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V. Y. Skorokhoda, N. B. Semenyuk, Yu. Ya. Melnyk, I. Z. Dzjaman, O. V. Suberlyak
Lviv PolytechnicNational University,
Department of Chemical Technology and Plastics Processing

THE BACTERICIDAL HYDROGEL MATERIALS AND SOFT CONTACT LENSES ON THEIR BASES

A hydrogel polymeric material with bactericidal properties based on 2-hydroxyethyl methacrylate and polyvinylpyrrolidone copolymers for soft contact lenses was developed. The regularities of copolymers obtaining by the graft copolymerization reaction, which occurs through a stage of complex formation between the reagents, were investigated. The relation between the complexation constant, the polymerization reaction kinetic parameters and structural parameters of the copolymers grid were established. The basic performance properties of hydrogels depending on their composition were investigated. The effect of silver nanoparticles on hydrogel coefficient of light permeability and its antibacterial properties were determined.

Key words: contact lenses, polyvinylpyrrolidone, 2-hydroxyethy methacrylate, hydrogel, permeability.

В. Ю. Скорохода, Н. Б. Семенюк, Ю. Я. Мельник, І. З. Дзяман, О. В. Суберляк

БАКТЕРИЦИДНІ ГІДРОГЕЛЕВІ МАТЕРІАЛИ І М’ЯКІ КОНТАКТНІ ЛІНЗИ НА ЇХНІЙ ОСНОВІ

Розроблено гідрогелевий полімерний матеріал із бактерицидними властивостями на основі кополімерів 2-гідроксіетилметакрилату з полівінілпіролідоном для м’яких контактних лінз. Досліджено закономірності одержання кополімерів реакцією прищепленої кополімеризації, яка відбувається через стадію комплексоутворення між реагентами. Встановлено взаємозв’язок між константою комплексоутворення, кінетичними параметрами реакції полімеризації і структурними параметрами сітки кополімерів. Досліджено основні експлуатаційні властивості гідрогелів залежно від їх складу. Досліджено вплив наночастинок срібла на світлопропускання гідрогелю та його бактерицидні властивості.

Ключові слова: контактні лінзи, полівінілпіролідон, 2-гідроксіетилметакрилат, гідрогель, проникність.

Introduction. The intensive development of polymeric chemistry and technology has resulted in wide introduction of polymers in various areas of human activity, the special interest among which represents the use of polymers in medicine. At early stages of development of biomedical polymers they were only substitutes of already known materials, later – as medicines, in the production of instrumentation, stomatological instruments, and synthetic bodies of a human body (synthetic bones and joints, blood vessels, heart valves, lungs, kidneys) [1].

The basic demands to synthetic bodies are absolute harmlessness for an organism, absence of cancerogenic or allergic influence, constancy of properties in time etc. Besides depending on specificity of that or other synthetic body, the material should also meet many other specific demands.

Besides mentioned above synthetic bodies the mankind is in great need of ophthalmologic implants, treating as well as correctional contact and intraocular lenses. The contact lenses are made in two modifications – solid and soft. Their well-known advantage is hyper permeability for an eye-water liquid and oxygen, the property which appreciably reduces a discomfort of lenses at use. In their turn, the soft contact lenses are made either from hydrogels, or from silicones. The silicone lenses have a hyper permeability for oxygen, but they moisten badly, are impenetrable for an eye-water liquid and are rather inconvenient for long using.

Investigations of the creation of contact lenses of long usage, are directed on the development of materials, which should have a necessary permeability for oxygen and eye-water liquid, as well as provide high optical and mechanical characteristics at minimum thickness and mass of a lens. However, while using the lenses is getting polluted and on its surface may appear fungus and bacteria. It requires periodic flushing lenses with the specific disinfecting solutions. This issue could partially be solved via contact lenses saturation (infusion) with a small amount of silver salts derived from its aqueous solutions. However, the introduction of silver salt in hydrogel creates only short-term effect, since the salts will be washed from the lens during operation.

Analysis of recent research and publications. For more than 35 years already the Department of Chemical Technology of Plastics Processing of the Lviv Polytechnic National University carries out investigations in the field of synthesis and application of medical polymers, for ophthalmology including [2]. Basically, these investigations are directed on synthesis of new and modification of already existing polymers. After long approbation, polyvinylpyrrolidone (PVP) has been chosen as the base starting product. Uniqueness of properties and application of PVP are caused by its structure and physical-chemical properties – the presence of carbamatic group promotes high selective-sorption properties, complex formation with iodine and other inorganic and organic compounds, formation of and ionic form of macromolecules in an aqueous medium [2]. PVP is non-toxic and biologically compatible, it is successfully applied in medicine as a substitute of a blood plasma. Alongside with the expected physiological activity and its function ability PVP positively influences the character of polymerization reaction in the synthesis of its copolymers. Besides, the PVP turned out to be an effective reducing silver agent by its salts [3]. This reaction opens up new opportunities by ensuring the PVP crossed linked hydrogels contain antibacterial properties.

Work purpose. The work purpose was to develop a material with antibacterial properties which would be useful for the contact lenses production and also research its basic properties.

Materials and methods. 2-Hydroxyethyl methacrylate (HEMA, Bisomer) were vacuum distilled before use, Poly(ethylene glycol) dimethacrylate (PEGDMA-13) purified by chromatography through a double column of Al_2O_3, Benzoyl peroxide (BPO, 97 %, Fluka) was twice recrystallized from ethanol. Polyvinylpyrrolidone (PVP, M_W = 12 600 g/mole, Povidone, Sintvita), Butanol, Cyclohexanol, Diethylen glycol, Dimethyl sulfoxide (DMSO), Ethylen glycol were used as received.

Hydrogel lens materials were obtained by block polymerization of compositions [2]. Structural parameters of the polymeric net in hydrated state were estimated by means of the molecular weight of macrochain section (M_n) between neighboring cross-linking nodes determined using module of high elasticity. The molecular weight of chain section between neighboring cross-linking nodes was investigated by the procedure described in [4].

Mechanical properties of hydrogels were determined by breaking sample with probe indenter. To ensure the research in the aqueous medium, we have constructed a special adjustment [4].

Oxygen permeability of the synthesized hydrogels was investigated by the polarographic method on changing the concentration of oxygen that penetrated through the hydrogel film with thickness of 0,5 mm. For this, a special polarographic cell was designed (Fig. 1).

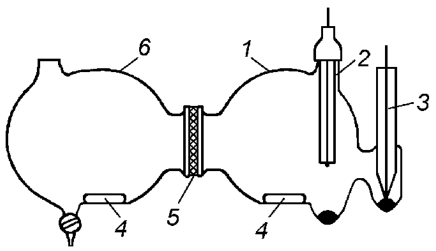

Fig. 1. Scheme of cell for hydrogel oxygen permeability investigation: 1, 6 – compartment; 2 – dripping mercury electrode; 3 – mercury electrode; 4 – magnetic stirrer; 5 – hydrogel

Study of oxygen diffusion through the hydrogel samples was carried out follows. The sample was placed between compartments *1* and *6* after they were filled with sodium chloride and purged with argon to remove oxygen from the solution and the sample. The completeness of oxygen removal was checked by polarography. The solution was then decanted from the compartment *6*, compartment was filled with saline and bubbled by air compressor for oxygenation. From that moment the countdown of experiment time began. For uniform distribution of diffused oxygen throughout the solution a magnetic stirrer was used. At regular intervals the polarograms of solution were filmed. Using calibration curve oxygen concentration in the solution was found. Based on the volume of the solution and its concentration amount of diffused oxygen was calculated. The rate of oxygen diffusion through the hydrogel sample was determined using Deynes-Barrer method [5]:

$$D = \frac{l^2}{6 \cdot q},$$

where: D – diffusivity, m^2/s, l – sample thickness, m; q – "delay time" (time from the experiment beginning to oxygen appearance in compartment 1), s.

Permeability of hydrogels for water and NaCl was investigated by the procedure offered by Karelin [6], optical transparency – by the standard procedure [7].

Results and Discussion. Investigations carried out at the Department of Chemical Engineering of Plastics Processing of the Lviv Polytechnic National University in the direction of the establishment of hydrogels with controlled structure and permeability, found that HEMA polymerization in the presence of PVP going through a stage of complex formation (CCT) between them [2], which actively affect the rate of polymerization (Table 1).

Table 1

The influence of the solvent nature on complexation parameters and on the rate of polymerization (*V*) of HEMA-PVP composition

№	Solvent	Constant of complex stability, K, $dm^3 \cdot mole^{-1}$	Viscosity*, $h \cdot 10^3$, Pa·s	$V^* \cdot 10^4$, $mole \cdot dm^{-3} \cdot s^{-1}$ (at 60 °C)
1.	Dimethyl sulfoxide	0	2,4	0
2.	Cyclohexanol	0,06	17,6	0,6
3.	Butanol	0,12	2,1	0,8
4.	Ethylen glycol	0,17	14,4	1,1
5.	Diethylen glycol	0,21	22,3	1,5
6.	Water	0,28	5,3	3,8

** HEMA : PVP : solvent = 9:1:10 mass. p. (non initiation)*

The resulting HEMA-PVP complex acts as a initiating system that is highly effective even in the absence of more traditional initiators of peroxide type or azo compounds and is largely independent of changes of the viscosity of the reaction mixture, caused by the nature of the solvent (Table 1). In this case, the polymerization proceeds in a complex-radical matrix mechanism with formation of rarely-cross-linked copolymers [2]. In the dry state the following (co)polymers are solids. Due to absorption of water they swell, resulting in the formation of diphasic systems consisting of chains of polymer, chemically and physically interconnected, and water that fills the free intermacromolecular space.

As a result of such swelling, hydrogel becomes permeable to water and substances dissolved in it. The higher water absorption of hydrogel, the higher its permeability it.

Another CCT effect in polymerization of HEMA in a composition with PVP was found out by the researches. It shows that the constant of complex formation K_C is interconnected with structural parameters of copolymer grid and their properties (Table 2).

Using these two revealed effects, we have developed ways of regulated synthesis of PVP copolymers, which are characterized by high sorption and selective diffusive properties (Table 3, 4).

Table 2

Dependence of PVP inoculation efficiency (*f*) and molecular weight of net internodal fragment (M_n) from a constant complex formation (*K*) in the system PVP–HEMA – a dissolvent

№	*K*, $dm^3 \cdot mole^{-1}$	M_n, $kg \cdot mole^{-1}$	*f*, %	PVP content in copolymers, %
1.	0,28	24	87	20
2.	0,13	34	60	30
3.	0,05	46	47	45
4.	~0	64	35	60

Table 3

Properties of hydrogels

№	Composition content for hydrogel synthesis mass. p.				Water permeability $K \cdot 10^4$, $m^3 \cdot m^{-2} \cdot h^{-1}$	Coefficient of permeability of NaCl, $mole \cdot m^{-2} \cdot h^{-1}$	Tensile strength, *s*, MPa	Relative elongation under under rupture, *e*, %
	HEMA	PVP	H_2O	DMSO				
1.	100	–	100	–	5,1	80	0,53	165
2.	80	20	100	–	52,3	181	0,40	235
3.	80	20	95	5	54,6	193	–	–
4.	80	20	90	10	56,5	212	0,41	240
5.	80	20	80	20	62,4	240	0,41	245
6.	80	20	200	–	74,2	234	0,38	245
7.	80	20	300	–	90,3	263	0,37	255
8.	70	30	100	–	71,4	232	0,31	270

Coefficient of permeability of light for polymers of composition: 1–5, 8, 9–90…96 %; 6,7 – opaque polymers

It was mentioned, that during water sorption optical properties of copolymers change differently depending on structure. The conditions of copolymers synthesis and their compositions have been determined and they are characterized during hydration by stability of optical properties (Table 4). In order to provide the materials with bactericidal properties during the hydrogels synthesis in their structure, the silver nanoparticles were synthesized by reacting silver nitrate with PVP. This reaction has been researched in detail [3].

Table 4

Physical-mechanical characteristics of polymers in a hydrated condition

№	Composition content for hydrogel synthesis, mass. p.			Coefficient of oxygen permeability, 10^{10}, $m^2 \cdot s^{-1}$	Water contain, %	Coefficient of permeability of light, %
	HEMA	PVP	PEGDMA-13			
1	100	–	–	0,29	39,2	96/95
2	80	20	–	1,13	42,3	96/96
2	70	30	–	1,51	44,1	95/94
4	80	20	5	0,45	40,9	95
5	80	20	10	0,42	40,6	94

** The denominator for compositions in the initial composition containing 0.1 wt. % $AgNO_3$.*

PVP copolymers are characterized by much higher permeability to oxygen compared with poliHEMA, resulting in lens made of such materials are more acceptable to the human eye. At the same time the copolymers optical transparency is almost unchanged, even if polymers contain the silver nanoparticles in its structure.

The hydrogels derived from the compositions containing at least 0.2 % of silver nitrate proved high bactericidal and fungicidal properties against Escherichia coli, Staphylococcus aureus bacteria and Aspergillus niger. This enabled to refuse the utilizing of such auxiliary materials as antibacterial liquid for cleaning lenses.

It is necessary to note, that the change of the structure and composition of copolymers may considerably influence the size of refraction index n_D. This was consequently used for optimization of copolymers composition for contact lenses. It allowed to receive correctional soft contact lenses with the following operational properties (Table 5).

Table 5

The characteristics of a polymeric material for soft contact lenses

№	Properties in hydrated condition	Parameter meaning
1	Absorption of water, %	51
2	Oxygen permeability, 10^{10} $m^2 \cdot s^{-1}$	1,2
3	Water permeability, 10^4 $m^3 \cdot m^{-2} \cdot h^{-1}$	52
4	NaCl permeability, $mole \cdot m^{-2} \cdot s^{-1}$	180
5	Toughness at a stretching, MPa	0,4
6	Relative tensile elongation , %	250
7	Permeability of light, %	96
8	Refraction index n_D	1,4253

At the expense of increased oxygen permeability and high refraction index n_D of a lens differ by comfort at operation. The presence of silver nanoparticles provides lenses with fungi-bactericidal properties.

Conclusions. A performed investigation allows developing hydrogel material for soft contact lenses with bactericidal properties based on 2-hydroxyethyl methacrylate and polyvinylpyrrolidone copolymers. Such lenses excel increased oxygen, water and ion permeability that provides their effective application.

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