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# Effect of sodium hyaluronate on mechanical and sorption properties of IPN hydrogels based on acrylic acid and acrylamide.

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**Abstract.** Acrylic hydrogels are popular medical materials. However, acrylic hydrogels, consisting of a single polymer network, do not have sufficient mechanical characteristics. Modified hydrogels have increased strength and mechanical characteristics, and their sorption properties also change. In this work, IPN hydrogels based on a copolymer of acrylic acid and acrylamide filled with various amounts of sodium hyaluronate and bentonite were synthesized. For these hydrogels, we studied the water sorption capacity and mechanical characteristics: relative elongation at break and tensile strength. It was shown that for hydrogels filled only with bentonite, a nonlinear decrease in the equilibrium moisture absorption and an increase in the concentration of bentonite in the composite is observed. For IPN hydrogel filled with sodium hyaluronate, the characteristic of equilibrium sorption has a maximum of sorption around 0.05 mas.% strength. An increase in the durability of samples modified with both bentonite and sodium hyaluronate is shown. The relative elongation of the samples at the time of rupture for hydrogels with bentonite decreases linearly with increasing concentration of bentonite. The relative elongation at the time of rupture of the samples modified with both bentonite and sodium hyaluronate has a characteristic with a maximum around -of 0.05-0.1 mas.% of sodium hyaluronate.

## 1. Introduction

Recently, there has been growing interest in biocompatible materials that well reproduce the properties of highly hydrated body tissues. One type of such materials are rarely cross-linked polyelectrolytes - polymer hydrogels [1].

Hydrogels are hydrophilic three-dimensional networks formed by chemical or physical bonds [5]. Acrylic hydrogels attract attention as soft, moisture-containing and moisture-retaining materials that can absorb water hundreds of times the original mas. This property gives them a resemblance to the natural extracellular matrix [6–8]. However, at the same time, acrylic hydrogels, consisting of one polymer network, do not have sufficient mechanical characteristics for wide practical use [2,9]. An ideal biomaterial must satisfy certain requirements, such as given mechanical parameters, biocompatibility, a certain degree of degradation and resistance to physiological environments, in the absence of adverse effects at the site of implantation [2,3]. Due to the rapid polymerization and

biocompatible properties, acrylamide monomers (AAm) and acrylic acid (AA) monomers are widely used to obtain medical hydrogels [4].

There are several approaches to increase the strength parameters of polymer materials: the introduction of fillers or modification of the polymer matrix [3, 10]. The mixing of two polymers or polymer systems has become a common approach for the development of a new class of biomaterials that demonstrate combinations of properties that are not achievable when using individual polymers [11]. In particular, mixtures of synthetic and natural polymers make it possible to obtain composite materials that combine a wide range of physicochemical properties of synthetic polymers, as well as biocompatibility, safety, and prevention of side effects when implanting natural polymers [12–14].

Interpenetrating polymer networks (IPNs) are mixtures of two crosslinked polymers, regardless of the nature of the crosslinking, chemical or physical. If one polymer is crosslinked and the other is linear, the structure is called semi-IPN [15]. IPN based materials are preferred in a number of biotechnological and biomedical applications because of their unique biophysical properties, such as the ease of manufacturing of various geometric shapes; soft and rubber texture; minimal mechanical irritation of surrounding tissues; unusual resistance to biological fluids, etc. [16]. IPN structures are also used to control the overall hydrophilicity of the hydrogel and drug release kinetics [17].

One of the polysaccharides widely used in bioengineering is sodium hyaluronate (or hyaluronan, SH), which is a linear glycosaminoglycan consisting of a repeating disaccharide unit of D-glucuronic acid and N-acetyl-D-glucosamine. SH is one of the main components of the extracellular matrix and is present in high concentrations in all connective tissues, such as cartilage, vitreous body and synovial fluids, where it performs structural and lubricating functions. The biological functions of SHs have been extensively studied, and the great interest in SHs is due primarily to its biocompatibility and the ability to interact with specific cellular receptors that can selectively recognize and bind SH. Numerous SH derivatives are used for tissue repair, wound healing, joint disease treatment, drug delivery, and as the basis for tissue engineering [18, 19].

In the present work, in order to combine the high sorption characteristics of acrylic hydrogels and sodium hyaluronate, as well as increase the mechanical parameters, hydrogels with a semi-interpenetrating network based on a copolymer of acrylic acid and acrylamide filled with sodium hyaluronate were synthesized.

## **2. Materials and methods**

### *2.1. Synthesis of hydrogels*

In this work, we synthesized composite hydrogels based on interpenetrating meshes of a copolymer of acrylic acid (AA) / acrylamide (AAm) and sodium hyaluronate (SH) with a concentration in the range of 0.01 - 1 mas.% And a bentonite concentration of 1-10 mas.%. A series of IPN hydrogels was obtained by radical polymerization [20]. IPN structures were prepared using methylenebisacrylamide (MBA) as a crosslinking agent.

Prepared 0.01 mas.%, 0.03 mas.%, 0.05 mas.%, 0.1 mas.%, 0.24 mas.%, 0.5 mas.% and 1 mas.% Filled with sodium hyaluronate composites, 1 mas.%, 3 mas.% , 5 mas.%, 7 mas.%, 10 mas.% Filled with bentonite composites and composites jointly filled (0.01 mas.% - 0.5 mas.%) With sodium hyaluronate and (1 mas.% - 10 mas.%) Bentonite. 3.5 ml of distilled water was mixed with monomers AA (10 ml) and AAm (3 g) in a beaker. Acrylic acid was pre-neutralized by 80%. The total volume of the mixture was 19 ml. A constant amount (0.01 g) of MBA was added to the glass as a crosslinking agent. After adding 4 ml (2%) / 4 ml (2%) (NH<sub>4</sub>)<sub>2</sub>S<sub>2</sub>O<sub>8</sub> / TEMED as an initiator, it was transferred from the glass to a Petri dish in this mixture.

### *2.2. The study of sorption properties.*

The degree of swelling of the samples was measured in distilled water with a volume of 300 ml. The weight of the sample was measured every hour for the first 7 hours, then once a day, until it reaches 48 hours. The degree of swelling ( $Q$ ) was determined by the amount of liquid absorbed by 1 g of dry matter according to the following formula:

$$Q = \frac{m - m_0(1 - \gamma)}{m_0(1 - \gamma)}, \quad (1)$$

where  $Q$  is the degree of swelling of the hydrogel, g / g;  $m$  is the mas. of the swollen sample, g;  $m_0$  is the initial mas. of the gel sample, g;  $\gamma$  is the moisture content of the gel sample, mas. fraction [21].

The swelling kinetics was estimated by the Fick diffusion coefficient and swelling rate constants.

To calculate the diffusion coefficient, the formula was used:

$$\frac{Q_t}{Q_\infty} = kt^n, \quad (2)$$

where  $Q_t$  and  $Q_\infty$  - sorption capacities represent the amount of solvent diffused into the gel at time  $t$  and at infinite time (i.e., upon reaching the state of equilibrium sorption capacity), respectively,  $k$  is a constant associated with the network structure, and the exponent  $n$  is a number that determines the type of diffusion. This equation is applicable only to the initial stages of swelling, that is, to increase the hydrogel mas. by 60% ( $Q_t / Q_\infty \leq 0.6$ ;  $\log(Q_t / Q_\infty) \leq -0.22$ ) [22].

The calculation of the exponent  $n$  and the constant  $k$  was achieved by plotting the data in logarithmic coordinates according to equation 3 and estimating the obtained curves using linear functions.

$$\log\left(\frac{Q_t}{Q_\infty}\right) = \log k + n \log t, \quad (3)$$

To determine the rate constants of swelling, a pseudo-second order kinetic model of sorption was used; the sorption capacity in this model is determined by the formula:

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

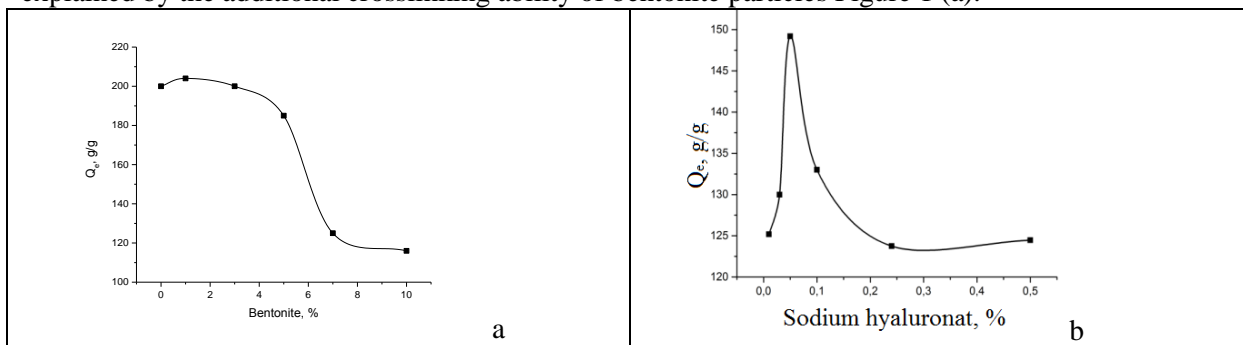
where  $k_2$  is the sorption rate constant of the pseudo-second order model, dimension (g • (mmol • min)<sup>-1</sup>);  $t$  is the time (min). In this case, it is possible to calculate the sorption rate constant without knowing the equilibrium sorption capacity  $Q_e$ . When the sorption process is well described by a pseudo-second order model, the experimental data constructed in the  $t / Q_t$  ( $t$ ) axes should fit into a linear dependence, from which  $Q_e$  and  $k_2$  can be determined from the slope and free term [23].

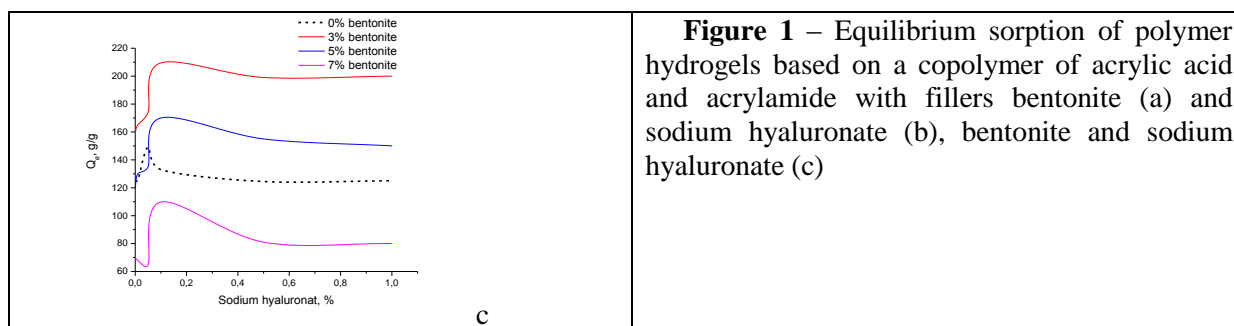
### 2.3. The study of mechanical properties.

The tensile test was carried out on a Shimadzu AGS X 5kN instrument. Estimated - elongation at the time of rupture;  $\varepsilon$  (%) - increase in the estimated length of the sample, related to its original length, tensile strength;  $\sigma$  (MPa) - the maximum stress withstand the sample in tension; Young's modulus,  $E_p$  (MPa) - was determined by the slope of the stress-elongation curve  $\sigma$  ( $\varepsilon$ ), for the interval from  $\varepsilon_1 = 0.05\%$  to  $\varepsilon_2 = 0.25\%$ .

## 3. Results and discussions

In the course of the work, it was found that for hydrogels filled only with bentonite, a nonlinear decrease in the equilibrium moisture absorption value with an increase in the concentration of bentonite in the composite is observed. The decrease in equilibrium moisture absorption can be explained by the additional crosslinking ability of bentonite particles Figure 1 (a).

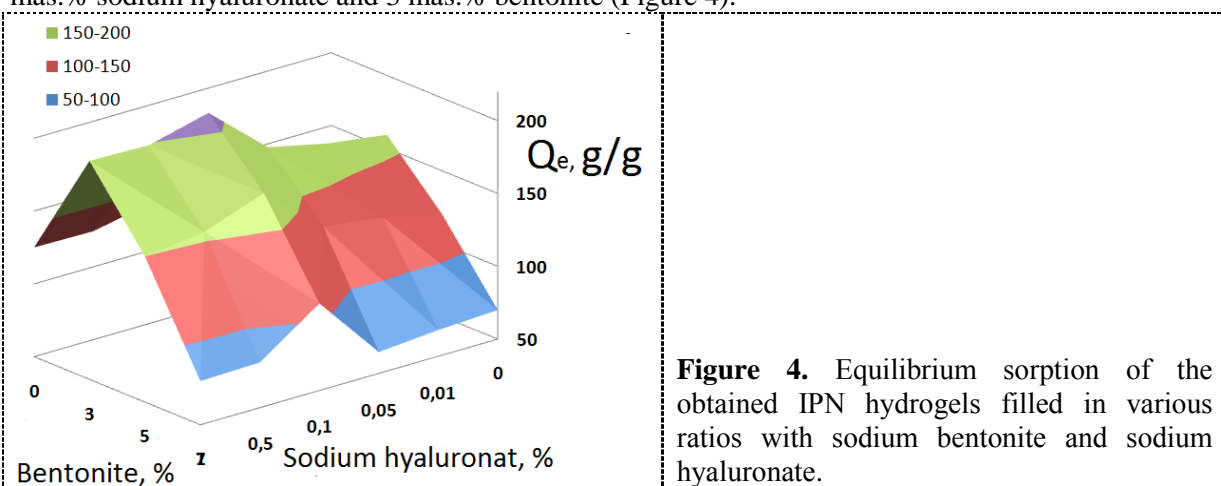




**Figure 1** – Equilibrium sorption of polymer hydrogels based on a copolymer of acrylic acid and acrylamide with fillers bentonite (a) and sodium hyaluronate (b), bentonite and sodium hyaluronate (c)

For a hydrogel filled with a different content of sodium hyaluronate, the characteristic of equilibrium sorption passes through a maximum of sorption in the concentration region of 0.05 mas.%, see Figure 1 (b).

With the combined introduction of bentonite and sodium hyaluronate, equilibrium moisture absorption is described by a surface having a displaceable maximum along the axis of the sodium hyaluronate content - from 0.05 mas.% to 0.1 mas.% and a decrease in equilibrium sorption along the axis of the bentonite content. The maximum equilibrium sorption corresponds to the content of 0.1 mas.% sodium hyaluronate and 3 mas.% bentonite (Figure 4).



**Figure 4.** Equilibrium sorption of the obtained IPN hydrogels filled in various ratios with sodium bentonite and sodium hyaluronate.

The coefficient of diffusion of water into a hydrogel, for all samples of hydrogels calculated according to Fick's law, has values in the range 0.5-1, i.e. The rates of water penetration into the composite and relaxation of polymer chains are approximately the same. Table 1.

The polymer network parameter  $k$  determined from equation 2, with the introduction of sodium hyaluronate into hydrogels filled with bentonite, decreases significantly (by  $\sim 10$  times), which is associated with a decrease in the size of free spaces in the hydrogel.

Table 1 Fick's diffusion coefficient, sorption rate constant for composites with bentonite and sodium hyaluronate.

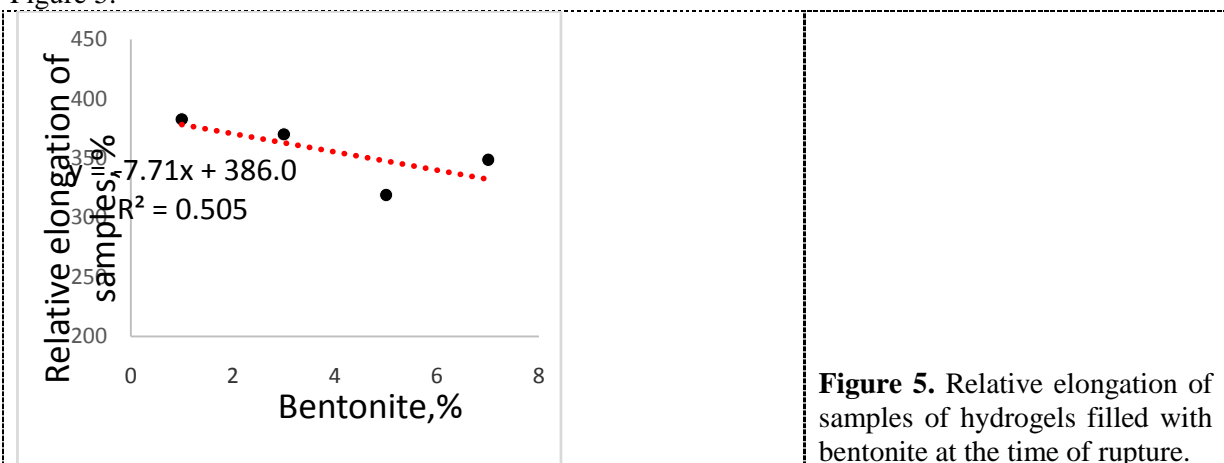
Sample	Fick's diffusion coefficient, n	Fick polimer network parameter, k	Moisture absorption rate constant, $g \cdot (mmol \cdot min)^{-1}$	Equilibrium degree of swelling, g / g
Sample without filler	0,530	0,038	5,3E-5	199
bentonite1%	0,796	0,011	7,0E-5	204
bentonite3%	0,893	0,007	3,0E-5	205
bentonite5%	0,706	0,018	6,0E-5	181
bentonite7%	0,529	0,065	4,1E-4	84

bentonite10%	0,530	0,060	3,4E-4	119
bentonite5%- 0.01%SH	0.818	0.004	1.00E-05	196
bentonite5%- 0.05%SH	0.788	0.009	2.40E-05	187
bentonite5%- 0.1%SH	0.912	0.002	5.50E-06	241
bentonite5%- 0.24%SH	0.815	0.006	3.10E-05	106
bentonite5%- 0.5%SH	0.787	0.006	2.00E-05	129

A pseudo-second order model was chosen as a kinetic model for achieving thermodynamic equilibrium during sorption of water by a hydrogel composite with bentonite, because it is consistent with the results of the experiment with the largest R2.

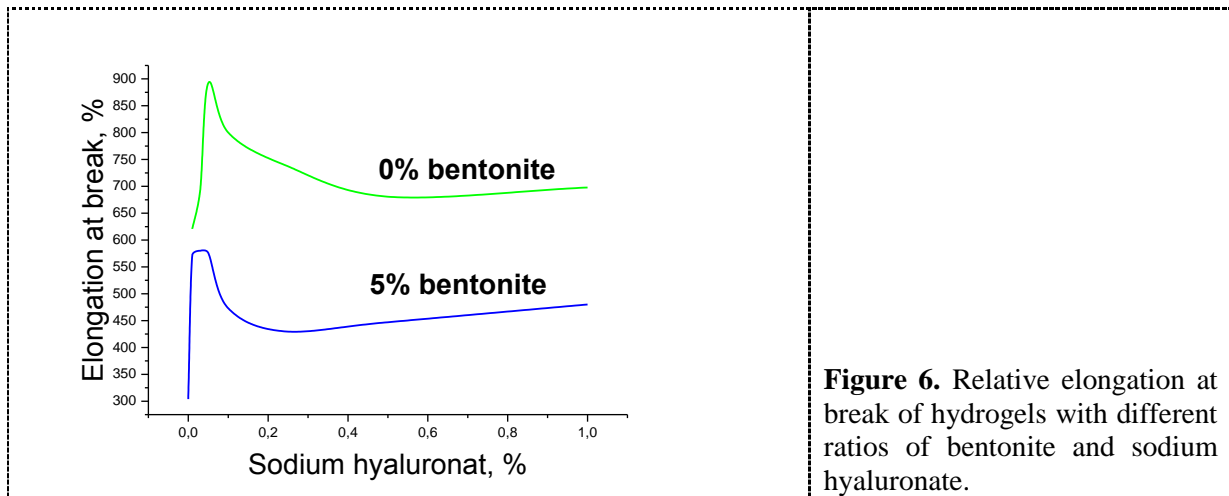
The sorption rate constants for a composite with bentonite and a composite with different contents of bentonite and sodium hyaluronate are presented in Table 1. The constant of sorption rate for water for composites with bentonite increases with increasing bentonite content in the composite. For hydrogels with bentonite and sodium hyaluronate, the rate constant as a whole decreases slightly, which can also be associated with a decrease in the free space in the gel polymer network.

The mechanical properties of the hydrogels obtained were measured on a Shimadzu AGS X 5kN tensile testing machine. The relative elongation of the samples at the time of rupture for hydrogels with bentonite decreases linearly with increasing bentonite concentration, the dependence is shown at Figure 5.



**Figure 5.** Relative elongation of samples of hydrogels filled with bentonite at the time of rupture.

At the same time, the relative elongation at the time of rupture of the samples modified with both bentonite and sodium hyaluronate has a characteristic passing through a maximum in the region of 0.05-0.1 mas.% of sodium hyaluronate (Figure 6).



**Figure 6.** Relative elongation at break of hydrogels with different ratios of bentonite and sodium hyaluronate.

For samples with bentonite and sodium hyaluronate, the elongation at the time of rupture is less, and the tensile strength is higher than for hydrogels filled only with sodium hyaluronate. Higher tensile strengths indicate that it was necessary to exert a greater force to rupture the sample, see Table 2.

Table 2. The mechanical characteristics of the obtained hydrogels with a modifier sodium hyaluronate and bentonite

	The content of sodium hyaluronate, mas. %	Elongation of the sample at break, average, %	Tensile strength, MPa
	0	710	0.2
	0.01	621	0.2
	0.03	694	0.3
	0.05	892	0.2
Sample AA-co-AAm 0% bentonite	0.24	740	0.2
	0.5	680	0.3
	1	698	0.3
	0	304	1.1
	0.01	571	0.4
	0.05	573	0.6
Sample AA-co-AAm 5% bentonite	0.1	473	0.4
	0.25	430	0.6
	0.5	447	0.4

**4. Conclusion**

The obtained IPN hydrogels modified with bentonite showed a nonlinear decrease in the equilibrium moisture absorption with an increase in the concentration of bentonite in the composite. For a hydrogel filled with various contents of sodium hyaluronate, the characteristic of equilibrium sorption passes through a maximum of sorption in the concentration region of 0.05 mas. %

The equilibrium moisture absorption with the combined introduction of bentonite and sodium hyaluronate is described by a 3D surface having a displaceable maximum along the axis of the sodium hyaluronate content - from 0.05 mas. % to 0.1 mas. % and a decrease in equilibrium sorption along the

axis of the bentonite content. The maximum equilibrium sorption corresponds to a content of 0.1 mas.% sodium hyaluronate and 3 mas.% bentonite

The mechanical properties measured on a Shimadzu AGS X 5kN analyzer show an increase in the strength of samples modified with both bentonite and sodium hyaluronate. The relative elongation of the samples at the time of rupture for hydrogels with bentonite decreases linearly with increasing concentration of bentonite. At the same time, the relative elongation at the time of rupture of the samples modified with both bentonite and hyaluronate has a characteristic passing through a maximum in the region of 0.05-0.1 mas.% of sodium hyaluronate.

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