Розроблено нову технологію формування сріблонаповнених гідрогелевих пов'язок медичного призначення. Для одержання металонаповнених композиційних гідрогелів запропоновано високотехнологічний одностадійний метод, який полягає у полімеризації полімер-мономерних композицій на основі полівінілпіролідону та 2-гідроксіетилметакрилату з одночасним хімічним відновленням йонів срібла з його нітрату етанолом. Термометричними дослідженнями встановлено, що температурні умови, необхідні для хімічного відновлення йонів срібла, досягаються за рахунок тепла, яке виділяється під час екзотермічної реакції полімеризації. Визначені часові та температурні параметри полімеризації залежно від складу вихідної полімер-мономерної композиції, вмісту розчинника та ініціатора, концентрації нітрату срібла. Серед них – початкова температура полімеризації, максимальна температура екзотермії, час досягнення максимальної температури екзотермії, тривалість гель-ефекту.

Використання комбінованої ініціювальної системи феруму (II) сульфат+пероксид бензоїлу забезпечує можливість здійснення процесу одержання сріблонаповнених гідрогелів за кімнатної температури, на повітрі. Синтез є технологічно неускладненим, здійснюється без складного апаратурного оформлення. Авторами запропоновано нову технологію формування гідрогелевих плівок відцентровим методом. Полімеризація з осадженням срібла відбувається у відцентровій формі одночасно з формуванням плівки, що дозволяє одержати матеріали з прогнозованими властивостями, які володіють рівномірним розподілом наповнювача в полімерній матриці, рівнотовщинністю та високою якістю поверхонь. Одержані за розробленою технологією плівкові вироби здатні набрякати у воді та інших полярних розчинниках, відзначаються міцністю, пружністю, бактерицидними та антифунгальними властивостями. Результати клінічного дослідження виявили достатню клінічну ефективність використання розроблених гідрогелевих пов'язок медичного призначення на основі сріблонаповнених гідрогелів. Такі матеріали, у поєднанні з комплексною терапією, сприяють підвищенню швидкості та інтенсивності лікування трофічних венозних виразок нижніх кінцівок

Ключові слова: гідрогелеві медичні пов'язки, сріблонаповнені гідрогелі, відцентрове формування, металополімерні композити, трофічні виразки

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TECHNOLOGICAL FEATURES IN OBTAINING HIGHLY EFFECTIVE HYDROGEL DRESSINGS FOR MEDICAL PURPOSES

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1. Introduction

Over the past decade, researchers have paid much attention to the development of new methods [1], optimization of synthesis conditions [2] and properties [3] of composite metal-filled polymeric hydrogels, which is a prerequisite for the creation of new materials with unique properties for various spheres of application. The uniqueness of such materials is the combination of the properties of a polymer matrix and the metal-filler. A polymer matrix is characterized by the ability to absorb low molecular substances, including medicines, to swell in solvents, retain a significant amount of water while

being in a highly elastic state. Depending on the nature of metal, composite hydrogel can acquire electro-conductive, magnetic and anti-bacterial properties, which significantly expands the fields of its usage. Composite metal-hydrogels with antibacterial and antifungal properties are ideal materials in the medical field for the creation of dressings to treat wounds, burns, ulcers of various kinds, including venous ulcers of lower limbs. More than 35 % of the working population and over 50 % of the population of retirement age suffer from chronic diseases of veins. In all cases, the ulcers are included in the group of risk of developing wound infection. The treatment of venous ulcers of the lower limbs is lengthy and often comes with complications. The traditional cotton-gauze dressing provides only a reliable mechanical protection, but when absorbing the lymph that flows from a wound, it becomes a medium for the pathogenic microflora. Therefore, for the prevention of pyo-inflammatory complications, it is advisable to use the dressings with antimicrobial action. One of the promising methods for the treatment of venous ulcers is considered to be covering (in order to prevent the development of wound infection) with the sorption hydrogel film materials with antibacterial properties and the combination of therapy using medical preparations [4]. The main problem that occurs during the creation of such materials is to select the optimal ways of introducing the filler in a polymer matrix and the formation of a film product. The magnitude and the character of distribution of the particles of filler in the volume of the composite, and, consequently, its structure and properties depend on the method of filling. The method of formation, in turn, ensures the quality of hydrogel films, as well as the productivity and cost effectiveness of the process.

Given the prevalence of venous ulcers among the population and considerable difficulties of their treatment, it is necessary to consider that the research, aimed at the development of new therapeutic methods and materials and technologies of their obtaining, is relevant.

2. Literature review and problem statement

The modern practice of the treatment of venous ulcers of lower limbs implies a combination of various methods for conservative treatment and surgical interventions. At appropriate treatment, we can observe a relatively rapid closure of the defect within the nearest 4 months in 50 % of cases of venous ulcers, ulcers remain open for 2 years in 20 % of cases, and the signs of skin defect epithelization are not observed for five years in 8 % of patients [5, 6]. This indicates the high relevance of the problem of the treatment of venous ulcers and creates the need for the search and implementation of new methods of therapy. Most trophic venous ulcers are characterized by a high degree of bacterial colonization with high probability of development of wound infection. According to many researchers, an important condition, necessary to prevent recurrence of venous ulcers, is the application of the adequate systemic and local therapy with antibiotics and antiseptic preparations in combination with lower limb compression [7].

Silver is widely used at the present stage to solve the problem. There is a known method of treatment, which involves a temporary closure of wounds using lyophilized silver-containing xenoderm transplants as antiseptic means [8]. However, the disadvantage of this method of treatment is the difficulty in using it due to the technological problems of manufacturing xenoderm transplants. One of the ways of local treatment of venous ulcers is the use of silver in ointments or liniments [9]. At the same time, this way of treatment is too lengthy. In addition, the use of silver-containing ointments or liniments is characterized by the low osmotic and absorption properties. The shortcomings of the treatment with the use of traditional dressings with antiseptics include the non-uniform penetration into the tissues of wound surface accumulation of discharge, poor penetration of oxygen into tissues, traumatization and pain sensations of a patient during changing the dressings.

It is obvious that the effectiveness of antibacterial activity of silver will be preserved after its impregnation on the film hydrogel materials, which at the same time will make it possible to achieve the desired clinical effect with a reduction of treatment duration and a decrease in its costs. We established experimentally the prospects of using silver-filled film hydrogel products based on co-polymers of polyvinylpyrrolidone (PVP) with 2-hydroxyethylmethacrylat (HEMA) during the treatment of venous ulcers [4]. The most common methods for obtaining such materials is polymeric filling with metal powders [10] and deposition of metal particles directly into the pores of a polymer matrix [11]. However, filling with powders does not always give the desired result from the technological point of view. During mixing the components of the composition, it is not always possible to achieve the uniform distribution of metal particles in the hydrogel due to their limited compatibility, as well as the possibility of sedimentation, which causes the heterogeneity of the composite properties. That is why in some cases, it is advisable to perform synthesis of the particles of the metal filler directly in a matrix polymer. In such composites, a polymer matrix plays the role of a reactor for the synthesis of metal particles [12]. During analysis of scientific sources, no specific dominant method for obtaining particles of metallic filler was found, however, a significant prevalence of chemical methods over physical, specifically, chemical reduction in solutions, is observed [2]. The process is implemented in the presence of reducing agents of various types. In the case of silver, it is formalin, sodium and potassium hypophosphates, sodium borohydride, and hydrazine borane [13]. The use of toxic reducing agents during filling hydrogels with chemical reduction of metals is a significant shortcoming, which greatly limits their application, especially in the biomedical area. Depending on the conditions and the nature of the redox system, the reduction temperature is 60–140 C [13]. The ways of chemical synthesis of metal particles without the use of additional reducing agents, when a solvent [14] or [15] a polymer play the role of a reducing agent, are worth attention. However, filling by reduction of the metal ions in the lattice of a polymer matrix requires the use of large quantities of solutions of an oxidant and a reducing agent, which requires an additional stage of regeneration and is accompanied by over-consumption of reagents. In addition, this method, like the other currently existing methods for obtaining metal-filled polymers, is, at least, double-stage and contains the stage of synthesis of a polymeric matrix and the stage of obtaining particles of the metal filler.

Without a doubt, the effectiveness of manufacturing technology and the properties of hydrogel film products for medical purpose are affected by the selection of the formation method. Currently, the most common method for obtaining hydrogel films in Ukraine and abroad is pouring

into the form between two glass [16] or Teflon plates [17]. Glazing on the glass or other surface [18] or dipping [19] are also used.

The simplest, from the technological point of view, is glazing and dipping, because these methods are simple to use and do not require sophisticated apparatus design. However, it is difficult to obtain the films of the assigned thickness with high-quality surface through the formation of coating by glazing. It is possible to obtain an ultra-thin film by dipping, but there is a problem in obtaining the product of the same thickness. The films, made in molds, are characterized by an increased quality of the surface and the absence of different thickness. However, in this case, there are difficulties in filling a mold with a composition without air inclusions. The problem is complicated at an increase in viscosity of the compositions, as well as at an increase in the dimensions of a mold and a decrease in the distance between its walls, that is, at a decrease in the thickness of a film.

Thus, the lack of highly effective film products for medical purposes and a simple productive technology of their obtaining nowadays cause the need for research in this direction.

3. The aim and objectives of the study

The aim of this research is to study the features of the new uncomplicated technology of obtaining silver-filled hydrogel films, suitable for using as medical dressings with antibacterial properties.

To accomplish the set goal, the following objectives were set:

– to establish the possibility of obtaining composite hydrogels based on copolymers of HEMA with PVP by the method of chemical deposition of silver at the stage of formation of a polymer matrix, using the thermal effect of polymerization;

– to explore the effect of the composite structure, content and nature of the initiator, initial temperature of polymerization on the duration of the polymerization process and maximum exothermic temperature as the main technological parameters of the polymerization method with simultaneous reduction;

– to explore the ability for swelling, physical-mechanical, bactericidal and antifungal properties of silver-filled hydrogels

4. Materials and methods of research

4. 1. Materials and procedures for obtaining metal-filled hydrogels

2-hydroxyethylmethacrylat (Sigma Chemical Co) and high-purity polyvinylpyrrolidone (AppliChem GmbH) with MM 12000 were used for co-polymerization. The initiator of the radical type benzoyl peroxide (BP) was selected as the polymerization initiator. Such choice was determined by its wide use for the synthesis of HEMA-PVP co-polymers [20]. HEMA was distilled in vacuum (residual pressure was 130 N/m^2, T_{boil}=351 K), PVP was dried at 338 K in vacuum for 2–3 h, BP was re-crystallized from ethanol.

The compositions of the structure HEMA:PVP= =90÷70:10÷30 mass parts using 10÷100 mass parts of solvent (H_2O) were studied. The need for the presence of the solvent in the original composition was caused by dissolving reduction precursors in it. The concentration of BP during the research was changed within 0.1÷0.5 % by weight.

The possibility of obtaining metal-filled hydrogels based on copolymers of HEMA with PVP by the polymerization method with simultaneous deposition of metal was experimentally proved in [21]. A prerequisite for using this method for obtaining silver-filled hydrogels is a high reactivity of HEMA–PVP compositions and exothermal polymerization effects that can provide the needed temperature conditions for the reduction of Ag^+.

Given that the silver-filled hydrogel is meant for medical purposes, silver deposition was carried out from argentum nitrate (of chemically pure brand) in the aqueous-ethanol solution. The recovery process goes on intensively at the temperature of 70 °C [14] according to the following reaction:

$$2AgNO_3+C_2H_5OH\rightarrow 2Ag\downarrow+2HNO_3+CH_3CH=O.$$

4. 2. Research into technological and operational characteristics of the obtained materials

To estimate the kinetic regularities of the reaction of copolymerization of HEMA with PVP, the procedure based on the thermometric method [21] was developed. On the resulting graphic dependences of $T=f(\tau)$, we separated the typical parameters that correspond to the start of gel formation ($\tau_{s.g.}$), time of reaching maximum exothermic temperature (τ_T), duration of gel-effect (τ_g), initial temperature of polymerization (T_0) and maximum exothermic temperature (T_{max}). The volume of the reaction mass for all the experiments was the same and made up 5 cm^3.

Water content (W, %), hardness number (H, MPa), plasticity number (P, %), elasticity number (E, %) were determined using the procedures described in [22].

4. 3. Medical-biological study of the obtained samples

Bactericidal and antifungal properties of the samples were studied on the test cultures of bacteria Escherichia coli (E. coli), Staphylococcus aureus (S. aureus), Staphylococcus epidermidis (S. epidermidis), Streptococcus viridans (S. viridans) and diploid fungus Candida albicans (c. albicans). We examined diffusion of active substance in agar on solid culture medium (for E. coli – meat-peptone agar, for Staphylococci – yolk-salt agar by Chistovich, for Streptococci – 5 % blood agar, for fungi – agarized medium by Saburo).

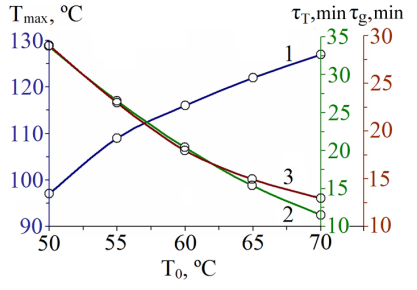
As inoculation material, we used 16–24–hour agar cultures brought to the density of 3.0×10^8 CFO/cm^3, which by the visual control corresponds to turbidity standard of 1.0 for McFarland. The diameter of the zones of microorganism growth inhibition around the plates was determined taken into account the diameter of the plates. The samples of the composites were used in the form of film products of 20×20 mm and a thickness of 1 mm.

5. Results of research into the technological features of obtaining silver-containing hydrogel dressings for medical purposes

5. 1. Technological features of obtaining composite hydrogels with silver deposition using thermal effect of polymerization

BP is the initiator of the "hot hardening" and is used at the temperatures of 80–90 °C. However, it was established

that in the case of HEMA-PVP composition, polymerization in the presence of BP takes place at a high rate at the temperature of 50 °C with T_{max}=96.8 °C, which is achieved in 34 min with τ_g=29 min (Fig. 1, *a*). That is why T_0=50 °C was accepted as the initial temperature of polymerization for subsequent research.



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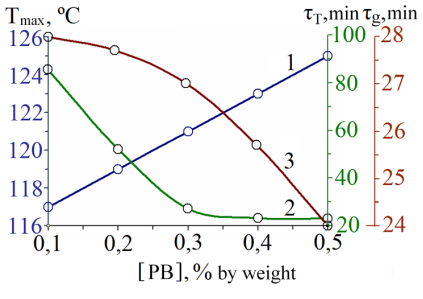

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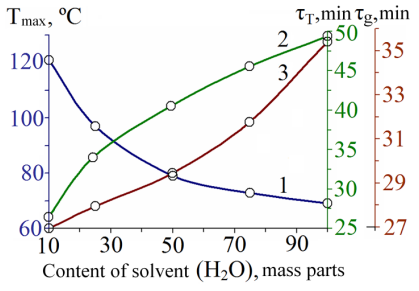
Fig. 1. Dependence of maximal exothermic temperature, T_{max} (1), time of achieving maximum exothermic temperature, τ_T (2) and duration of gel-effect, τ_g (3) on: *a* – initial temperature (HEMA:PVP:H_2O=80:20:25 mass part; [BP]=0.3 % by weight); *b* – concentration of initiator BP (HEMA:PVP:H_2O=80:20:10 mass part; T_0=50 °C)

At the initial temperature of 50 °C and the content of the initiator of 0.1% by weight, the process is characterized by lengthy induction period with the subsequent gel-effect, which manifests itself after 67 min (Fig. 1, *b*). The maximum exothermic temperature in this case is achieved after 86 minutes and is 116.8 °C. At an increase in the concentration of initiator, T_{max} increases with decreasing τ_T. The time of starting gel-effect decreases significantly. At an increase in the content of BP to 0.3 % by weight, the minimal time τ_T is achieved, which with the further increase [BP] varies slightly, which causes the use of its concentration [BP]=0.3 % by weight.

A decrease in the concentration of monomer due to dilution of the composition with the solvent naturally causes a decrease in the initial polymerization rate, as evidenced by an increase in time of achieving T_{max} with its significant decrease (Fig. 2, *a*). An increase in the content of the solvent from 10 mass part to 100 mass part causes a decrease in T_{max} from 121 °C to 69 °C and an increase in τ_T, accordingly, from 26 min to 49 min.

At the same time, it should be noted that the duration of the gel effect in this case change only by 8.5 min. It was established that existence of even a small content of reduction precursors in the original composition has an impact on the rate of the polymer formation process. The simultaneous implementation of the reactions of chemical deposition of metal and polymerization causes a decrease in T_{max} and an increase in $\tau_{s.g}$, τ_T, τ_g (Table 1).



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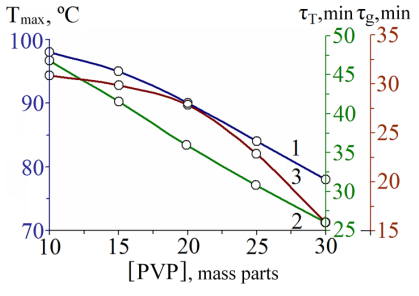

b

Fig. 2. Dependence of maximum exothermic temperature, T_{max} (1), time of reaching maximum exothermic temperature, τ_T (2) and duration of gel-effect, τ_g. (3) on: *a* – content of solvent H_2O (HEMA:PVP=80:20 mass part; [BP]=0.3 % by weight; T_0=50 °C); *b* – content of PVP in the original composition (K:P=4:1 mass part; P – EtOH:H_2O=1:3 % by weight; [$AgNO_3$]=0.22 mol/l; [BP]=0.3 % by weight; T_0=50 °C)

Table 1

Influence of the process of chemical reduction of metal on parameters of gel-effect of polymerization of PVP–HEMA compositions (HEMA:PVP:P=80:20:25 mass part, [BP]=0.3 % by weight, T_0=50 °C)

No.	[$AgNO_3$], mol/l	Solvent (P)	$\tau_{s.g}$, min	τ_T, min	τ_g, min	T_{max}, °C
1	–	H_2O	16	34	28	97
2*	0.22	EtOH+H_2O	20	36	28	90
4*	1.10	EtOH+H_2O	22	40	27	88

*Note: * – EtOH:H_2O=1:3 % by weight*

It is possible that an increase in duration of $\tau_{s.g}$, τ_T, τ_g and a decrease in T_{max} is associated with the steric factors due to the growth in the reaction medium of the number of Ag^+ ions, blocking the active centers of PVP, preventing the formation of CPC between PVP and HEMA.

The polymerization rate is significantly influenced by the composition of the polymer-monomer mixture – at an increase in the content of PVP in the composition, its polymerization ability increases, which is proved by a reduction in the time of onset of exothermia and duration of gel-effect (Fig. 2, *b*). At the same time, a decrease in T_{max} was observed, which can be explained by a decrease in the monomer content in the original composition, the number of double bonds of which affects the exothermic intensity.

An increase in the initial polymerization temperature, of course, contributes to an increase in the rate of the polymerization processes, maximum exothermic temperature, and therefore the rate of metal reduction. However, due to the high rate of heat release and poor thermal conductivity

of the polymer, there occurs thermal expansion and occurrence of internal stresses, which is the cause of cracking in the volume of the sample [21]. Polymerization in the presence of $FeSO_4$ is one of the methods of polymerization of PVP–HEMA of the compositions at low temperatures [22]. Under the influence of metal ions of the alternating degree of oxidation, the process occurs at a high rate at the room temperature, in the air and finishes after 5–30 minutes. Due to the research into kinetics of co-polymerization of PVP with HEMA in the presence of metal ions of alternating degree of oxidation, it was established that the process goes on by the ion-radical mechanism with a clearly pronounced gel-effect and minimum induction period [23]. The results of thermometric studies (Fig. 3, curve 1) prove the exothermal nature of the polymerization of PVP-HEMA compositions under the action of Fe^{2+}. However, the maximum exothermic temperature is 52 °C and is insufficient for intensive reduction of Ag^+, although it starts in 10 min, and polymerization occurs without the induction period. At the same time, the possibility of polymerization of PVP–HEMA compositions at the room temperature in the presence of the combined initiation system of $FeSO_4$+BP was established. Polymerization of HEMA in the presence of PVP under the action of the BP at the temperature of 50 °C is characterized by the maximum exothermic temperature of 118 °C, which starts in 27 min after its beginning (Fig. 3, curve 2). The use of the combined initiation system $FeSO_4$+BP for polymerization of PVP-HEMA of the composition reached T_{max}=83 °C in a relatively short period of time of 33 min and under conditions of the initial room temperature (Fig. 3, curve 3).

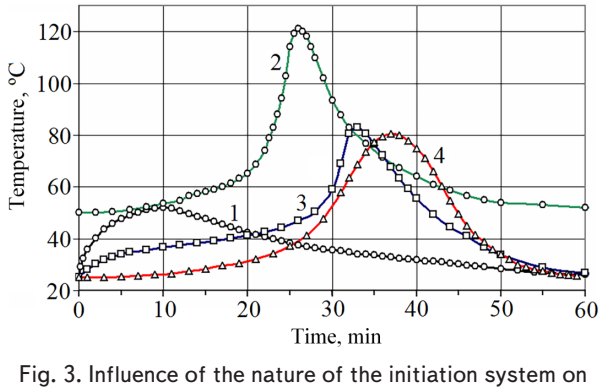

Fig. 3. Influence of the nature of the initiation system on T_{max} of polymerization (HEMA:PVP:H_2O=80:20:10 mass part, T_0=25 °C, [$FeSO_4$]=0.01 % by weight, [BP]=0.3 % by weight): 1 – $FeSO_4$; 2 – BP (T_0=50 °C); 3 – $FeSO_4$+BP; 4 – $FeSO_4$+BP+EtOH+$AgNO_3$

The resulting effect was used for the polymerization of the HEMA-PVP composition in the presence of the redox system of EtOH+$AgNO_3$ (Fig. 3, curve 4). The maximum exothermic temperature in this case is 80 °C.

Coloration of the samples, obtained by the method of polymerization with simultaneous reduction of Ag^+, changes from silver-gray to brown, depending on the conditions of formation, components of the original polymer-monomer composition and concentration of $AgNO_3$. Such change in the coloration is obviously connected with the appearance of metal silver in the structure of the polymer.

To prove obtaining zero-valence silver due to its chemical deposition during polymerization, the X-ray structural analysis of the obtained composites was conducted (Fig. 4, curve 1).

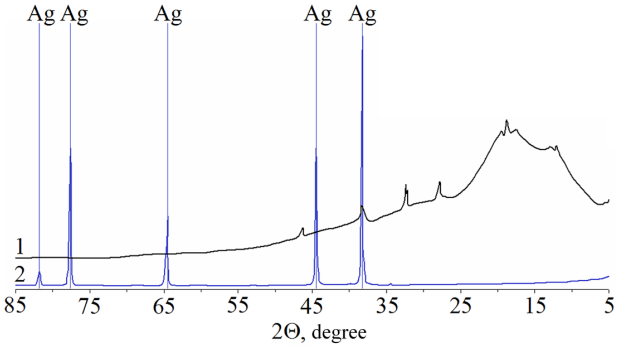

Fig. 4. Diffractograms of silver-filled PVP-HEMA copolymers: 1 – before thermal treatment; 2 – after thermal treatment

However, analyzing the resulting roentgenogram, it is possible to note that on the curve, there are no peaks that correspond to zero-valence metal. It might be assumed that X-ray amorphous silver that is not manifested in roentgenograms, is formed during reduction with the simultaneous polymerization. To prove the assumption that was put forward, the X-ray structural analysis of the sample after its heat treatment was carried out (Fig. 4, curve 2). As it can be seen, the peaks characteristic of zero-valence silver appear after recrystallization. Given the fact that for the analysis we used the samples that were washed off from the residues of the oxidant, reducing agent and the reduction reaction products, it is possible to draw an affirmative conclusion that the peaks, characteristic of zero-valence silver, appeared after recrystallization of X-ray amorphous metal, obtained through chemical reduction of Ag^+ during the polymerization process.

An additional proof of the formation of the graft co-polymer during the polymerization of the HEMA in the presence of PVP with simultaneous silver deposition is the IR spectra of PVP and the acquired composite. Analysis of IR spectra showed that the characteristic bands of PVP in the regions of 650 cm^{-1}, 1,415 cm^{-1}, 1,480 cm^{-1} exist in the spectrum of copolymer, indicating the existence of PVP chains in it.

5. 2. Results of research into characteristics of the obtained materials

Polymeric hydrogels differ from the other materials by the fact that they become limitedly swollen in water and aqueous solutions of various substances. However, without receiving moisture, these materials are in the glass-like condition. Since such materials are mainly used in the swollen form, including medical dressings, there is a need to study the mechanical properties and swelling capacity (Table 2). The properties of copolymers depend mainly on its structure, which is determined by the structure of the original composition. Analyzing the influence of the composition structure on the properties of silver-filled copolymers, it is possible to follow the regularity: an increase in the content of PVP (Table 2, pos. 1–3) and of the solvent (Table 2, pos. 2, 4, 5) in the original composition decreases the strength (hardness number) and elastic characteristics (elasticity number, E) of copolymers. At the same time, the ability of composites to swell improves and moisture content and swelling coefficient increase.

The medical-biological studies of the resulting film products were carried out under the laboratory conditions at the Department of Microbiology of Danylo Halytskyi

Lviv National Medical University. A comparative analysis of the results of medical-biological tests of the obtained materials and non-filled hydrogel films regarding the used micro-organisms revealed that non-filled films do not show any bactericidal and antifungal properties.

The film products that contain silver particles block the growth of bacteria and fungi (Table 3).

Table 2

Influence of composition structure on properties of silver-filled copolymers in the hydrated state (K:P=1:1 mass part, $[AgNO_3]$=0.11 mol/l)

No. of entry	Composition structure, mass parts		$H\times10^2$, MPa	E, %	P, %	W, %	k
	HEMA	PVP					
1	90	10	9.5	88.7	11.3	49.2	1.20
2	80	20	8.7	86.7	13.3	55.7	1.29
3	70	30	7.5	86.0	14.0	64.9	1.34
4*	80	20	10.6	89.5	10.5	49.8	1.22
5**	80	20	9.9	88.2	11.8	51.4	1.27

*Notes: * – content of the solvent (EtOH:H_2O=1:3 % by weight) – 50 mass parts; ** – content of the solvent (EtOH:H_2O=1:3 % by weight) – 75 mass parts*

Table 3

Bactericidal and antifungal activity of silver-filled hydrogel films, obtained based on copolymers of HEMA with PVP

Duration of storage of hydrogel films	Magnitude of the zone of inhibition of microorganism growth, mm				
	S. aureus	S. epidermidis	Str. viridans	E. coli	C. albicans
1 month	12, 10, 9	12, 8, 9	11, 11, 9	3, 3, 0	11, 11, 7
18 months	5, 4, 8	5, 4, 5	11, 8, 8	–	0, 4, 2

It was established that the bactericidal and antifungal properties of silver-filled hydrogel films under conditions of storage in distilled water deteriorate over time and disappear in relation to bacteria Escherichia coli.

6. Discussion of results of studying the technological features of obtaining silver-filled hydrogel dressings for medical purposes

High elasticity, strength, sorption capacity, bactericidal and antifungal properties of the obtained materials make them effective to use as hydrogel dressings for medical purposes. A unique porous structure, combined with the existence of hydrophilic functional groups ensures swelling of a polymer matrix in water and high permeability for dissolved low molecular substances. This, in turn, determines the suitability of the obtained hydrogel dressings for the preparation treatment by introducing medicines through the material by the transdermal method.

At the same time, due to the ability to absorb and retain moisture, elasticity and stability of the form in aqueous medium, such materials are compatible with a variety of biological systems.

The proposed method for obtaining – polymerization with the simultaneous deposition of silver – makes the developed materials promising for the implementation and usage. The method is especially attractive both from the practical and the scientific point of view, because the particles of metal are formed at the same time with the formation of a polymer matrix. This approach makes it possible to achieve a better, uniform distribution of the filler and to obtain the material with the isotropic properties.

High reactivity and possibility to regulate within wide limits the time of HEMA–PVP compositions being in liquid state is a prerequisite of their recycling in film products by the method of centrifugal formation [24]. The technological characteristics, cost effectiveness of the centrifugal formation and low quality of the films, obtained by the other currently existing methods, contribute to this. The samples of hydrogel film materials, obtained by centrifugal formation, are characterized by various thickness, which does not exceed 1 %, high-quality surfaces and a complex of physical and mechanical properties.

Processes for copolymer synthesis, reduction of Ag^+, filling hydrogel with silver, as well as the formation of a hydrogel film take place simultaneously in the reduced form. The implementation of polymerization in the presence of a solvent contributes to achievement of high porosity of a polymer matrix, which makes it possible to withdraw the products of the reduction reaction from the volume of the composite.

The uniformity of silver distribution in the volume of a polymer matrix is provided at the stage of mixing the components of the original composition due to the process of complexing. The formation of the CPC is accompanied by the formation of intermolecular contacts between the monomer, the metal ion and the carbamate groups of the PVP chain (Fig. 5) and thus, by the Ag^+ fixation.

The existence of the ternary complex between PVP, HEMA and a metal ion was proven in paper [23].

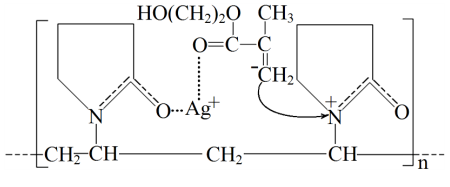

Fig. 5. The ternary complex with transfer of discharge of PVP – Ag^+ – HEMA

No doubt, the technological features of obtaining polymers (original structure of the composition, duration and temperature of the process) depend on the kinetic regularities of polymerization. It is particularly important to study the regularities of polymerization, which occurs simultaneously with chemical deposition of metals and the establishment of the mutual influence of two chemical processes that are different by nature. However, due to multi-component original composition, the existence of precursors and products of reduction in the reaction system, specific determining the kinetic parameters of polymerization is much more complicated. At the same time, polymerization of HEMA in the presence of PVP goes on by the radical mechanism and is the exothermal process – it occurs with the gel-effect, which causes self-heating of the system [20].

Thermometric research revealed that the temperature conditions needed for chemical reduction of Ag^+ are achieved due to the heat that is released during the exothermic reaction of polymerization. The use of the combined initiation

system of $FeSO_4$+BP allows carrying out the process of obtaining composites at room temperature, in the air. The formation of films by the centrifugal method provides a high quality of products without additional vacuum evacuation of the original composition.

Based on the obtained silver-filled films, we developed hydrogel medical dressings, clinical testing of which was successfully carried out at the surgical department of the Lviv hospital at ZT PAT "Ukrainian Railway" in the treatment of venous ulcers of lower limbs [4]. It was established that the use of the silver-filled hydrogel films improves the treatment results, accelerates cleaning, granulation and healing trophic ulcers and, as a result, reduces the duration of patients staying at hospital. Due to its unique properties, the developed materials can be also used for the treatment of burn and post-operative wounds.

The proposed technology is easy to implement into production, does not require sophisticated apparatus design. One of its advantages is the minimum amount of waste and no need of recycling or recuperation of solutions of an oxidant and a reducing agent. Such technology is a priority and needs development, taking into consideration the prospects of the obtained composites.

At the same time, establishing the optimal possible content of silver, which would ensure bactericidal and antifungal properties of the films without a toxic action on the human body, requires additional research.

It should also be noted that equally important is the problem of studying the temperature and temporal parameters of polymerization exothermia, depending on the volume of the original composition. Exothermia in the operation was studied for the compositions of the volume of 5 cm^3, which limits the use of the obtained results when the composition volume changes.

Subsequent studies will also be aimed at enhancing the strength and sorption ability of composite film hydrogels to enable their multiple use.

7. Conclusions

1. The conducted research proved the possibility of obtaining silver-filled copolymers of PVP with HEMA with simultaneous chemical reduction of silver ions using the exoeffect of the polymerization reaction. The proposed method ensures the deposition of silver particles without preliminary heating the polymer-monomer composition.

2. The developed compositions in the presence of benzoyl peroxide together with ferrum (II) sulfate are highly reactive and can harden in the air at room temperature within 10–40 minutes with the maximum temperature of exothermia at 70–127 °C.

3. The fundamentally new method for obtaining high-quality metal-filled hydrogel films based on the reactive compositions of HEMA with PVP by the centrifugal formation was proposed. The developed method is simple to implement in production, single-stage, does not need complex apparatus design. The film products, obtained using the developed technology, are characterized by a high quality of the surface, strength and elasticity. The antibacterial and antifungal properties of the obtained silver-filled hydrogel films were proved on the example of the test cultures of bacteria Escherichia coli, Staphylococcus aureus, Staphylococcus epidermidis, Streptococcus viridans and diploid fungus Candida albicans.

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