseudomonas aeruginosa ATCC 27853; Candida albicans ATCC 10231. During the experiments, nutrient media were used: NutrientAgar (nutrient agar); SabouraudAgar (Sabouraud agar). In the experiments the followings were studied: a standard sample solution containing methyluracil 0.8 mg/ml, chloramphenicol 0.4 g/ml, chlorhexidine digluconate 0.2 mg/ml; test sample - a mixture of films containing active ingredients with 10 ml of water; the placebo sample is a mixture of placebo films with 10 ml of water. The results of studies of the antimicrobial activity of films after 24 hours of incubation are shown in Table 6.

Table 6

Results of studying the antimicrobial activity of complex action films

Nutrient medium	Test strains	The zone of inhibition of the growth of test-microorganisms, mm

		Placebo sample	Standard sample	Test sample
Nutrient Agar	St.aureus	-	26.1	26.0
	Ps.aeruginosa	-	24.5	24.5
	E.coli	-	27.0	27.1
Sabouraud Agar	C. albicans	-	25.5	25.6

The research results showed that the tested samples of films exhibit pronounced antimicrobial activity **against** the following microorganisms: St. aureus, E. coli, Ps. aeruginosa, C. albicans. Figure 7 shows the results of a study of the antimicrobial activity of films in relation to the test microorganisms St. Aureus after 6, 12, 24 hours of incubation, respectively.

In order to standardize the proposed polymer medicinal films, methods for the quantitative analysis of the active substances of the films were developed using the method of high performance liquid chromatography (HPLC).

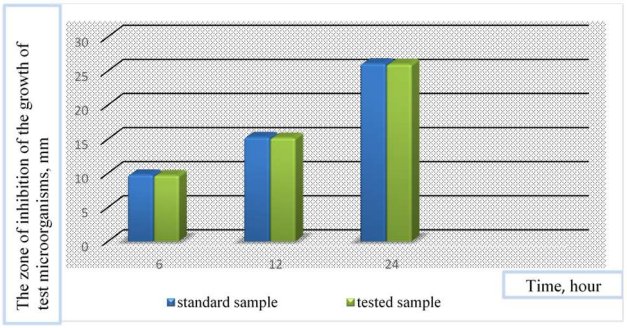

Fig.7. Kinetics of diffusion in agar of antimicrobial substances from films, complex action on zones of inhibition of growth of test-microorganisms St. Aureus

For this, studies were carried out to ascertain the optimal conditions for the chromatographic separation of methyluracil, chloramphenicol and chlorhexidine in the studied films. The studies were carried out on an AGILENT high pressure liquid chromatograph (model HPLC 1200) with a UV detector. As a result of the experiments, the following optimal chromatographic conditions were developed, shown in Table 7.

Table 7

Optimal conditions for the chromatographic separation of active substances in the investigated films of complex action

Chromatographic conditions	Methyluracil	Chlorhexidine and chloramphenicol
Mobile phase composition	phosphate buffer solution pH = 3.5	phosphate buffered solution pH = 3.5-methanol
UV detection at wavelength	254nm	
Mobile phase speed;	1.0 ml/min	
Column oven temperature	40°C;	
Injected sample volume	20 µl;	
Chromatographic column	Zorbax Eclipse filled with C-18 sorbent, 150 mm x 4.6 mm, particle size 5 microns or similar	

Chromatograms of active substances in a solution of a test sample of medicinal films are shown in Figure 8. The results of quantitative determination of active substances in films of complex action are shown in Table 8.

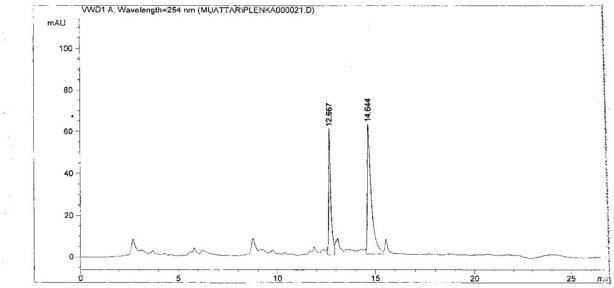

Fig.8. Chromatogram of chlorhexidine and chloramphenicol in a solution of the tested samples of medicinal films

Table 8
Results of quantitative determination of active substances in medicinal films
(t (P;f)=2,78; P=95 %; n=5; f=4)

Active substance	Film weight, g	Found, g	Metrological characteristics
Chloramphenicol	3.6999 3.6998 3.7001 3.7001 3.7002	0.01061 0.01064 0.01077 0.01075 0.01072	X_{av}=0.01069; S^2=0.000000005 S=0.00006979; S_X=0.00003120 ΔX=0.000194 ; ΔX_{av}=0.00008676 ε=1.8134% ; ε_{av}=0.8110%
Methyluracil	3.6998 3.6998 3.7001 3.6999 3.6999	0.02180 0.02173 0.02180 0.02174 0.02177	X_{av}=0.02177; S^2=0.000000001 S=0.00003271; S_X=0.00001462 ΔX=0.00009094 ; ΔX_{av}=0.00004066 ε=0.4178% ; ε_{av} =0.1868%
Chlorhexidine	3.6999 3.7001 3.7001 3.7002 3.6998	0.00541 0.00542 0.00534 0.00531 0.00530	X_{av}=0.00535; S^2=0.000000003 S=0.00005792; S_X=0.00002590 ΔX=0.0000161 ; ΔXav=0.0000072 ε=0.3008% ; ε_{av} =0.1345%

A preliminary biomedical study of the specific activity of the developed medicinal films was carried out according to the results of studying their effect on the course of an experimental burn ulcer of the distal part of the rabbits, as well as the anti-inflammatory effect of the drug in comparison with placebo films and Levomekol ointment. The research results showed that the developed medicinal films have a pronounced therapeutic - antiulcer effect and have an inhibitory effect on the development of formalin and histamine inflammation. At the same time, in terms of wound healing and anti-inflammatory effect, the films are not inferior to the well-known drug Levomekol.

CONCLUSION

The composition of the active components of polymeric medicinal films of complex action, including methyluracil, chloramphenicol and chlorhexidine, has been scientifically substantiated. The results of the research have selected the optimal film-forming polymer-NaCMC for the production of films. The optimal concentration of the selected polymer and glycerin plasticizer in the film mass was substantiated, which was 2% for the polymer and 1% for glycerin. The nature of the interaction that occurs in the studied films between medicinal substances and a solution of the film-forming polymer Na-CMC has been studied. Using microbiological methods, the antibacterial activity of the recommended films was studied and it was found that they exhibit pronounced antimicrobial activity **against**: St. aureus, E. coli, Ps. aeruginosa, C. albicans. Methods have been developed for the quantitative determination of the active substances of films of complex action by the HPLC method. The results of preliminary biomedical studies have shown that the films have wound healing and anti-inflammatory effects.

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