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## Study of the Properties of Semi-Interpenetrating Networks Based on Acrylic Hydrogel and Collagen

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**Abstract.** Interpenetrating networks based on acrylic hydrogel and collagen were obtained by the method of free-radical polymerization. The effect of the degree of neutralization of acrylic acid and the temperature of synthesis of acrylic composites on the duration of the onset of gelation, of the obtained ratio of polymeric materials was studied. A decrease in the duration of the onset of gelation, with an increase in the degree of neutralization of acrylic acid from 0.6 to 1 and an increase in temperature from 25 to 45 °C was shown. During the work, the kinetics of swelling of the obtained samples on the basis of a pseudo-second order model and a mathematical model in distilled water, saline and phosphate--buffered saline was investigated. It was shown that synthesized polymer samples upon solvent sorption are described by Fick's low diffusion ( $n < 0.5$ ).

**Keywords:** Acrylic hydrogel, collagen, duration of the onset of gelation, sorption, sorption kinetics, wound dressing.

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## Исследование свойств полувзаимопроникающих сетей на основе акрилового гидрогеля и коллагена

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**Аннотация.** Методом свободно-радикальной полимеризации были получены взаимопроникающие сетки на основе акрилового гидрогеля и коллагена. Изучено влияние степени нейтрализации акриловой кислоты и температуры синтеза на время начала гелеобразования полученных образцов. Показано уменьшение продолжительности начала гелеобразования при увеличении степени нейтрализации акриловой кислоты с 0,6 до 1 и повышении температуры с 25 до 45 °С. В ходе работы была исследована кинетика набухания полученных образцов на основании модели псевдвторого порядка и математической модели в дистиллированной воде, физиологическом растворе и фосфатно-солевом буфере. Показано, что все синтезированные полимерные образцы при сорбции растворителя описываются малой диффузией Фика ( $n < 0,5$ ).

**Ключевые слова:** акриловые гидрогели, коллаген, время начала гелеобразования, сорбция, кинетика сорбции, раневые повязки.

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### Introduction

Hydrogel wound dressings are an effective alternative to traditional wound healing methods. One of the advantages of using polymeric hydrogel materials for epithelialization is the controlled release of drugs and regulation of the level of exudate secreted [1–3].

That is why an important characteristic of hydrogel dressings is the sorption capacity of the material, which, first of all, depends on the nature and proportion of the initial components. Most often, synthetic or natural polymers and / or biological molecules are used as raw materials for hydrogel dressings.

Whatever the nature of the used polymer, the most important characteristics are biological activity, biodegradability and biocompatibility. One of the fibrillar proteins widely used in medicine is collagen, which is characterized by low antigenicity and biocompatibility [4]. Among synthetic polymers, acrylic hydrogels are the most promising for creating a wound dressing. Thus, hydrogels based on acrylic acid, possessing hemocompatibility, demonstrate accelerated wound healing (Intrasite Conformable® hydrogel) [5, 6]. However, the effect of prescription and technological parameters on the sorption properties of semi-interpenetrating (semi- IPN) nets based on acrylic hydrogel and collagen has not been sufficiently studied.

Thus, the purpose of this work was to study the effect of synthesis conditions on the sorption characteristics of compositions based on acrylic hydrogel and collagen as the basis of a wound dressing.

## Materials and research methods

### *Synthesis of hydrogels*

During the work, hydrogel acrylic compositions based on acrylic acid (AAc, “Vekton”), acrylamide (AAm, “Vekton”) by free radical polymerization in an aqueous medium with varying prescription and technological parameters: 1) the degree of neutralization by 2 N sodium hydroxide solution (60–100 % with a step of 10 % (synthesis temperature 40 °C)); 2) synthesis temperature (20° ÷ 45°C (neutralization degree 80 %)). Ratio of monomers: AAc: AAm = 30:70 %, accordingly and collagen with a concentration of 10 %. An oxidizing agent – ammonium peroxydisulfate (PSA, “LenReaktiv”) and a reducing agent – N, N, N', N'-tetramethylethylenediamine (TEMED, “SIGMA-ALDRICH”) were used as an initiating system. The crosslinking agent was N, N-methylbisacrylamide (MBA, “Vekton”) with a concentration of 0.2 wt% per monomer feed [7].

### *FTIR spectroscopic analysis*

IR spectra were obtained on a Bruker Tensor 37 FTIR spectrometer using a Pike ATR attachment (attenuated total reflectance) MIRacle (Pike) with a diamond-coated ZnSe crystal. The spectra were recorded in the range 4000–600 cm<sup>-1</sup> with a resolution of 2 cm<sup>-1</sup> and averaging over 32 spectra.

### *Thermogravimetric analysis*

The thermogravimetric analysis data of the composites were recorded using a TG 209 F1 LibraNETZSCH thermal analyzer in temperature range from 25 °C to 450 °C at a heating rate of 10 °C / min in a nitrogen atmosphere with a gas flow of 40 ml/min.

### *Measurement of sorption capacity*

Swelling of hydrogels was carried out in distilled water (pH = 7), physiological solution (pH = 7.0–7.5), phosphate buffer (pH = 7.2–7.6) for three days.

- The degree of swelling was calculated by the formula:

$$Q_{\infty} = \frac{m_s - m_0}{m_0} \quad (1)$$

where,  $m_s$  is the mass of the swollen sample, g;  $m_0$  is the mass of the dried sample, g/g;

The moisture content was determined as follows: the samples were dried in a thermostatic oven at 110°C to remove the water to constant weight. The moisture content was calculated using the formula:

$$\gamma = \frac{m_0 - m_c}{m_0} \times 100\% \quad (2)$$

where,  $m_0$  is the initial mass of the sample, g;  $m_c$  is the mass of the sample dried to constant mass, g; The following models were used to describe solvent diffusion into the hydrogel:

- Fickian mathematical model [8],

$$\frac{Q_t}{Q_{\infty}} = kt^n \quad (3)$$

where,  $Q_t$  and  $Q_\infty$  are the degree and equilibrium degree of swelling, respectively, representing the amount of solvent diffused into the hydrogel at time  $t$  and at infinite time (equilibrium state), referred to 1 gram of dry material;  $k$  is a constant associated with the structure of the polymer network and the exponent;  $n$  is a number that determines the type of diffusion;

- kinetic model of pseudo second order sorption [9],

$$Q_t = \frac{t}{\frac{1}{k_2 \cdot Q_c^2} + \frac{t}{Q_c}} \quad (4)$$

where,  $k_2$  is the rate constant of sorption of the pseudo second order model ( $\text{g} \cdot (\text{mmol} \cdot \text{min})^{-1}$ ),  $t$  is the time (min).

## Results and discussion

During the work the composite hydrogels based on the semi-IPN copolymer of acrylic acid/acrylamide and collagen were prepared by varying the degree of neutralization of the acrylic acid and the synthesis temperature by free radical polymerization in an aqueous medium (Fig. 1a). In this

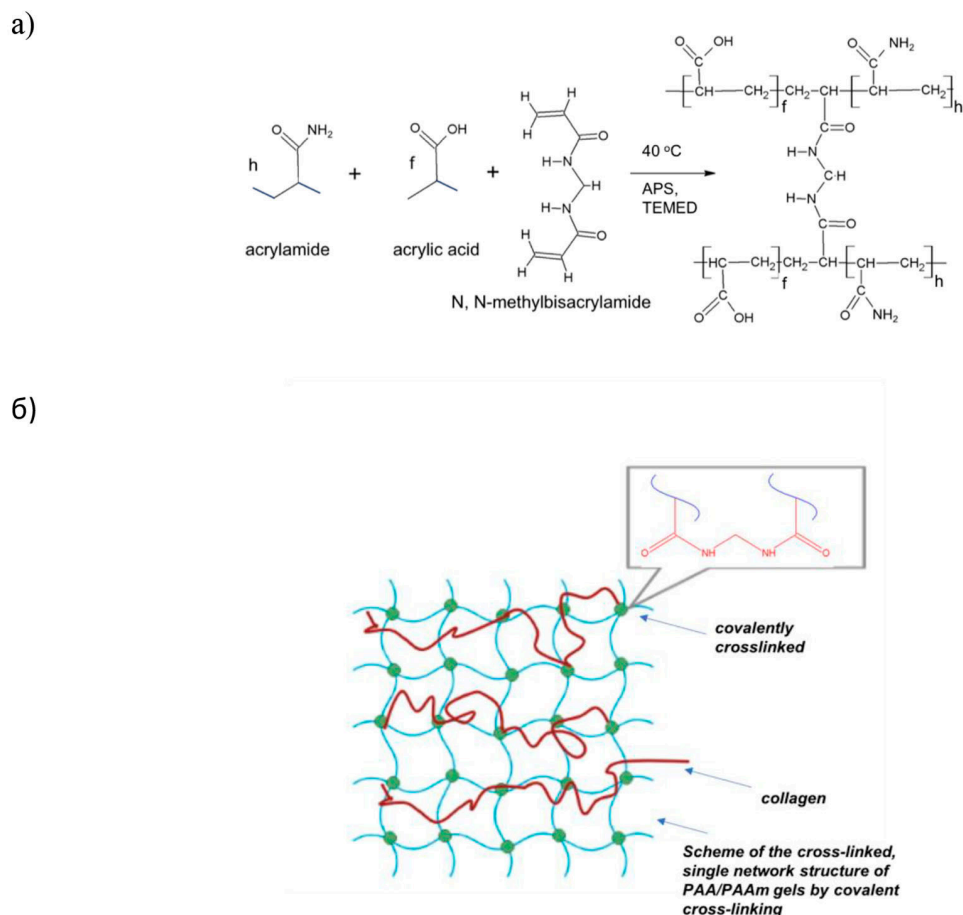


Fig.1. a) Polymerization of acrylic acid and acrylamide by radical polymerization; b) Schematic representation of an acrylic acid/acrylamide-collagen semi-IPN copolymer

process, neutralized acrylic acid was crosslinked with acrylamide in the presence of a crosslinker, which was N, N'-methylbisacrylamide. The macromolecular linear chains of collagen are embedded in the acrylate semi-IPN of the acrylic acid/acrylamide copolymer network by electrostatic attraction (Fig. 1b).

Fig. 2a shows the dependence of the time of the onset of gelation (GT) on the degree of neutralization of acrylic acid ( $\alpha$ ). The gelation time is the starting point for the loss of fluidity of the reaction mixture [10]. GT in this work was determined by the standard tilting method, i.e., establishing the point in time at which the mixture of reagents stopped to fall in the inclined position of the glass [11]. As Fig. 2a shows, an increase in the degree of neutralization of AAc led to a decrease in GT exponentially, which is associated with an increase in the rate of polymerization of acrylic derivatives, according to the theory of the formation of ion pairs.

A similar correlation of a decrease in GT on an increase in the synthesis temperature ( $T$ ) is shown in Fig. 2b, described by the equation:  $\tau_{GT} = -16.61 \ln(T) + 67.373$ , the coefficient of accuracy of the approximation:  $R^2 = 0.874$ . This dependence is naturally explained by the acceleration of the thermal motion of the reacting molecules, which leads to an increase in the total fraction of particles with the necessary internal energy, which makes it possible to pass into the active form.

Fig. 3 and Fig. 4 show the IR spectra of the polymer composite with the neutralization degree of acrylic acid 60–100 % before and after the sol-gel analysis. Fig. 3 shows the IR spectra of the obtained polymer compositions with different degrees of neutralization of acrylic acid ( $\alpha$ ).

The broad absorption band refers to vibrations of valence – O-H groups ( $3550\text{--}3450\text{ cm}^{-1}$ ), the band  $3171\text{--}3078\text{ cm}^{-1}$  characterizes the vibration of secondary amides (valence N-H). Stretching vibrations of asymmetric  $\text{-CH}_3$  bonds are characterized by a peak in the region of  $2954\text{ cm}^{-1}$ . The range from  $1747\text{ cm}^{-1}$  to  $1708\text{ cm}^{-1}$  characterizes the vibration of the valence carboxyl groups  $\text{C=O}$ . The absorption band at  $1663\text{ cm}^{-1}$  refers to the absorptions of the  $\text{C=O}$  group of acrylamide monomers, and the absorption at  $1550\text{ cm}^{-1}$  refers to the carboxylate groups of potassium acrylate monomers. The absorption at the wave number  $1612\text{ cm}^{-1}$  is mainly contributed by collagen (in addition, multiple  $\text{C=C}$

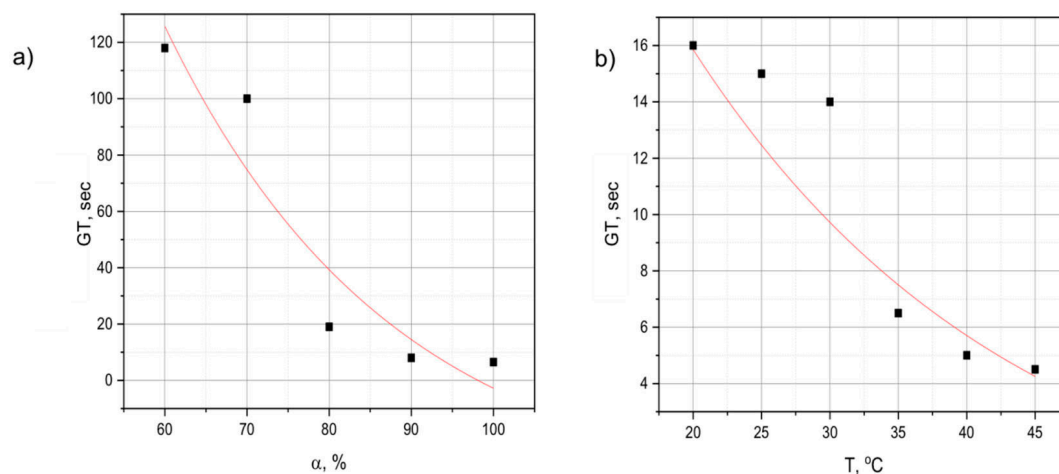


Fig.2. Gelation time dependence of the acrylic composite on: a) of the degree of neutralization of acrylic acid at a temperature of 40 °C; b) on the temperature of synthesis with the degree of neutralization of AA – 0.8

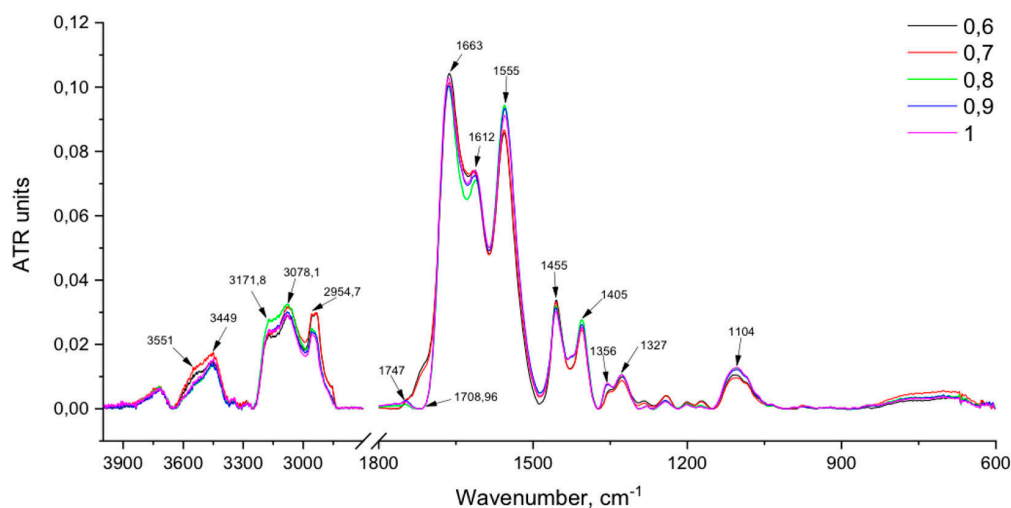


Fig. 3. IR spectra of the polymer composite with degrees of neutralization of acrylic acid 60–100 %.

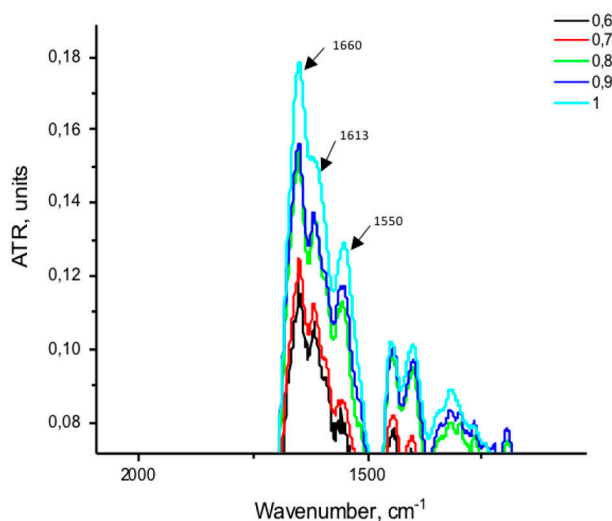


Fig. 4. IR spectra of the polymer composite with degrees of neutralization of acrylic acid 60–100 % after sol-gel analysis characterizing the presence of C=O carbonyl groups

bonds of both monomers can also absorb here). The peak at  $1405\text{ cm}^{-1}$  characterizes the vibrations of valence COO-symmetric bonds, while the maximum is observed in polymer samples with  $\alpha = 80\%$ .  $1356\text{ cm}^{-1}$ ,  $1327\text{ cm}^{-1}$  and  $1104\text{ cm}^{-1}$  characterize valence C–N bonds [12, 13].

Table 1 presents the spectral coefficients – the ratio of the intensities of the absorption bands characterizing the stretching vibrations of the carbonyl groups of acrylate monomers and collagen to assess the final composition of the gels

The proportion of residual monomers in the composition of the hydrogel was determined by studying the process of extraction of the remaining monomers using IR spectroscopy. When analyzing

Table 1. Relationships of the intensities of absorption bands at the picks characterizing valence vibrations of the carbonyl groups

Parameter		As-prepared samples					
		Intensities of absorption bands at the picks			Relationships of the intensities of absorption bands at the picks		
		1633 cm <sup>-1</sup>	1612 cm <sup>-1</sup>	1553 cm <sup>-1</sup>	1633 cm <sup>-1</sup> / 1555 cm <sup>-1</sup>	1633 cm <sup>-1</sup> / 1612 cm <sup>-1</sup>	1555 cm <sup>-1</sup> / 1612 cm <sup>-1</sup>
$\alpha$ , %	100	0,1027	0,0743	0,0909	1,130	1,382	1,223
	90	0,1004	0,0725	0,0934	1,075	1,385	1,288
	80	0,1004	0,0712	0,0943	1,065	1,410	1,324
	70	0,1011	0,0737	0,0868	1,165	1,372	1,178
	60	0,1044	0,0739	0,0858	1,217	1,413	1,161
Parameter		Sol-gel analysis samples					
		Intensities of absorption bands at the picks			Relationships of the intensities of absorption bands at the picks		
		1660 cm <sup>-1</sup>	1613 cm <sup>-1</sup>	1550 cm <sup>-1</sup>	1660 cm <sup>-1</sup> / 1550 cm <sup>-1</sup>	1660 cm <sup>-1</sup> / 1613 cm <sup>-1</sup>	1550 cm <sup>-1</sup> / 1613 cm <sup>-1</sup>
$\alpha$ , %	100	0,1559	0,1363	0,1173	1,329	1,144	0,861
	90	0,1565	0,1369	0,1173	1,334	1,143	0,857
	80	0,1525	0,1351	0,1124	1,357	1,129	0,832
	70	0,1229	0,1117	0,0857	1,434	1,100	0,767
	60	0,1146	0,1053	0,0796	1,440	1,088	0,756

the intensity ratios of the absorption bands of the C=O bonds of acrylamide monomers and the COO<sup>-</sup> group of potassium acrylate, the following trend was observed: depending on the neutralization degree of acrylic acid monomers, this spectral coefficient varies from 1.329 to 1.440, because as the degree of neutralization decreases, the intensity of the 1550 cm<sup>-1</sup> band decreases. The intensity of the absorption band of the COO<sup>-</sup> group reaches a maximum at neutralization degree of acrylic acid of 0.8 and then decreases with a further increasing in the neutralization degree. This dependence can be explained by an increase in the electrostatic interaction of COO<sup>-</sup> groups of potassium acrylate with NH<sub>3</sub><sup>+</sup> groups of collagen. After a sol-gel analysis, the ratio of the intensities of the indicated absorption bands decreases, which reflects the process of extraction of components containing carboxylate groups to a greater extent than acrylamide ones. It follows from this that the proportion of potassium acrylate monomers that did not enter into polymerization is greater than that of acrylamide monomers (or oligomers). When comparing the intensity ratios of the absorption bands of the carbonyl groups of acrylamide/collagen and potassium acrylate/collagen, the following trend was preserved – as a result of the sol-gel analysis, the spectral coefficients decrease in both cases, which indicates the extraction of acrylate monomers, while the intensity of the bands naturally increase with an increase in the neutralization degree of acrylic acid. In acidic environments, as a result of the protonation of the amino groups of collagen, a positive charge arises, which allows collagen to be tightly embedded in the network due to electrostatic attraction.

The presence of the maximum value of the equilibrium degree of swelling ( $Q$ ) at 25 °C in distilled water, saline and phosphate-buffered saline for synthesized semi-IPN based on acrylic

Table 2. Sorption properties of acrylic composite materials

Parameter		$\gamma$ , %	$Q_{\max}$ , g/g		
			Distilled water	Saline	PBS*
$\alpha$ , %	60	72	20	8	9
	70	74	25	9	9
	80	75	45	15	12
	90	75	42	12	11
	100	76	40	11	10
T, °C	20	74	35	11	11
	25	81	30	11	11
	30	76	40	11	11
	35	76	40	12	11
	40	76	45	15	12
	45	78	40	11	11

\*PBS – phosphate-buffered saline

hydrogel and collagen with a degree of neutralization of AAc equal to 80 % is shown in Table 2 and Fig. 5, which is explained by the ionic contribution to the total swelling pressure of the material. As can be seen from Fig. 5, materials obtained at a synthesis temperature of 40 °C have the highest degree of swelling and reach values up to 45 g/g. An increase in the temperature of the synthesis of acrylic hydrogel composites with 5 °C leads to an increase in the maximum degree of swelling of polymer samples and averages 30–40 g/g. 1.5–2 times and averages 40–50 g/g. It should be noted that in all cases, the average time to reach the values of the equilibrium degree of swelling was 4–7 hours.

As can be seen from the data in Table 2, the value of the moisture content ( $\gamma$ ) of acrylic composite materials varies in the range of 72–78 %. Fig. 5 shows the kinetic curves of the swelling in distilled water at a temperature of 25 °C of the obtained semi-IPN depending on the degree of neutralization of AAc and the synthesis temperature. Table 2 presents some characteristics of swelling in distilled water, saline and PBS (diffusion coefficient ( $n$ ), Fick grid parameter ( $k$ ), swelling rate constant ( $k_2$ )) of new hydrogel collagen-containing composites depending on the synthesis temperature and degree of neutralization of AAc.

As can be seen from Table 3, the values of the exponent  $n$  of hydrogel collagen-containing samples obtained with different degrees of neutralization of acrylic acid take values  $n < 0.5$ , which indicates that the limiting factor affecting the swelling rate is the relaxation of the polymer chain, the so-called pseudo-Fick diffusion.

It is natural for the synthesis temperature changes did not affect the diffusion coefficient of obtained hydrogel composites in distilled water, physiological saline and PBS.

The use of a pseudo-second order model based on the assumption of adsorbate chemisorption on adsorbents makes it possible to calculate the swelling constants  $k_2$  [14]. Based on the pseudo-second order equation (4), the rate of diffusion of the solvent into the network at the initial stage is higher the greater the values of the obtained constants.



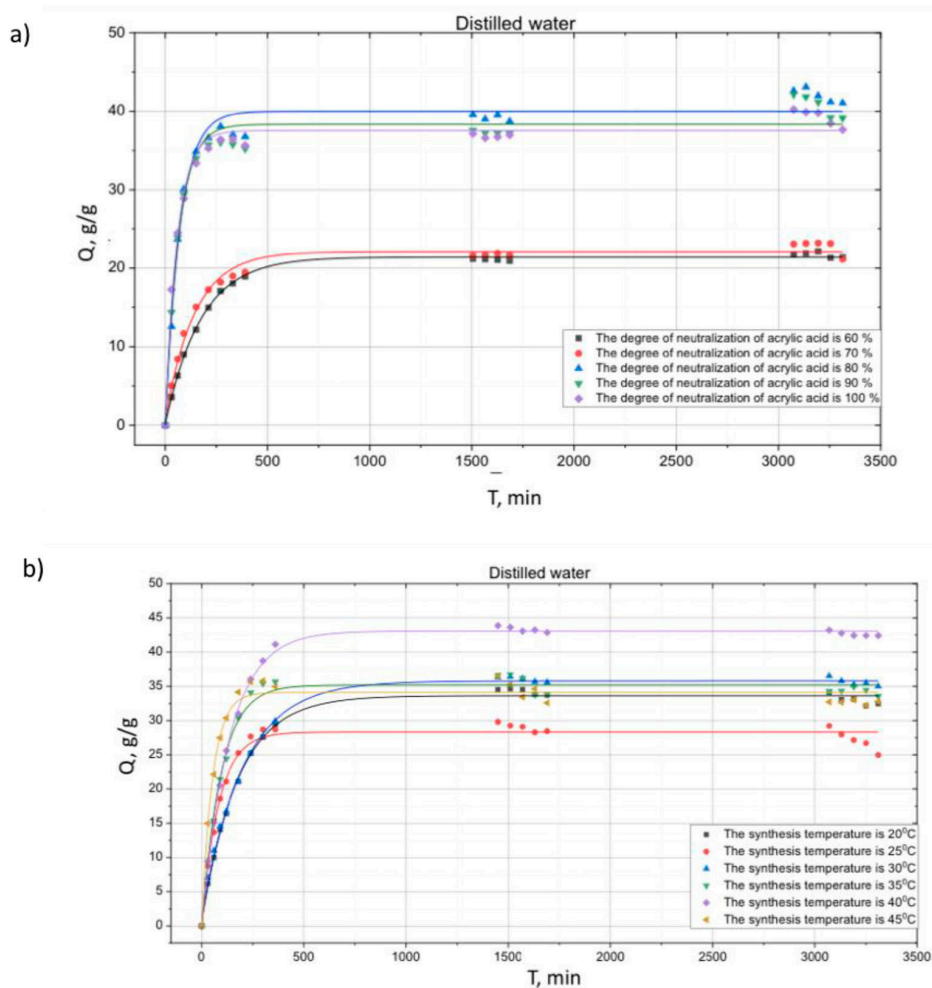


Fig. 5. Kinetic curves of swelling in distilled water of a polymer composite at different: a) the degree of neutralization of acrylic acid at a synthesis temperature of 40 °C; b) synthesis temperature

Table 3. Some kinetic characteristics of acrylic composite materials

Parameter		Distilled water			Saline			PBS*		
		$k_2 \cdot 10^3$	n	k	$k_2 \cdot 10^3$	n	k	$k_2 \cdot 10^3$	n	K
$\alpha$ , %	60	0,4	0,5	0,04	1,3	0,4	0,085	0,8	0,4	0,06
	70	0,5	0,4	0,08	4,2	0,2	0,227	0,75	0,4	0,06
	80	0,6	0,3	0,18	3,1	0,2	0,331	0,74	0,3	0,09
	90	0,4	0,2	0,22	1,4	0,2	0,204	0,9	0,3	0,11
	100	0,5	0,2	0,28	3,1	0,2	0,506	1,39	0,2	0,14
$T$ , °C	20	0,4	0,5	0,05	0,4	0,3	0,1	0,9	0,3	0,1
	25	4,5	0,3	0,13	0,8	0,2	0,2	1,6	0,2	0,2
	30	0,3	0,4	0,05	2,7	0,2	0,15	0,8	0,2	0,15
	35	1,3	0,3	0,13	1,4	0,3	0,16	1,4	0,3	0,16
	40	0,4	0,3	0,18	3,1	0,2	0,331	0,74	0,3	0,09
	45	1,5	0,2	0,25	2,4	0,2	0,15	1,0	0,3	0,15

The maximum swelling rate at the initial stage is possessed by polymer samples obtained at a synthesis temperature of 25 °C and a degree of neutralization of acrylic acid equal to 80 %. It should be noted that the equilibrium degree of swelling of the obtained polymer samples is achieved on average in 4–7 h.

### Conclusion

During this work, composite hydrogels based on a semi-IPN copolymer of acrylic acid and acrylamide and collagen were obtained by free radical polymerization at various degrees of neutralization of acrylic acid and synthesis temperatures.

The dependence of the time of the onset of gelation on the degree of neutralization and the synthesis temperature was studied. It was found that GT naturally decreased with an increase in the degree of neutralization of acrylic acid and an increase in the synthesis temperature.

The sorption characteristics of collagen-acrylic composites in distilled water, physiological saline, and phosphate-buffered saline have been studied. The process of solvent sorption into the polymer network is described by a low Fick diffusion.

The obtained polymeric semi-IPN based on acrylic hydrogels and collagen have reach an equilibrium degree of swelling for 4–7 hours.

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