

doi: 10.15407/ujpe62.05.0402

V.B. NEIMASH, H.D. KUPIANSKYI, I.V. OLKHOVYK, V.YU. POVARCHUK,
I.S. ROGUTS'KYI

Institute of Physics, Nat. Acad. of Sci. of Ukraine
(46, Prosp. Nauky, Kyiv 03028, Ukraine)

**PHYSICAL PROPERTIES
OF RADIATION-CROSSLINKED
POLYVINYL ALCOHOL–POLYETHYLENE
GLYCOL HYDROGELS FROM THE VIEWPOINT
OF THEIR APPLICATION AS MEDICAL DRESSINGS**

PACS 61.82.Pv, 82.35.-x

The influence of component composition, as well as hydration and electron irradiation conditions, on mechanical, optical, diffusion, and hydrophilic properties of radiation-crosslinked hydrogels prepared on the basis of the polyvinyl alcohol–polyethylene glycol system has been investigated from the viewpoint of their application to the fabrication of medical dressings to treat burns and wounds. A significant impact of the electron irradiation intensity and the temperature of initial solutions on the processes of polymer radiation crosslinking is experimentally revealed and analyzed. The hydrophily of crosslinked hydrogels is demonstrated to depend more strongly on the exposure dose than on the gel composition. The optimal intervals of radiation doses and polymer concentrations, at which the radiation-crosslinked hydrogel satisfies requirements for medical dressing materials are determined.

Keywords: radiation crosslinked hydrogels, polyvinyl alcohol–polyethylene glycol system, medical dressing materials.

1. Introduction

The structure of radiation-crosslinked hydrogels (RCLHG) is a three-dimensional network consisting of molecules of multiatomic polymers linked with one another by means of radical bonds (links) and “filled” with water [1]. Radiation-crosslinked hydrogels are classed to the “soft matter”, one of the forms of the substance in the condensed state. They are hydrophilic, i.e. they are capable of absorbing a significant amount of external water or aqueous solutions.

Polar water molecules are held in RCLHGs due to both the forces of their weak dipole interaction with the corresponding sections of polymer molecules and the forces of surface tension in the capillary structure of three-dimensional network [2]. Since the covalent links do not allow the polymer network of RCLHGs to dissolve, its ability to hold water is much higher than that of hydrophilic linear polymers [2, 3]. The water content in RCLHGs can reach 90–95%. As a result, RCLHGs have a soft consistence,

and they are characterized by a combination of properties, which makes them closer to the natural living tissue than any other class of synthetic materials [4].

The RCLHG porosity allows certain substances to be dissolved in the gel matrix and, afterward, released at the surface (or the inverse process, e.g. the surface contaminant is absorbed into the bulk, can take place). The rate of admixture transport between the surface and the bulk depends on the admixture diffusion coefficient and the parameters of the crosslinked gel network [5]. Those parameters can be controlled in wide intervals by varying the density of crosslinks between the molecules in the gel matrix, which is an aqueous solution of hydrated polymer molecules [5–7].

Radiation-crosslinked hydrogels can be biologically compatible with the human body not only because of a high water content, but also owing to their component composition. Therefore, they are manufactured from such chemically inert substances as agar-agar, gelatin, chitosan, some kinds of cellulose, polyacrylamide, polyvinylpyrrolidone, polyethylene glycol

(PEG), polyvinyl alcohols (PVAs), various polysaccharides, and others [8, 9].

Radiation-crosslinked hydrogels are widely applied in medicine, in particular, as a wet dressing material to cure wounds, burns, and various skin diseases. The maintenance of the moist environment of a wound substantially stimulates the metabolic and regenerative processes in damaged tissues and, as a result, considerably accelerates healing [10]. The application of a dressing with RCLHG to a wound or a burn provides an instant anesthetizing effect owing to the wound cooling by a considerable mass of water, which possesses a high heat capacitance. Afterward, the wound is maintained in the cooled state due to the water evaporation from RCLHG. In this case, very soft and elastic RCLHG closely contacts with the wound relief and isolates it from external infection. The very RCLHG, by definition, is a sterile material, because it is disinfected by radiation during the radiation-induced crosslinking process.

The RCLHG transparency allows the state of a wound to be monitored without removing the dressing. Antiseptics, analgetics, and anesthetizing substances that are contained in the gel matrices disinfect, anesthetize, and heal the wound during the following time period. The diffusion-driven equilibration of the concentrations of water-soluble substances in the bulk and on the surface of RCLHG can last for several hours. In the case of RCLHG dressings, this process looks like the oppositely directed diffusion fluxes of medicines from the dressing to the wound, and the wound exudates to the dressing.

An important circumstance consists in that RCLHGs, owing to their high water content, do not stick to wounds. Therefore, unlike ordinary cotton dressings, the RCLHG ones can be changed without serious consequences and without damaging the newly formed epidermis.

Concerning the scope of RCLHG application in medicine as dressings, the following physical, chemical, and biological properties of those materials are important:

- their mechanical strength has to be high enough for the long storage in a hermetically sealed but flexible container like a polyethylene bag in order to provide a quick access and convenient application to a wound under extreme field conditions;
- their water content has to be not lower than 80%, provide an effective anesthesia of the wound by cool-

ing, create a moist environment at the wound surface, and prevent the sticking to the wound;

- their hydrophily (the ability to absorb water) has to be substantial, which is beneficial for the sorption and subsequent removal of physiological exudates from the wound, as well as for the impregnation of a dressing with medical solutions;

- they have to be characterized by a high diffusion permeability for aqueous solutions and oxygen used to feed the wound from the external dressing surface;

- they must be surgically sterile;

- they must be impermeable for microorganisms responsible for external infection;

- their operating abilities have to be stable within a temperature interval of 0–45 °C and restorable after the material storage in a hermetic package within a temperature interval from –60 to +60 °C;

- they must be not toxic, being biologically compatible with human skin and tissues of open and purulent wounds (the absence of irritations or rejections).

The difficulty consists in that those kinds of RCLHGs that are known today do not fully correspond to the mentioned requirements. Each type of RCLHGs has its advantages with respect to certain parameters, which is usually attained due to shortcomings with respect to others. Moreover, a considerable number of RCLHG kinds have such component compositions or the features in their production technology that they do not provide both the profitability of their fabrication and the production affordability for the mass consumer. Therefore, the research of the properties of new RCLHG types, as well as the influence of various physical factors on the processes of RCLHG formation and the final RCLHG parameters, remains challenging.

The aim of this work was to study the physical properties of RCLHGs prepared on the basis of the PVA–PEG system and the influence of the following factors on them:

- the component composition of the PVA–PEG system;

- conditions of polymer hydration in the course of hydrogel preparation before irradiation;

- the energy, intensity, and dose of electron irradiation at the radiation crosslinking;

- the thermal prehistory of hydrogel before the radiation crosslinking and its temperature during this process.

2. Experimental Part

2.1. Hydrogel preparation

In this work, we used polyethylene glycol PEG-6000, and polyvinyl alcohols PVA 8/1 and PVA 11/2. Distilled water was used as a solvent. When preparing hydrogel, PEG and PVA were separately dissolved in distilled water with the use of a water bath with a temperature of up to 100 °C. After the solutions had become transparent, the PEG solution was added to the PVA one, and the mixture was stirred until a homogeneous state was obtained. The obtained mixture was isolated from the air environment and



a



b

Fig. 1. Typical example of radiation-crosslinked hydrogel: in the technological packing (a) and unpacked (b)

put into a water bath for another 90 min in order to complete the hydration of polymers. Then hydrogel was so packed into polyethylene zip-lock bags that the latter did not contain air bubbles. Bags of various standard dimensions ranging from 3×4 to 15×20 cm² were used. The bags were filled with gel to obtain a uniform layer 3 mm in thickness over the bag plane.

The mixtures of PVAs of both kinds (the total PVA content $x = 2$ –25%) taken in various combinations with polyethylene glycol (the PEG content $y = 1$ –10%) were prepared and studied.

2.2. Radiation crosslinking of hydrogel

Samples of liquid hydrogel were packed into hermetically sealed polyethylene bags and put into a flat metallic case. The latter provided the formation of a plane layer of liquid hydrogel 2–3 mm in thickness. Then the case was arranged perpendicularly to the electron flux generated by a pulse electron accelerator.

Two electron accelerators were used for the radiation crosslinking of hydrogels: “ARGUS” (the electron energy $E_e = 1$ MeV) and “Elektronika” ($E_e = 4$ MeV). The electron flux intensity was varied within an interval from 0.1 to 2.5 $\mu\text{A}/\text{cm}^2$. The researched interval of radiation doses amounted to 1–50 Mrad. The current density in the electron beam and the total exposure dose were monitored, by using the Faraday cup method.

The temperature of hydrogel under the electron irradiation was measured with the help of an alumel-chromel differential thermocouple. The required temperature of the hydrogel sample was maintained by a balance between its heating (by means of the electron beam and an incandescent lamp) and cooling (using an air fan). The researched interval of hydrogel temperatures during irradiation amounted to 15–95 °C.

Under the influence of electron irradiation, the radiation crosslinking of hydrogel, i.e. the formation of covalent bonds between various polymer molecules, takes place [2]. As a result, the polymer molecules form a spatial network, which is capable to hold its shape under the influence of the gravitation. In Fig. 1, a typical view of a sample of radiation-crosslinked hydrogel in the technological packing (panel a) and without it (panel b) is shown.

2.3. Methods for the measurement of RCLHG properties

2.3.1. Mechanical properties

There are no standard values for such parameters as hardness, elasticity, ultimate rupture strain, and so forth, which could definitely characterize the requirements to RCLHGs applied as a dressing material. It is evident that hydrogel has to be rather soft and elastic in order to conform to the wound by reproducing body's relief. At the same time, it must be rather firm, not tear when being packed, and serve as a wound sheeting.

As an integrated parameter of the RCLHG mechanical strength, we used the ratio (expressed in percent) between the ultimate elongation of a material sample before its rupture at stretching to the initial sample length: $UE(\%) = (L_{\max} - L_0)/L_0 \times 100$. For RCLHGs used in hydrogel dressings from the leading trade marks "Paul Hartmann" and "Aqua-Gel", this parameter equals 50–100%. If the value of the parameter UE fell within this interval, it was considered as a criterion of the optimum quality of hydrogel crosslinking.

The dose of electron irradiation that provided such a value for UE was called the "optimum crosslinking dose", D_{OCL} . This parameter characterizes the efficiency of radiation crosslinking, because it is proportional to the exposure dose that is required for one intermolecular bond to be formed, and the sum of those doses results in the given UE .

2.3.2. Hydrophilily

In order to analyze the ability of RCLHGs to absorb water, we studied the dependence of the relative growth of the sample mass m with respect to its initial mass m_0 , $WU(\%) = (m - m_0)/m_0 \times 100$, on how long the sample was held in water. Samples with identical dimensions (disks 5 mm in diameter and 3 mm in thickness) but made of RCLHGs with different chemical compositions or subjected to different thermoradiation treatments were used.

2.3.3. Diffusion permeability

Diffusion permeability for aqueous solutions was estimated on the basis of the penetration rate of water-soluble dyes from one surface of the flat RCLHG sample to the other one (Fig. 2). For this purpose, we also

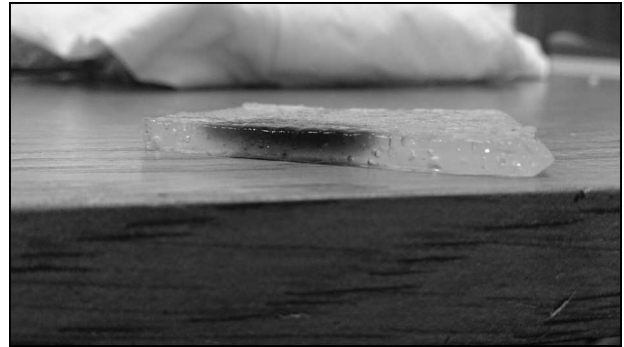


Fig. 2. Cross-section of a RCLHG plate at the site, where a droplet of brilliant green solution diffuses from the upper sample surface. The plate thickness equals 5 mm

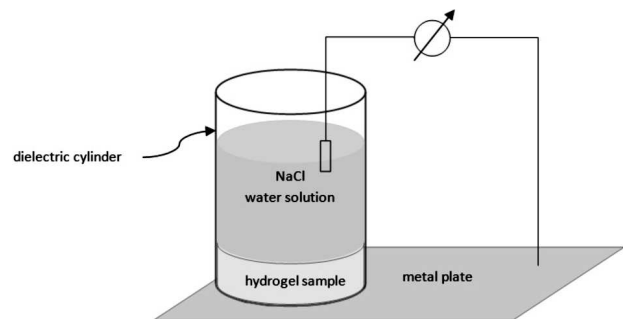


Fig. 3. Schematic diagram of the measurement of the RCLHG electrical resistance change during the diffusion of an external solution

used the variation rate of the RCLHG electrical resistance in the course of diffusion of the aqueous NaCl solution from one surface of the sample to the other one (Fig. 3).

3. Results and Their Discussion

The aqueous PVA solution looks like a transparent fluid, the viscosity of which is proportional to the PVA-to-water mass ratio and reciprocal to the temperature. The maximum of this ratio increases with the solution temperature and decreases with the PVA molecular weight. When being cooled down, the PVA solution becomes more viscous, is transformed into gel, and becomes less transparent. For example, at room temperature and mass concentrations higher than 15–20%, the PVA solution is transformed into a dense plastic mass, which does not leak out from the vessel, but becomes liquid again when being heated on a water bath. The solution of PVA 8/1 with a mass concentration of 20–25% behaves similarly.

Irradiation of the hydrated PVA solution (hydrogel) with electrons results in its transition from the liquid state into a more dense gelled state owing to the radiation crosslinking between polymer molecules. As the exposure dose increases, the specific viscosity of hydrogel gradually grows, as was observed, e.g., in work [11], and, accordingly, its fluidity decreases. The fluidity vanishing means that hydrogel has been transformed into the radiation-crosslinked state. In other words, the sample can now hold its shape under the gravitation action. It reveals attributes of elastic deformation and is characterized by a certain rupture strength. Being subjected to further irradiation, RCLHG hardens, starts to release water, and comes unstuck from bag's walls. It is probable that radiation crosslinks are accumulated, and they squeeze the three-dimensional network formed by them so strongly that RCLHG cannot contain anymore the whole initial volume of a solvent. This conclusion completely agrees with the data of work [12]. The growth of the exposure dose also gives rise to the accumulation and size growth of gas bubbles in the RCLHG bulk. It is remarkable that the heating of radiation-crosslinked hydrogel to $T = 100$ °C does not transform it into the liquid state. This fact may testify to the covalent character of radiation crosslinks between polymer macromolecules, which govern the mechanical properties of RCLHG.

A radiation crosslink is formed as a result of the interaction between a radical (a dangling bond) in one polymer macromolecule and an atom in another macromolecule. Ionizing radiation creates radicals in the hydrated polymer following two basic mechanisms: the direct interaction of a high-energy particle with atoms in the polymer macromolecule, which gives rise to ionization and breaks the bonds between them, and the interaction of radiation with water molecules, which gives rise to their radiolysis, i.e. the excitation of the electron subsystem, ionization, and dissociation into free (mobile) radicals. Mainly, this is the reaction $\text{H}_2\text{O} \rightarrow \text{OH} + \text{H}$. Afterward, the mobile radicals chemically interact with the polymer and create radicals (dangling bonds) in its structure [13, 14]. For instance, a hydroxyl OH group can capture a hydrogen atom H from the C–H bond in the polymer and can form a water molecule H_2O , leaving a dangling bond at the carbon atom in the polymer chain. The radicals that emerged following this scenario form crosslinks with

other sections in the same polymer macromolecule or with other macromolecules. In the examined hydrogels, the number of water molecules was approximately an order of magnitude larger than the number of all others. Therefore, it is the former that are the main absorbers of high-energy irradiation. Therefore, the second mechanism of radical formation in polymer molecules should be considered as dominating.

Some of the hydrogen atoms that had emerged in the course of water radiolysis united to form H_2 molecules. As a result, there appeared gas bubbles 0.3–3.0 mm in diameter in the bulk of RCLHG samples (Fig. 1). Their size and concentration correlated with the exposure dose. Later, when the samples were stored at room temperature, the dimensions of the gas bubbles gradually decreased, which probably took place owing to the hydrogen diffusion outward.

The influence of PEG on the properties of the researched RCLHGs fabricated on the basis of the $\text{PVA}_x\text{-PEG}_y$ system becomes noticeable, when its concentration in the initial solution exceeds 1%. The addition of PEG to the initial PVA solution to a concentration of 1–5% substantially increases the elasticity and the rupture strength of RCLHG. It is probable that PEG plays the roles of low-molecular crosslinking sensitizer and polymer solution plasticizer following the mechanism discussed in work [15]. This scenario is implemented despite a reduction of the gel fraction, when PEG is added [16, 17]. If the PEG concentration in the initial solution of the $\text{PVA}_x\text{-PEG}_y$ system exceeds 5%, opaque clusters characterized by a high density are formed. The PEG content optimum for the radiation crosslinking falls within an interval of 1–3%, depends on the molecular weight and concentration of applied PVA, and is determined experimentally.

The D_{OCL} parameter means the irradiation dose, at which the optimum concentration of crosslinks is formed in hydrogel with the given composition. As a result, mechanical properties are obtained that are close as much as possible to the requirements to the RCLHG medical application [18]. It turned out that, for every hydrogel composition, the value of D_{OCL} depends on the intensity of an electron flux used for the crosslinking. In Fig. 4, this dependence is illustrated for two kinds of hydrogel. A more than two-fold decrease of D_{OCL} with the growth of the irradiation intensity is observed provided approximately identical temperatures of the samples. This

fact means that if the irradiation intensity is high, half as many electrons are required to create the same number of crosslinks in comparison with the low-intensity case. In other words, the efficiency of radiation crosslinking grows with the irradiation intensity.

A similar dependence is observed for elastomers [19] and hydrocarbons [20]. The authors of the cited works explained it by the fact that the intensity (the radiation flux density) growth gives rise to a higher average concentration of transient products (radicals) and, hence, to the acceleration of reactions, in which they participate. In the case of pulse irradiation, the dependence of the crosslinking process on the radiation intensity can be driven by the ratios between the radical lifetimes, as well as between the duration of pulses and the intervals between them [21]. The number of crosslinks is proportional to the stationary concentration of radicals, R_{st} , which is established as a result of the equilibrium between the processes of radical formation and recombination (or passivation), including the crosslink formation.

In the absence of specially introduced passivating admixtures and considering the indicated interval of exposure doses, we may regard that all radicals participate in the formation of crosslinks. During the electron pulse action, t_p ($t_p = 4 \mu\text{s}$ for the linear electron accelerator “Elektronika”), radicals are formed at the rate λ_R and disappear as a result of the crosslink formation. The time constant for the radical accumulation process will be denoted as τ_1 . In the time interval between pulses, $t_{off} \sim 10^3 t_p$, only the radical concentration R exponentially decreases as a result of the crosslink formation. The time constant for the process of R reduction, i.e. the radical lifetime, will be denoted as τ_2 . The resulting time dependence of R has a sawtooth profile, as is demonstrated in Fig. 5. The figure illustrates three time dependences of the radical concentrations created in hydrogels by high-energy electrons in the course of pulse irradiation with three different irradiation intensities.

One can see that if $\tau_2 \ll t_{off}$ and if the electron pulse intensity, J , is low, the radical concentration R can fall to zero before the next pulse begins. If the intensity increases to $2J$ and $4J$ (provided the same τ_2), the residual concentration grows (${}^J R_1 < {}^{2J} R_2 < {}^{4J} R_3$) for those radicals, which had not recombined before the next pulse began. They are accumulated with further pulses. The minimum concentration of radicals within the period (dashed

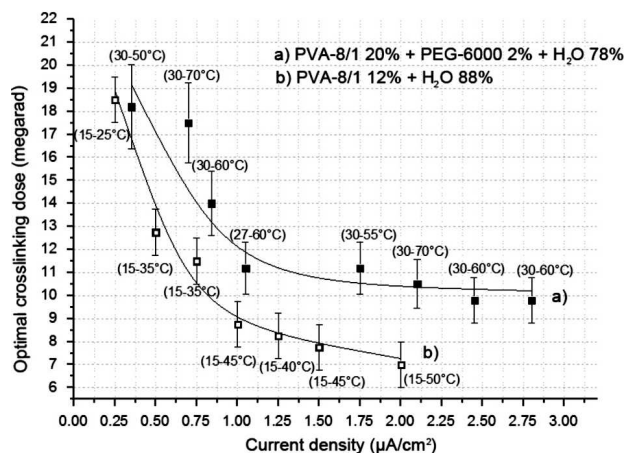


Fig. 4. Dependence of the exposure dose for the optimal crosslinking, D_{OCL} , on the integrated (averaged over 1 s) density of a pulse electron flux. The pulse duration is $4 \mu\text{s}$, and the pulse frequency is 250 Hz

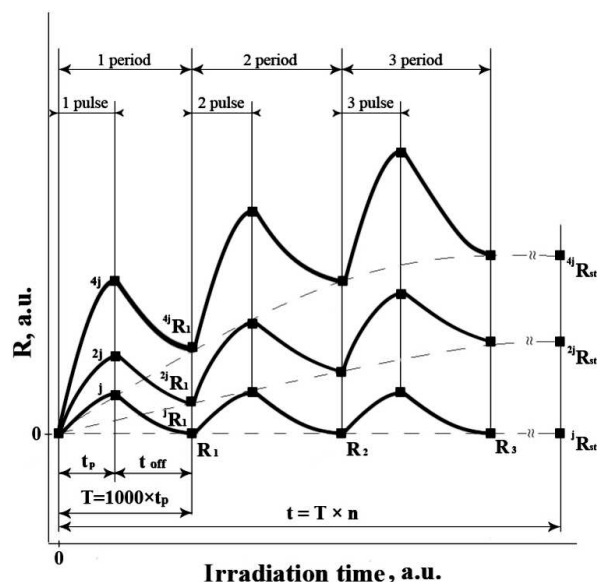


Fig. 5. Variations of the radical concentration in hydrogel during three first periods of pulse electron irradiation with the intensities J , $2J$, and $4J$; t_p is the pulse duration, and t_{off} is the interval between pulses

curves in Fig. 5) grows faster at the higher intensity. Ultimately, the stationary concentration R_{st} , which is proportional to the irradiation intensity, is established.

Let us imagine the process of radiation crosslinking as the formation of a complex consisting of a radical in one polymer molecule and an atom in another

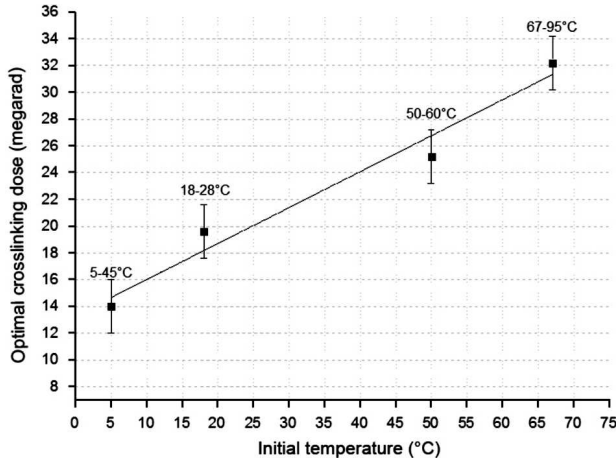


Fig. 6. Dependence of the optimal crosslinking dose on the initial sample temperature ($j = 0.35 \mu\text{A}/\text{cm}^2$). Near each point, the final temperature of a sample heated by the electron flux is indicated. Solution 20% PVA-8/1 + 2% PEG-6000

molecule. The notation N_x will stand for the concentration of those atoms, R for the concentration of radicals, and Z for the concentration of crosslinks. Then the kinetics of crosslink accumulation can be written in the form

$$\frac{dR}{dt} = \lambda_R - \chi_{RX}RN_x, \quad (1)$$

$$\frac{dZ}{dt} = \chi_{RX}RN_x, \quad (2)$$

where λ_R is the radical generation rate, and χ_{RN} the effective cross-section of the interaction between the radical and polymer atoms.

As one can see from Fig. 5, the initial rate of radical accumulation, $\frac{dR}{dt}(t \rightarrow 0)$, depends on the irradiation intensity. Lately, a stationary value of radical concentration, R_{st} , is established, by owing to the equilibrium between the processes of radical generation and passivation in the course of crosslink formation. The R_{st} magnitude also correlates with the irradiation intensity.

The stationary state means that $\frac{dR}{dt} = 0$. In this case, Eq. (1) looks like $\chi_{RX}RN_x = \lambda_R$, and, substituting this expression into Eq. (2), we obtain that $\frac{dZ}{dt} = \lambda_R$. A solution of this equation is $Z(t) = \lambda_R t$. In other words, the crosslinks are accumulated proportionally to the irradiation time and, accordingly, to the exposure dose. Taking into account that $dZ/dD = (1/J)dZ/dt$, where $J = dD/dt$ is

the irradiation intensity, we obtain that $dZ/dD = \lambda_R/J$. However, by definition, $\lambda_R \sim J$. Therefore, the crosslink formation efficiency, dZ/dD , should be independent of the radiation intensity. The same is valid for the reciprocal quantity, the optimum crosslinking dose, $D_{OCL} \sim dD/dZ$, which is required to create the optimum (i.e. the same) concentration of crosslinks. However, the computer approximation of experimental data presented in Fig. 5 brought about the dependence $D_{OCL} \sim 1/J$, which means that $dZ/dD \sim J$, so that the crosslinking efficiency is proportional to the radiation intensity. In our opinion, this conclusion confirms the consideration given above concerning the role of irradiation intensity at the pulse irradiation.

The importance of the temporal parameters of pulse irradiation for the processes of radiation crosslinking is illustrated in Table. The table exhibits the experimental values obtained for D_{OCL} and the crosslinked layer thickness d_z in liquid hydrogel (10% PVA 11/2 + 3% PEG + 87% H₂O) irradiated with 1- and 4-MeV electrons. The average intensities J and the total doses obtained during the irradiation time t_{int} are the same, but the pulse durations t_p and the pauses T between them are different. One can see that, according to the parameter D_{OCL} , the less intensive (1 MeV) irradiation unexpectedly crosslinks hydrogel more efficiently than the more intense (4 MeV) one does. It is of interest that the D_{OCL} ratio between those two irradiation modes is equal to the ratio of the pauses between the pulses. The thickness of a crosslinked layer expectedly correlates with the energy of electrons.

We also studied the dependence of the hydrogel crosslinking efficiency on the temperature of hydrogel at its irradiation. Figure 6 demonstrates the experimental dependence of D_{OCL} on the gel temperature. One can see a substantial reduction of D_{OCL} , when the temperature at irradiation decreases. For the examined temperature variation, the gel viscosity considerably increased, which means the en-

Radiation crosslinking parameters

E_e , MeV	t_{puls} , μs	t_{off} , ms	J , μA	t_{int} , μs	D_{OCL} , Mrad	D_z , mm
1	3.3	2.5	0.25	1320	5	1.5
4	4.5	4.0	0.25	1125	8	6.0

hancement of the role of the dipole interaction between polymer macromolecules. The dipole interaction brings about a diminishing of the distance between macromolecules, as well as their spatial rearrangement and restructuring. In our opinion, these processes can substantially increase the probability of radical crosslink appearance, so that it can be responsible for the reduction in D_{OCL} .

The capability to absorb water (hydrophily) is an important property of RCLHG from the viewpoint of their medical application. Hydrophily allows them to absorb wound's exudates and to be impregnated with medicine solutions before their application as dressings. The RCLHG hydrophily was found to depend on the irradiation dose. Figure 7 demonstrates the dependences of the relative mass growth of RCLHG samples irradiated to various electron doses on the time of their holding in distilled water. One can see that the rate of water absorption and the amount of absorbed water at the saturation substantially grow with the irradiation dose. This behavior differs from that observed for hydrogels of the PVA-pyrrolidone [22] and pyrrolidone-polyacryl [23] systems. The PVA_x-PEG_y system with the given composition content can increase its weight by 50% during an hour and a half owing to adsorbed moisture.

The reduction of hydrophily with the growth of the PVA concentration in the initial mixture at close (4–5 Mrad) irradiation doses looks somewhat unexpected (the similar event was observed in work [24]). This conclusion follows from the comparison of plots depicted in Figs. 7, *a* and *b*, where analogous dependences are exhibited for hydrogel with twice as high mass concentration of PVA-8/1. This fact may mean that the hydrophily of RCLHG is less associated with the polar binding of water molecules at PVA owing to hydration, than with something similar to the surface tension in capillaries created by the radiation crosslinking of polymers. It is probable that radiation affects the gel hydrophily by branching those capillaries due to the formation of radiation crosslinks. As is seen from Fig. 7, *b*, the hydrophily of the PVA_x-PEG_y system with the given composition content amounted to 92% after the water absorption for 4 h, and it can be regulated in a wide interval by means of the irradiation dose. The maximum hydrophily of the RCLHG belonging to the considered system amounts to 200–250%. This value is reached

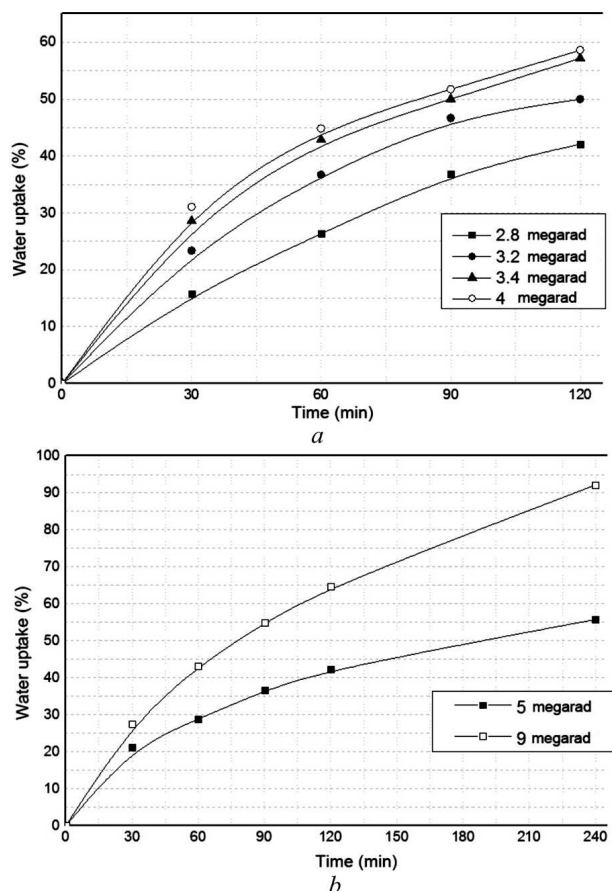


Fig. 7. Dependences of the relative mass growth, $WU(\%) = (m - m_0)/m_0 \times 100$, of RCLHG samples irradiated to various exposure doses on the time of their holding in water at room temperature: solution 10% PVA-8/1 + 1.5% PEG-6000 + 88.5% H₂O (*a*), solution 20% PVA-8/1 + 2% PEG-6000 + 78% H₂O (*b*)

after holding the sample for more than a day at room temperature or after an hour at $T = 60^\circ\text{C}$.

It is typical that the hydrophily drastically decreases with the PEG concentration growth. In particular, if the concentration of PEG-6000 exceeds 5%, the sample that has been radiation-crosslinked in the interval of D_{OCL} almost does not absorb water.

Hydration of polymer macromolecules in the course of solution preparation is an important factor for the radiation crosslinking. Depending on the hydration degree, macromolecules have a wrapped (like a ball) or unwrapped (quasilinear) configuration. This circumstance substantially affects their reactivity with respect to low-molecular radicals that arise in the

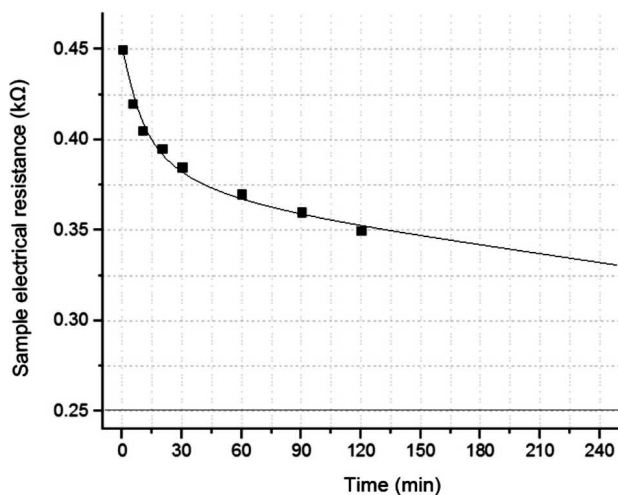


Fig. 8. Variation of the electrical resistance of the RCLHG disk sample (Fig. 3) in the course of diffusion of 3.2% NaCl solution at $T = 18^\circ\text{C}$. The sample thickness is 0.25 cm, and the diameter is 1.7 cm. Solution 20% PVA-8/1 + 2% PEG-6000 + 78% H_2O . Line $R = 0.25\text{ k}\Omega$ marks the resistance of the initial NaCl solution

course of water radiolysis. As a rule, the unwrapped configurations are more reactive than wrapped ones [13].

In our experiments, the researched $\text{PVA}_x\text{-PEG}_y$ system was hydrated by holding the aqueous solution of polymers at $T = 100^\circ\text{C}$ for 90 min. This procedure provides the unwrapping of polymer macromolecules that is sufficient for the radiation crosslinking at room temperatures. However, the further long-term (for 3 months) holding of gel samples at room temperature and without access of air resulted in a considerable change of their properties, which can hardly be explained by the growth of hydration. First of all, this concerns mechanical properties; namely, the samples were transformed from the liquid state into a more viscous one, which was close to the RCLHG state after irradiation. The relative elongation at the rupture of those samples amounted to 50% without irradiation. But they were not heat-resistant: when being heated to 60–70 $^\circ\text{C}$, the samples were transformed into the liquid state again. Moreover, after the long-term storage, the transparency of hydrogel samples became substantially lower. This effect completely disappeared, when the temperature was elevated to 60–70 $^\circ\text{C}$. The same effect, but much quicker (for hours), was produced, when hydrogel was cooled down before its irradiation to temperatures close to

0 $^\circ\text{C}$. It is significant that the further irradiation of samples (either stored for a long time interval or cooled down) with electrons at temperatures of 20–30 $^\circ\text{C}$ gave rise to a decrease of D_{OCL} by a factor of 1.5 to 2. In this case, the mechanical properties acquired in the course of irradiation remained thermostable, even when the samples were heated up to 100 $^\circ\text{C}$.

In our opinion, the described effects and the reduction of D_{OCL} with decrease in the sample temperature before irradiation can be explained by a certain structuring in hydrogel, which takes place due to the forces of polar interaction acting between separate macromolecules in hydrated polymers. This structurization is not thermally stable, but it evidently diminishes the average distance between macromolecules, which substantially increases the probability for the radiation crosslinks to be formed under further irradiation.

The ability of aqueous drug solutions to diffuse quickly in RCLHGs is an important property of the latter for their medical applications. As an illustration of this property, Fig. 2 demonstrates a photo of the RCLHG plate cross-section. A droplet of brilliant green solution was deposited on the upper surface of the plate. One can clearly observe the diffusive profile of the dye concentration.

In Fig. 8, the dependence of the electrical resistance $R \sim 1/n$, where n is the concentration of charge carriers in the disk sample of RCLHG, is shown (see Fig. 3). One can see that, after two hours of diffusion, the electric resistance and, accordingly, the concentration of charges in the sample reach values that are average between those for pure RCLHG and a NaCl solution. This result allows the diffusion coefficient of solution ions, \tilde{D} , to be evaluated from the relation $L = \sqrt{\tilde{D}\tau}$, where L is the diffusion length, and τ the diffusion time.

Setting L equal to the sample thickness and τ to the time interval, during which the average concentration between the initial concentrations of charge carriers in pure RCLHGs and a NaCl solution is established, we obtain $\tilde{D} \sim 10^{-5}\text{ cm}^2/\text{s}$. Hence, the transport of a water-soluble preparation from the external surface of the RCLHG layer about 0.3 cm in thickness takes about 1 h at room temperature.

4. Conclusions

The radiation crosslinking of hydrogels prepared on the basis of the $\text{PVA}_x\text{-PEG}_y$ system (with $x = 8 \div 20\text{ wt}\%$ and $y = 1 \div 3\text{ wt}\%$, depending on the

molecular weights of components) provides them by the mechanical properties that are required for their application as a material for wet medical dressings. The efficiency of the radiation crosslinking grows, as the time of the hydration at room temperature increases and the temperature, at which the initial hydrogel PVA_x–PEG_y has been irradiated, decreases. This fact may result from the spatial ordering of polymer macromolecules during the hydration owing to their dipole interaction. The concentration of intermolecular crosslinks is proportional to the exposure dose at least within an interval of 2–50 Mrad. However, PVA_x–PEG_y hydrogel obtains mechanical properties that are optimal for medical applications only in a narrow interval of crosslinking exposure doses, $D_{\text{OCL}} \pm 0.5$ Mrad for every specific ratio $x : y$. The crosslinking efficiency is proportional to the integrated intensity of pulse electron irradiation applied to the radiation crosslinking of hydrogel. The parameters of this dependence are determined by the lifetime ratios between the radicals created by irradiation, and by the duration and ratio of irradiation pulses.

The dependence of the thickness of a radiation-crosslinked layer in liquid PVA_x–PEG_y hydrogel, d_z , on the energy of electrons, E_e , is evaluated experimentally: $d_z = kE_e$, where $k \approx 1.5$ mm/MeV. The efficiency of the radiation crosslinking is found to decrease with the growth of the hydrogel temperature during irradiation. This phenomenon may result from the annealing of the intermolecular ordering between polymer macromolecules, which is established in the PVA_x–PEG_y solution due to the polar interaction at hydration. The hydrophilicity of RCLHG on the basis of the PVA_x–PEG_y system correlates with the exposure dose obtained during the crosslinking much more strongly than with the concentrations and molecular weights of applied polymers. This circumstance may testify to the domination of the hydrophilicity mechanism associated with the surface tension in RCLHG capillaries over the mechanism associated with the polymer hydration owing to the polar interaction. The diffusion coefficient for aqueous solutions in PVA_x–PEG_y radiation-crosslinked hydrogels has an order of 10^{-5} cm²/s within the interval of room temperatures. Therefore, the transport of the working concentration of water-soluble drugs from the external side of the RCLHG dressing to a wound takes about 1 h.

The authors are sincerely grateful to the Head of the Chair of Traumatology of Bogomolets National Medical University, Dr.Sci. in medicine, Prof. A.A. Bur'yanova; the Head of the Division of Chemistry of High-Molecular Compounds of T. Shevchenko National University, Dr.Sci. in chemistry, Prof. A.Yu. Kolendo; and the Deputy of the General Director of the PJSC SIC "Borshchahivskiyi CPP", Ph.D. in chemistry A.S. Shalamaya for their assistance in this work.

1. J.M. Rosiak, F. Yoshii. Hydrogels and their medical applications. *Nucl. Instrum. Methods B* **151**, 56 (1999).
2. J.M. Rosiak, P. Ulański, L.A. Pajewski, F. Yoshii, K. Makuuchi. Radiation formation of hydrogels for biomedical purposes. Some remarks and comments. *Radiat. Phys. Chem.* **46**, 161 (1995).
3. A.K. Nayak, R. Maji, B. Das. Gastroretentive drug delivery systems: A review. *Asian J. Pharm. Clin. Res.* **3**, 2 (2010).
4. Sh.P. Shetye, A. Godbole, Sh. Bhilegaokar, P. Gajare. Hydrogels: Introduction, preparation, characterization and applications. *Int. J. Res. Methodol.* **1**, 47 (2015).
5. T.R. Hoare, D.S. Kohane. Hydrogels in drug delivery: Progress and challenges. *Polymer* **49**, 1993 (2008).
6. J.M. Rosiak, I. Janik, S. Kadlubowski, M. Kozicki, P. Kujawa, P. Stasica, P. Ulański. Nano-, micro- and macroscopic hydrogels synthesized by radiation technique. *Nucl. Instrum. Methods Phys. Res. B* **208**, 325 (2003).
7. T. Schmidt, I. Janik, S. Kadiubowski, P. Ulański, J.M. Rosiak, R. Reichelt, K.F. Arndt. Pulsed electron beam irradiation of dilute aqueous poly(vinyl methyl ether) solutions. *Polymer* **46**, 9908 (2005).
8. E.A. Kamoun, X. Chen, M.S.M. Eldin, E.S. Kenawy. Crosslinked poly(vinyl alcohol) hydrogels for wound dressing applications: A review of remarkably blended polymers. *Arabian J. Chem.* **8**, 1 (2015).
9. C.M. Hassan, N.A. Peppas. Structure and applications of poly(vinyl alcohol) hydrogels produced by conventional crosslinking or by freezing/thawing methods. *Biopolymers. PVA Hydrogels, Anionic Polymerisation Nanocomposites* **153**, 37 (2000).
10. T.N. Yudanova, I.V. Reshetov. Modern wound dressings: making and properties (A review). *Khim. Farm. Zh.* **40**, No. 2, 24 (2006) (in Russian).
11. S. Francis, L. Varshney. Studies on radiation synthesis of PVA/EDTA hydrogels. *Radiat. Phys. Chem.* **74**, 310 (2005).
12. A.J. Swallow. *Radiation Chemistry* (Longman, 1973) [ISBN: 058246286X].
13. A.K. Pikaev. *Modern Radiation Chemistry. Solid Body and Polymers. Applied Aspects* (Nauka, 1987) (in Russian).

14. J.M. Rosiak, P. Ulański. Synthesis of hydrogels by irradiation of polymers in aqueous solution. *Radiat. Phys. Chem.* **55**, 139 (1999).
15. M.A. Ghalia, Y. Dahman. Biodegradable poly(lactic acid)-based scaffolds: Synthesis and biomedical applications. *J. Polym. Res.* **22**, No. 11, 218 (2015).
16. J. Dutta. Synthesis and characterization of γ -irradiated PVA/PEG/CaCl₂ hydrogel for wound dressing. *Am. J. Chem.* **2**, No. 2, 6 (2012).
17. J. Park, H. Kim, J. Choi, H. Gwon, Y. Shin, Y. Lim, M.S. Khil, Y. Nho. Effects of annealing and the addition of PEG on the PVA based hydrogel by gamma ray. *Radiat. Phys. Chem.* **81**, 857 (2012).
18. M.T. Razzak, E. Zainuddin, S.P. Dewi, H. Lely, E. Taty, S. Sukirno. The characterization of dressing component materials and radiation formation of PVA-PVP hydrogel. *Radiat. Phys. Chem.* **55**, 153 (1999).
19. A.S. Kuzminskii, T.S. Fedoseeva, F.A. Makhlis. *Radiation Chemistry of Elastomers. Radiation Chemistry of Polymers* (Nauka, 1973) (in Russian).
20. G. Foeldiak. *Radiation Chemistry of Hydrocarbons* (Akademiai Kiado, 1981) [ISBN: 963-05-2249-7].
21. V.N. Shubin, T.A. Frunze, Yu.I. Sharanin. *Kinetic Studies in Pulsed Radiolysis* (Nauka, 1974) (in Russian).
22. M.T. Razzak, D. Darwis, E. Zainuddin, S. Sukirno. Irradiation of polyvinyl alcohol and polyvinyl pyrrolidone blended hydrogel for wound dressing. *Radiat. Phys. Chem.* **62**, 107 (2001).
23. S. Kadłubowski, A. Henke, P. Ulański, J.M. Rosiak, L. Bromberg, T.A. Hatton. Hydrogels of polyvinylpyrrolidone (PVP) and poly(acrylic acid) (PAA) synthesized by photoinduced crosslinking of homopolymers. *Polymer* **48**, 4974 (2007).
24. B. Jiang, B. Akar, T.M. Waller, J.C. Larson, A.A. Appel, E.M. Brey. Design of a composite biomaterial system for tissue engineering applications. *Acta Biomater.* **10**, 1177 (2014).

Received 14.03.17.

Translated from Ukrainian by O.I. Voitenko

В.Б. Неймаш, Г.Д. Купянський,
І.В. Ольховик, В.Ю. Поварчук, І.С. Рогуцький

ФІЗИЧНІ ВЛАСТИВОСТІ
РАДІАЦІЙНО-ЗШИТИХ ГІДРОГЕЛІВ
ПОЛІВІНІЛОВИЙ СПИРТ-ПОЛІЕТИЛЕНГЛІКОЛЬ
В КОНТЕКСТІ ЗАСТОСУВАННЯ
В МЕДИЧНИХ ПОВ'ЯЗКАХ

Резюме

Досліджено вплив компонентного складу, умов гідратації та електронного опромінення на механічні, оптичні, дифузійні та гідрофільні властивості радіаційно-зшитих гідрогелів на основі системи полівініловий спирт-поліетиленгліколь з точки зору їх застосування у виготовленні медичних пов'язок для лікування опіків та ран. Експериментально виявлено та проаналізовано значний вплив інтенсивності електронного опромінення і температури розчинів на процесі радіаційного зшивання високомолекулярних полімерів. Показано переважну залежність гідрофільності зшитих гідрогелів від дози опромінення над залежністю від композиційного складу. Визначено діапазони оптимальності режимів опромінення та концентрації полімерів, що забезпечують вимоги до радіаційно-зшитого гідрогелю як матеріалу для медичних пов'язок.