ВИСОКОМОЛЕКУЛЯРНІ СПОЛУКИ
ТА (НАНО)КОМПОЗИЦІЙНІ МАТЕРІАЛИ

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SYNTHESIS AND STUDY OF THE PROPERTIES
OF CROSSLINKED POLYACRYLIC ACID COPOLYMERS

The effect of synthesis conditions on the structure of acrylic acid and N,N-methylene bisacrylamide copolymers has been investigated. Optimal conditions for the synthesis of polymers with linear, tree-like, and crosslinked macromolecular structures have been established. The properties of the synthesized polymers, namely density, degree of swelling, gel fraction, etc., were investigated. It has been shown that copolymers with crosslinked macromolecules form hydrogels, the swelling degree of which considerably depends on the synthesis conditions. For copolymers forming hydrogels, the density of crosslinking units was determined based on the dependence of the density and equilibrium swelling degree.

Key words: acrylic acid; copolymer; structure; gel and sol fractions; crosslinking degree.

Introduction

Among synthetic polymers used in biomedicine, polyacrylic acid, which is considered a non-toxic, biocompatible, and biodegradable polymer, attracts the attention of scientists [1, 2]. In particular, products based on polyacrylic acid and its modified forms are proposed to be used in various fields of nanomedicine, such as antimicrobial, antitumor, imaging, biosensor, and tissue engineering [3–5].

The possibility of using a polymer in a particular field is determined by its nature and, to some extent, the structure of macromolecules [6]. To date, the production and use of several types of polyacrylic acid which differ in their macromolecule structures (linear, branched, comb-like, and star-like polymers) have been described [7]. It is known that macromolecules with branched structures, compared to those with linear ones, have unique characteristics (increased density of functional groups, presence of intramolecular cavities, lower viscosity, and improved solubility), which significantly expands the possibilities of their use [8–10].

Polyacrylic acid-based drug delivery systems have gained great importance for the delivery of various therapeutic agents by various routes of administration to achieve a controlled and sustained release profile [11–13]. Polyacrylic acid is used to make various architectures, such as hydrogels (including hydrogels for injection), microparticles, nanoparticles, etc. The possibility of delivering therapeutic agents via various routes, such as oral, buccal, transdermal, nasal, vaginal, and gene/vitamin/growth factor delivery, further diversifies the prospects for the use of polyacrylic acid in the biomedical field.

This work aims to synthesize polyacrylic acid with branched and crosslinked macromolecular structures and to study their properties.

Materials and research methods

Acrylic acid (AA) (Sigma-Aldrich) with a basic substance content of 99.5 %.

N,N'-Methylene bis-acrylamide ((b-MAA)) (Sigma-Aldrich) with a basic substance content of 99 %.

N,N'-Azo-isobutyronitrile (DAK) (Fluka) with a basic substance content of 98 %.

The copolymer of acrylic acid with a bifunctional agent, N,N`-methylene bisacrylamide, was obtained in methanol at a temperature of 70–80 °C. N,N'-Azo-isobutyronitrile was the initiator and conversion was 50–90 %. The copolymer was reprecipitated twice (hexane or propanone-hexane mixture, methanol solvent), dried to a constant weight, and the number of carboxyl groups in the copolymer was determined by potentiometric titration according to the method described in [14].

The swelling degree was determined at 20°C in distilled water according to the method given in [14].

To determine the gel fraction, polymer samples (0.5÷1 g) were weighed on an analytical balance and placed in pre-weighed bags. Extraction was performed in a Soxhlet apparatus, methanol solvent, and extraction time 2 hours (determined by previous studies). After extraction, the samples were dried to constant weight.

The density of polymers was determined according to the method described in [15]. Polymer samples were pre-dried to a constant weight. The medium was hexane. The measurement temperature was 20 °C.

Results and discussion

The polymerization of acrylic acid (AA) with a bifunctional agent, N,N`-methylene bisacrylamide (b-MAA), leads to the formation of branched (Fig. 1, *a*) and crosslinked (Fig. 1, *b*) macromolecules, depending on the synthesis conditions.
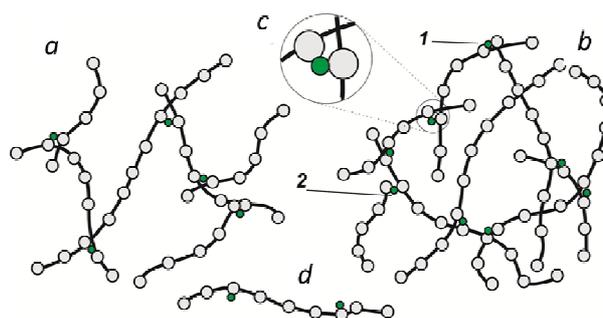
Fig. 1. Schematic representation of the macromolecule structure formed during AA copolymerization with b-MAA and their structural elements: a – structure of a macromolecule with a tree-like (branched) structure; b – structure of a molecule with a crosslinked structure; c – branch point the chemical structure of which is shown in d – conventional structure of a macromolecule formed without considering the branches according to the scheme in Fig. 2 (PP)

The involvement of b-MAA both chains in the copolymerization process leads to the formation of macro chain branching centers (schematic representation is shown in Fig. 1, *c*, and the chemical structure of the branch point is shown in Fig. 2, *b*).

The copolymerization of AA with b-MAA, especially at the initial stages, can be represented by the scheme shown in Fig. 2, *a*.

According to this scheme, the copolymerization of two monomers produces macromolecules (PP) with unsaturated groups in the side chains. According to Flory [15], the reactivity of unsaturated bonds to the chain of the PP macromolecule in radical polymerization reactions differs slightly from the unsaturated bonds in the b-MAA. Therefore, they take part in the copolymerization reaction, which leads to the formation of a branch point in the PP macromolecule.

a *b*
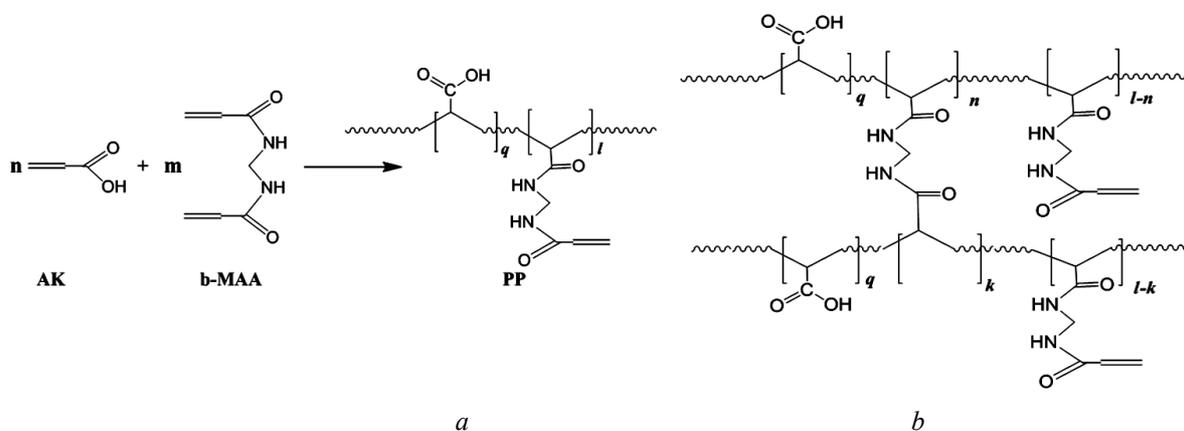
Fig. 2. Reaction scheme of AA and b-MAA copolymerization (a); chemical structure of the branching unit in PP macromolecules (b)

The chemical structure of such a branch point is shown in Fig. 2, *b*. It should be noted that the formation of linear copolymer macromolecules with the PP structure (Fig. 1, *d*) can be observed only at the initial stages of the reaction. Already at low degrees of conversion, while maintaining the reactivity of the grafted unsaturated bonds, branching of macromolecules with the formation of a tree-like structure of macromolecules is observed (Fig. 1, *a*). In the theory of the formation of branched and crosslinked macromolecules, such hypothetical linear macromolecules are called primordially formed linear macrochains. According to Flory's theory [16–18], the formation of crosslinked macromolecules is observed if the number of formed branch points per PP macromolecule exceeds one. It should be noted here that Fig. 2, *b* shows a structure in which there are 0.5 branches per PP macromolecule. With an increase in monomer conversion and an increase in the number of branches per macromolecule, the tree-like structure of macromolecules is gradually replaced by a crosslinked one (Fig. 1, *b*).
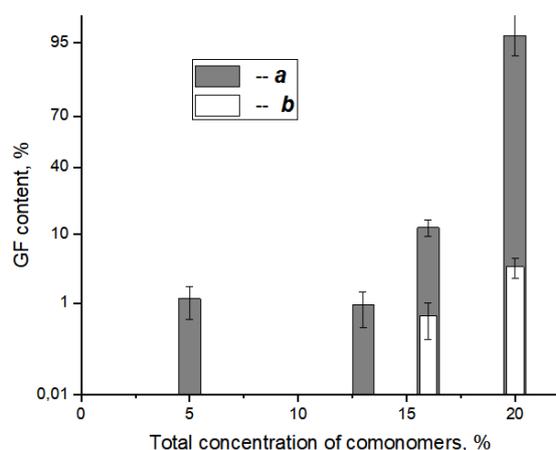
Fig. 3. GF content in copolymer samples at different total concentrations of comonomers. The b-MAA:AA ratio: a – 0.0055;, b – 0.0036

Although these two structures have approximately the same composition, their properties differ significantly. Macromolecules with a tree-like structure are unlimitedly soluble in solvents (for this class of polymers, in water). This property does not significantly differ from polymer molecules with a linear structure. In contrast, macromolecules with a crosslinked structure do not dissolve in solvents (in particular, in water), they only swell. This property

allows polymer samples to be separated. It should be borne in mind that this separation method is not absolute. When polymer samples are extracted in a Soxhlet apparatus, the fraction with a dominated branched structure of macromolecules passes into the solution. This fraction is infinitely diluted with the solvent, i.e., the "sol" fraction (SF), but there may be small amounts of fragments in the macromolecule structure that correspond to a crosslinked structure. In contrast, the non-extractable fraction consists almost entirely of macromolecules with a crosslinked structure. They swell to a limited extent in water and an equilibrium degree of swelling can be determined for them, i. e., the "gel" fraction (GF). The ratio of SF to GF in the polymer sample depends on the synthesis conditions to a large extent. The studies have shown that the main factors determining this ratio within the adopted synthesis conditions are the total initial concentration of monomers in the reaction mixture and the molar ratio of monomers (b-MAA and AA) in this mixture. This can be seen from the dependencies shown in Fig. 3.

Thus, at a b-MAA:AA ratio of 0.0055 and a total monomer conversion of more than 97 %, a significant amount of GF is observed only when the total monomer concentration exceeds 15 %. At a total concentration of about 20 %, this fraction becomes dominant in the resulting polymer. At the same time, even at a total concentration of 20 %, a decrease in the ratio to 0.0036 already leads to a GF content in the polymer sample of only about 4 %.

With a total conversion of monomers above 97 %, the b-MAA conversion by both groups can be considered almost complete. According to Fig. 3, this means that at a b-MAA:AA ratio of 0.0055 till their total concentration of 16 %, the number of reacted unsaturated groups from the b-MAA composition is insufficient to form elastically active crosslinks of PP macromolecules (Fig. 1, position 1) and points (Fig. 1, *c*), which lead to the macromolecule branching (Fig. 1, position 2). According to the theory of the formation of branched and crosslinked polymers, only those points that lead to the formation of a crosslinked macromolecule structure are considered elastically active. Within the framework of the present work, this means the need to form a PP fragment (network chain), which includes at least two branch points that are part of two other PP fragments, which also have at least two branch points. Flory's theory recommends

that the number of such elastically active points be determined by equation (1) through the concentration of the network chains:

$$n_s = f \cdot \frac{v_s}{2},\qquad (1)$$

where f is the functionality of the network node, for this type of copolymer it is equal to 3; v_s is the density of the network nodes, number of momomer units/dm^3 or mol//dm^3; n_s is the concentration of network chains, g/dm^3.

Before calculations it is necessary to pre-estimate the concentration of networkchains using equation (2) [15]:

$$n_s = -\frac{\ln(1-\upsilon_2)+\upsilon_2+\chi\cdot\upsilon_2^2}{V_0\left(\upsilon_2^{1/3}-2\upsilon_2/f\right)},\qquad (2)$$

where υ_2 is the volume fraction of the polymer in the hydrogel sample at equilibrium swelling; χ is the Huggins constant; V_0 is the molar volume of the solvent, dm^3/mol.

To use equation (2), it is necessary to experimentally determine the volume fraction of polymer in a hydrogel sample in the state of equilibrium swelling in a solvent (in this case, water). To do this, it is necessary to know the density of the polymer that forms the hydrogel and the degree of equilibrium swelling.

Table 1

Synthesis conditions and characteristics of b-MAA÷AA copolymers

Synthesis conditions			Xerogel characteristics*		Concentration of network nodes, mmol/dm^3		*Sh* are of hydrody-namically active network nodes in relation to their total number
Total concentration of monomers, %	Concentration of b-MAA, mmol/dm^3	b-MAA:AA molar ratio	Density, g/cm^3	Equilibrium swelling degree in water, g/g	In gel at equilib-rium swelling degree in water	In xerogel*	
13.2	7.4	0.0055	1.42±0.06	80±4	$7.0\cdot10^{-5}$	2.0	0.27
20.5	12.5		1.57±0.05	450±20	$1.5\cdot10^{-3}$	7.8	0.63

* *Xerogel is a dried sample of hydrogel.*

To perform the above-described evaluations, the samples with maximum gel fraction should be used. The synthesis conditions for such samples, as well as the values of the polymer (xerogel) density, the degree of equilibrium swelling, and the volume fraction of polymer in the hydrogel calculated from these values under equilibrium swelling conditions, are represented in Table 1.

The following conclusions can be drawn. An increase in the total monomer concentration from 13 % to 20 % decreases the equilibrium swelling degree of the polymer by 5÷6 times under the same other conditions of its synthesis (temperature, initiator concentration, ratio of co-monomers, and their conversion). This effect is due to a sharp increase in the number of elastically active network nodes (approximately 20 times). This suggests that an increase in the total monomer concentration to

18–20 % with a monomer ratio of 0.0055 leads to a sharp increase in the efficiency of elastically active network node formation.

This can be confirmed as follows. If we assume that all b-MAA molecules that entered the polymerization reaction by both unsaturated groups formed a branch point, then at a concentration of 13.2 %, less than a third of them participated in the formation of elastically active network nodes (Table 1), the rest leading only to chain branching. At a concentration of 20.5 %, this amount already increases to 63 %. The increase in the efficiency of the elastically active crosslinks formation with an increase in the monomer concentration under the same other conditions results in the increase in the polymerization degree of the PP chains. Moreover, the possibility of involving unsaturated b-MAA bonds contained in the

other two PPs and the formation of an elastically active node increases.

Conclusions

Polymers and copolymers of acrylic acid are of practical interest as special-purpose polymers, both with branched and crosslinked macromolecular structures. The research results presented in this article demonstrate that the methodology described here can be used to obtain samples of crosslinked polyacrylic acid with different macromolecular structures, which will significantly affect its properties. Thus, if it is necessary to obtain branched but water-soluble macromolecules, it is necessary to carry out the synthesis with a b-MAA:AA ratio of less than 0.0036 and at a total concentration of comonomers of less than 13–15 %. If it is necessary to obtain crosslinked polyacrylic acid capable of forming hydrogels or microhydrogels, the synthesis should be carried out at a total monomer concentration of at least 20 % and a b-MAA:AA ratio of 0.0052 or more.

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СИНТЕЗ ТА ДОСЛІДЖЕННЯ ВЛАСТИВОСТЕЙ РІДКОСТРУКТУРОВАНИХ КОПОЛІМЕРІВ ПОЛІАКРИЛОВОЇ КИСЛОТИ

Досліджено взаємозв'язок структури кополімерів акрилової кислоти та N,N-метиленбісакриламіду від умов їх отримання. Встановлені оптимальні умови одержання полімерів із лінійною, деревоподібною та просторово-структурованою будовою макромолекул. Досліджено їх властивості, а саме густину, ступінь набрякання, гель-фракцію тощо. Показано, що кополімери із просторово-структурованими макромолекулами утворюють гідрогелі, ступінь набрякання яких істотно залежить від умов одержання. Для кополімерів, що утворюють гідрогелі, на основі залежностей густини та рівноважного ступеня набрякання визначено густину вузлів зшивок.

Ключові слова: акрилова кислота; кополімер; структура; гель- та золь-фракція; ступінь зшивки.