Synthesis and Swelling Behaviour of Some Crosslinked Poly(vinyl alcohol)-acrylamide Hydrogels

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Hydrogels are networks consisting of crosslinked hydrophilic polymers that absorb and retain water or biological fluids. Poly(vinyl alcohol) (PVA) based hydrogels are non-toxic, non-carcinogenic, easily processed and therefore have been examined for tissue replacements, artificial skin, hemodialysis membrane and oral drug release systems. The research focuses on the synthesis of PVA–acrylamide based hydrogels, using glutaraldehyde, sodium tetraborate and N,N'-methylenebisacrylamide/sodium tetraborate mixture as crosslinking agents. The crosslinking copolymers were characterized by infrared spectroscopy (IR), thermal analysis (TG, DSC), and swelling behaviour in distilled water at 37.5 ^{0}C temperature.

Keywords: crosslinked copolymers, poly(vinyl alcohol)-acrylamide, glutaraldehyde, sodium tetraborate, N,N'-methylenebisacrylamide

Hydrogels are polymeric three-dimensional networks, which absorb and retain large amounts of water until equilibrium is reached, but keep their shape. The three-dimensional network is constituted of long polymer chains that are chemically (polymer network with covalent bonding), or physically (no covalent interactions) crosslinked. Chemically crosslinked hydrogels are obtained by radical polymerization procedure of low molecular weight monomers in the presence of crosslinking agents, as well as of some water soluble polymers with reactive side groups. Other chemically crosslinking methods include: chemical reactions of complementary groups, high energy radiation as well as using enzymes [1]. To design hydrogels from water soluble polymers (dextran, hydroxyethylstarch, albumin, poly(vinyl alcohol) and hyaluronic acid), they were previously derivatized with methacrylic groups.

Hydrogels have found applications in separation processes: microfiltration, ultrafiltration, gas permeation, dialysis, reverse osmosis [2]. In the biomedical field they are used in diagnosis, therapeutic and implantable devices (catheters, biosensors and artificial skin), protein separation, matrices for cells encapsulation and controlled release systems of drugs and bioactive substances. A relatively new application of hydrogels is as delivery vehicle in tissue engineering, also they can guide and support the formation of a new tissue *in vivo* [3]. Theories are unable to predict the physical properties of the gels from the synthesis conditions, due to different reactivity and conversion dependent of the vinyl groups, cyclyzation, and multiple crosslinking. As non-ideal networks, hydrogels include defects that affect their physical properties such as: swelling, elasticity, transparency, permeability, gel inhomogeneity [4].

Poly(vinyl alcohol) hydrogels are hydrophilic polymer networks whose properties are controlled by variation of the degree of residual acetylation (percent hydrolysis), as well by variation of the crosslinking density. Poly(vinyl alcohol) can be crosslinked through the use of difunctional crosslinking agents (glutaraldehyde, acetaldehyde, formaldehyde) [5]. When these crosslinking agents are used in the presence of sulfuric acid, acetic acid, or methanol acetal bridges form between the pendant hydroxyl groups of the PVA chains. Chemical crosslinking was also done on poly(vinyl alcohol) with the use of electron beam or γ-irradiation [6]. Poly(vinyl alcohol) modified with L(+)-lactic acid in different molar ratio was crosslinked with sodium tetraborate and triethylenetetramine as activator [7]. The hydrogels have swelling ratio values in phosphate buffer solution (*p*H=7.4) close to PVA, and the glass transition temperature values decreased. The physically crosslinked PVA gels presented a higher swelling degree in water, a rubbery and elastic structure and high mechanical strength [8, 9]. Poly(vinyl alcohol) hydrogels are used in biomedical and pharmaceutical applications, as they have high swelling in water. They are easily accepted in the organism and simulate natural tissues, being utilized in the reconstruction of vocal cords [10], biomembranes in artificial kidney applications [11]. *p*H-sensitive hydrogels composed of chitosan and polyacrylamide were prepared as semi-interpenetrating and interpenetrating networks, using chitosan in a two-fold molar excess to polyacrylamide [12]. Also, hydrogels based on acrylamide were synthesized by simultaneous crosslinking polymerization procedure with a bifunctional cross-linker N,N'-methylenebisacrylamide and potassium peroxydisulphate and ascorbic acid redox initiating system at established weight ratio. In real-time the gelation process is monitored by following the viscoelastic parameters throughout the in situ crosslinking (in the rheometer) and by temperature, pH and conductivity determination. It was found that the optimal weight ratio of the redox initiators pair from the viewpoint of elastic properties of the obtained hydrogel is 7/1 potassium persulfate/ascorbic acid [13, 14].

The aim of this study is the preparation of some PVA–acrylamide based hydrogels, their characterization and swelling behaviour in distilled water at 37.5 ^{0}C temperature similar to human body. The chemical crosslinking of the previously synthesized copolymers [15], was done in aqueous solution using different crosslinking agents: sodium tetraborate, glutaraldehyde in acid medium and N,N'-methylenebisacrylamide/sodium tetraborate mixture with triethylenetetramine activator.

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Table 1

SYNTHESIS OF THE CROSSLINKED COPOLYMERS

Sample	Copolymers		Hydrogels
	PVA/acrylamide gravimetric ratio	initiator	crosslinking agent 5%
1	1/1	POB	Sodium tetraborate
2			Glutaraldehyde
3			Sodium tetraborate/N,N'-methylenebisacrylamide
4	1/1	$K_2S_2O_8$/$FeSO_4$	Glutaraldehyde
5			Sodium tetraborate/N,N'-methylenebisacrylamide
6	2.33/1	$K_2S_2O_8$/$FeSO_4$	Glutaraldehyde
7			Sodium tetraborate/N,N'-methylenebisacrylamide
8	2.33/1	POB	Sodium tetraborate
9			Glutaraldehyde
10			Sodium tetraborate/N,N'-methylenebisacrylamide

Experimental part

Materials

The copolymers poly(vinyl alcohol)-acrylamide were previously synthesized by graft copolymerization procedure of PVA with acrylamide in the presence of redox (potassium persulfate and ferrous sulfate) or benzoyl peroxide as initiators. Glutaraldehyde, sodium tetraborate, N,N'-methylenebisacrylamide, and triethylenetetramine (Fluka reagents) were used without further purification.

Methods of investigation

IR spectra of PVA and some crosslinked copolymers were recorded on spectrophotometer M80 type using KBr pellets for sample preparation.

Thermogravimetric analyses (TG and DTG) were recorded using a derivatograph Q-1500D type MOM-Budapest (Hungary) under the following operational conditions: sample weight 50 mg, heating rate 10^{0}C/min, in air flow of 30 mL/min, the maximum heating limit 700 ^{0}C and reference material α-Al_2O_3

Thermal DSC analyses were carried out by means of a Mettler 12E type differential scanning calorimeter (Switzerland) with a heating rate of 10^{0}C/min in nitrogen atmosphere. The first heating run was carried out with a 10-12 mg sample in the temperature range between room temperature and 300^{0}C. The second heating run was performed with samples, which were suddenly cooled to room temperature. Pure indium was used as a standard for calorimeter calibration.

Swelling ratio (SR) of gels in distilled water was studied at 37.5^{0}C and was defined as:

$$SR = (W_1 - W_0)/W_0$$

where W_1 and W_0 are weights of gels in the swollen and dry states, respectively.

Equilibrium water content (EWC) was defined as:

$$EWC = [(W_1 - W_0)/W_1] \, . \, 100$$

The studied gel sample was cut into 1.0 cm x 1.0 cm x 0.8 cm pieces and immersed in distilled water. At established time intervals the samples were taken out of water and blotted with filter paper to remove the traces of water adherent to surface, then were weighed at the analytical balance. The distilled water was replaced after each determination.

Synthesis of hydrogels

Hydrogels were achieved by chemical crosslinking of some PVA-acrylamide copolymers previously synthesized [15]. Copolymers with PVA/acrylamide gravimetric ratio 1/1, benzoyl peroxide (POB) as grafting reaction initiator, reaction temperature 90 ^{0}C (copolymers 1-3), or redox initiator ($FeSO_4$+$K_2S_2O_8$), reaction temperature 75-80 ^{0}C (copolymers 4, 5), as well as copolymers with PVA/acrylamide molar ratio 2.33/1, redox initiators (copolymers 6, 7) and POB initiator (copolymers 8-10) were used. Synthesis of copolymers were achieved in aqueous solution. The swelling ratios in water (25 ^{0}C) of the non-crosslinked copolymers in the presence of redox initiator presented higher values comparative to the copolymers synthesized with POB (for the same PVA/acylamide ratios). This reality suggests that in the presence of these two initiators categories and different reaction temperatures, copolymers with different molecular weights can be obtained, that can influence the swelling ratios. In the presence of POB initiator copolymers with more raised molecular weight and viscosity than in presence of redox initiator are obtained.

To obtain hydrogels, we used aqueous solutions 10 wt.% of PVA-acrylamide copolymers that were submitted to crosslinking reactions. Different crosslinking systems were used: glutaraldehyde in acid medium, sodium tetraborate (aqueous solution 3 wt.%) and sodium tetraborate/N,N'-methylenebisacrylamide mixture with triethylenetetramine as activator. The copolymers composition and synthesis conditions of the hydrogels are presented in table 1. In all cases the concentration of the crosslinker was 5 wt.% reported to copolymer. Solutions of the copolymers and crosslinking agents were homogenized by stirring at 25^{0}C and placed into tight closed glass tubes. They were introduced in water bath and maintained at 80^{0}C for 48 hours. Finally, the tubes were broken and the product was recovered and dried under vacuum at 100^{0}C. The obtained crosslinked copolymers were studied concerning the swelling behaviour in distilled water at 37.5 ^{0}C temperature.

The possible structures of the copolymers crosslinked with sodium tetraborate, glutaraldehyde and sodium tetraborate/N,N'-methylenebisacrylamide are presented in schemes 1-3. By dissolving sodium tetraborate in water, this dissociate into sodium ions (Na^+) and tetraborate ions ($B_4O_7^{2-}$) [16]. The tetraborate ion reacts with water (hydrolyzes) to produce boric acid and the OH^- ion.

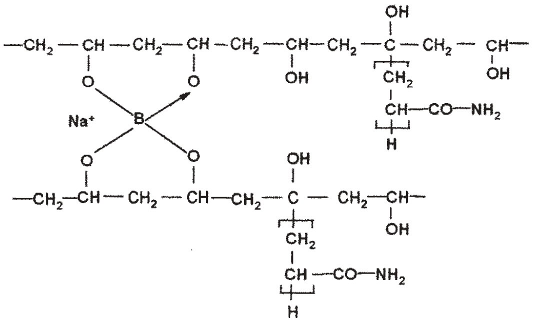
$$B_4O_7^{2-}(aq) + 7\,H_2O <\!\!—\!\!> 4\,H_3BO_3(aq) + 2\,OH^-(aq)$$

$$Na^+ + OH^- \longrightarrow NaOH$$

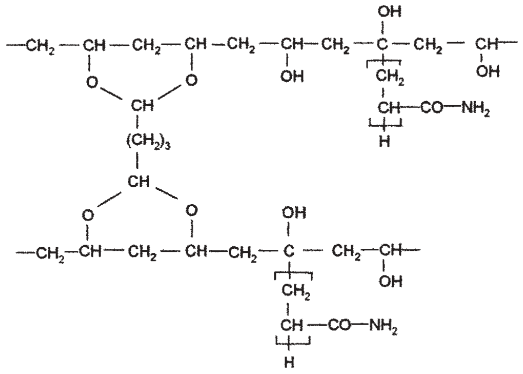
The boric acid further reacts with water to form the borate anion:

$$H_3BO_3(aq) + 2\,H_2O <\!— > B(OH)_4^-(aq) + H_3O^+(aq)$$

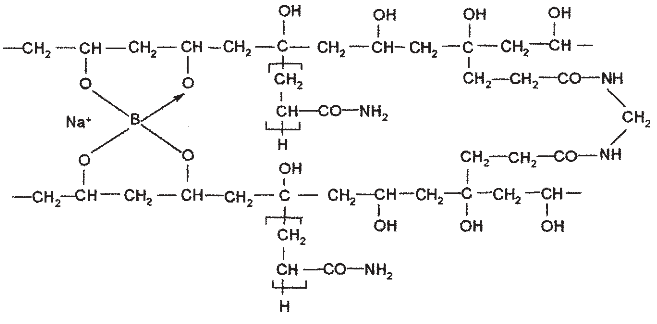
The borate anion can reacts with OH groups in two chains of PVA-acrylamide copolymer to form crosslinks, possibly with the elimination of water (scheme 1). Also, it is well-known that poly(vinyl alcohol) reacts with aldehydes in acid media to form water insoluble polyacetals [17]. Reaction cu dialdehyde (glutaraldehyde) is expected to form an acetal crosslinked structure as indicated in scheme 2. In accordance with the previous proposed mechanisms, when sodium tetraborate and N,N'-methylenebisacrylamide were used as crosslinking agents, we suggest the chemical structure presented in scheme 3.



Scheme 1



Scheme 2



Scheme 3

Results and discussion

IR spectra of PVA and PVA-acrylamide copolymer are presented in figure 1. The absorption bands at 1650 cm^{-1} corresponding to νCO absorption bands and at 1600 cm^{-1} corresponding to δNH absorption bands indicate the modification of PVA chemical structure.

The IR spectra of the crosslinked copolymers (hydrogels) are presented in figure 2. The large peaks between 3000 and 4000 cm^{-1} are normally assigned to symmetric and asymmetric stretching vibration corresponding to unreacted OH bonds in PVA polymer. The copolymers crosslinked with glutaraldehyde have pronounced bands (νCO) at 1675 cm^{-1} characteristic to the CHO group, and in the crosslinked copolymers with sodium tetraborate and N,N'-methylenebisacrylamide the presence of an supplementary absorption band at 1380 cm^{-1} characteristic to νBO group and at 1655 cm^{-1} respectively, characteristic to νCO group in the secondary amides, is ascertained. The absorption bands resulted from the carbonyl groups (C=O) of the crosslinking agents are superposed with the absorption bands of PVA-acrylamide copolymer, and intensity of the respective bands is not significantly modified because the crosslinking agent concentration is low.

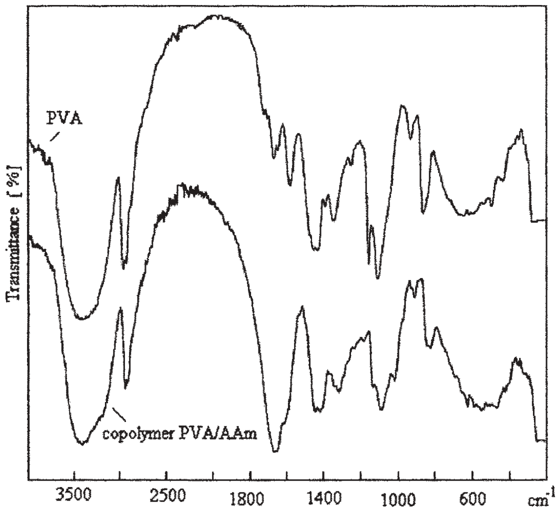


Fig. 1. IR spectra of PVA and PVA-acrylamide copolymer

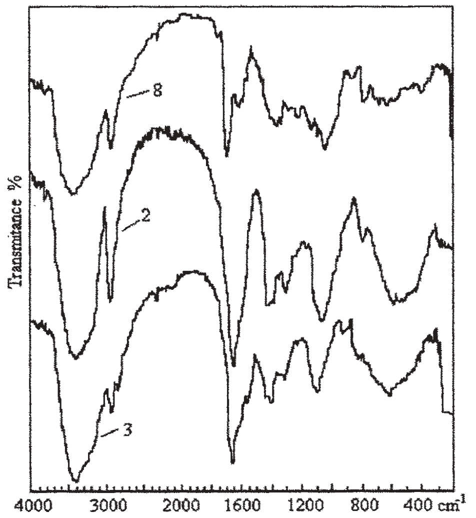


Fig. 2. IR spectra of the PVA-acrylamide copolymers crosslinked with: 2- glutaraldehyde; 3- sodium tetraborate/N,N'-methylenebisacrylamide; 8- sodium tetraborate

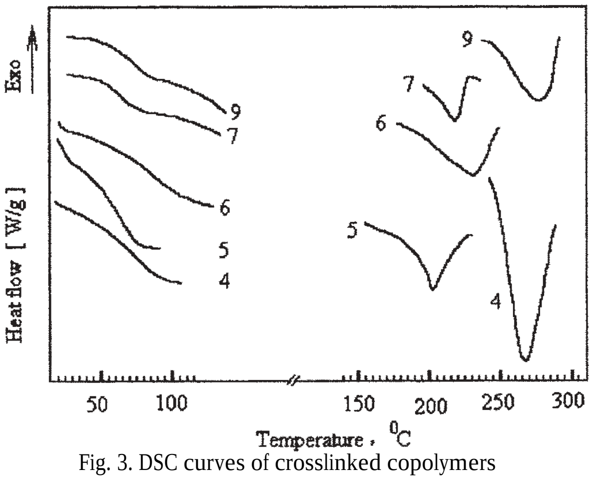


Fig. 3. DSC curves of crosslinked copolymers

Table 2

DSC CHARACTERISTICS OF THE MAIN SYNTHESIZED COPOLYMERS

Sample	Crosslinked copolymers			Uncrosslinked copolymers [15]		
	T_g (^{0}C)	T_m (^{0}C)	ΔH (J/g)	T_g (^{0}C)	T_m (^{0}C)	ΔH (J/g)
4	86	278	108.64	47	230	43.60
5	60	215	32.30	47	230	43.60
6	78	240	32.96	45	225	47.48
7	65	228	12.30	45	225	47.48
9	75	290	59.80	40	228	82.55

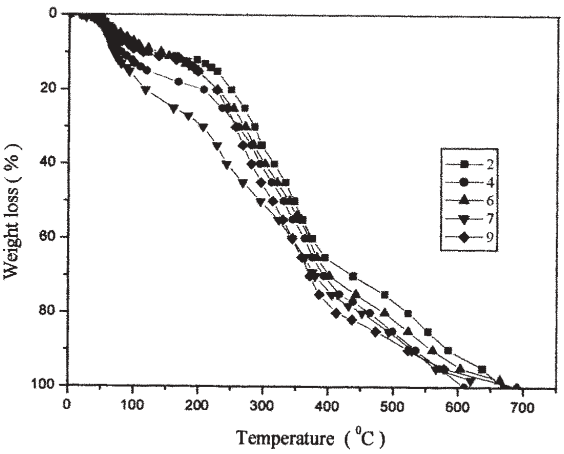


Fig. 4. TG diagrams of the main crosslinked copolymers

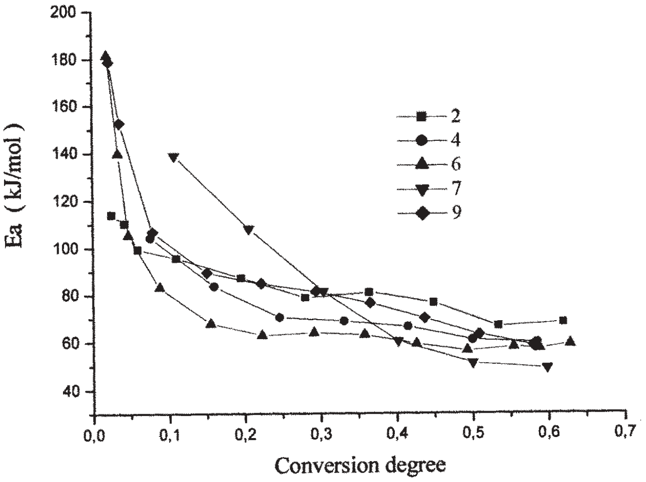


Fig. 5. Dependence of Ea versus conversion degree of thermal decomposition processes

In figure 3 and table 2 the thermal characteristics determined by differential scanning calorimetry are presented. In the case of non-crosslinked copolymers, the glass transition temperatures (T_g) and melting temperatures (T_m) doesn't influence significantly as PVA/acrylamide ratio in their structure. The glass transition temperatures and melt temperatures of the crosslinked copolymers have more raised values comparative to the uncrosslinked graft copolymers (table 2). Also, the melting heat (ΔH), T_g and T_m of the crosslinked copolymers with glutaraldehyde (samples 4, 6 and 9) have higher values comparative to the products crosslinked with sodium tetraborate/N,N'-methylenebisacrylamide mixture (samples 5 and 7). It is emphasized that glutaraldehyde is the best crosslinking agent for the synthesized copolymers, carrying out a higher density of crosslinks. This fact can be observed also from the swelling behaviour of the copolymers, when lower swelling ratio values were obtained.

In figure 4, TG curves referring to weight loss obtained by the thermal oxidative decomposition process of main crosslinked copolymers are presented. In table 3 characteristics concerning thermal stability of the same copolymers are listed. Crosslinked copolymers with glutaraldehyde are more thermally stable than crosslinked copolymers with sodium tetraborate/N,N'-methylene-bisacrylamide mixture. This fact can be concluded from the weight losses of 10 and 50% recorded by oxidative thermal decomposition. The crosslinked copolymers with glutaraldehyde presented weight losses of 10 % on temperature intervals 82-141^{0}C, and 50% on 314-348^{0}C intervals. In the case of crosslinked copolymer with sodium tetraborate/N,N'-methylenebisacrylamide mixture, weight losses of 10 % were recorded at 70 ^{0}C, and of 50% at 295^{0}C. Also, the final temperature of the main decomposition processes (where the weight losses had maximum values) was situated between 437-523^{0}C when glutaraldehyde was used as crosslinking agent, and 376 ^{0}C in the case of sodium

Table 3

THERMAL CHARACTERISTICS DETERMINED BY DTG ANALYSIS

Sample	T_{10} (^{0}C)	T_{50} (^{0}C)	T_i (^{0}C)	T_f (^{0}C)	W_{Ti-Tf} (%)	Ea (kJ/mol)	n	ln A
2	121	348	164	438	59	61.26	1.6	6.576
4	82	332	169	438	59	47.30	1.1	2.132
6	141	340	154	523	74	45.55	1.9	3.456
7	70	295	184	376	51	37.15	1.1	2.045
9	113	314	164	437	70	54.09	1.4	3.512

T_{10}, T_{50} –temperatures corresponding to 10 wt % and 50 wt % weight loss.

T_i, T_f –temperature of beginning of main process of thermal decomposition and ultimate temperature of the process, respectively.

W_{Ti-Tf} – weight losses.

Table 4
THE SWELLING RATIOS OF THE CROSSLINKED COPOLYMERS

Copolymer	Swelling time (h)									
	0.5	1	2	3	4	6	8	10	34	100
1	2.267	2.738	2.082	2.394	0.769	-	-	-	-	-
2	1.423	2.526	3.103	3.431	3.645	3.796	5.189	3.808	3.795	3.803
3	0.022	0.01	-	-	-	-	-	-	-	-
4	1.354	2.74	3.707	4.298	4.654	5.119	5.189	5.207	5.306	5.35
5	7.47	12.78	24.04	39.468	**41.159**	32.306	-	-	-	-
6	1.012	2.809	3.137	3.399	3.594	4.027	4.123	4.186	4.328	4.326
7	3.61	5.809	7.629	9.835	**10.425**	10.1	-	-	-	-
8	0.755	1.057	1.444	1.409	1.41	1.339	1.269	1.208	1.104	1.103
9	1.101	2.623	3.339	3.734	3.897	4.21	4.194	4.231	4.197	4.204
10	1.559	1.841	1.856	1.658	1.356	-	-	-	-	-

tetraborate/N,N'-methylenebisacrylamide mixture. The components ratio PVA/acrylamide used in the copolymers synthesis can have influence on thermal stability. The copolymers with gravimetric ratio 1/1 (copolymers 2 and 4) crosslinked with glutaraldehyde have a better thermal stability than those with gravimetric ratio 2.33/1 (copolymers 6 and 9), weight losses on T_i-T_f temperature interval are 59 % in the case of copolymers 2, 4 and between 70-74 % for copolymers 6, 9.

The activation energy (Ea) and the reaction order (n) were determined in each case on the main decomposition process (T_i-T_f), using methods cited in speciality literature [18-20], based on general equations:

$$\frac{d\alpha}{dT} = A\exp\left(\frac{-Ea}{RT}\right)\left[\alpha^{m}(1-\alpha)^{n}\right]\cdot\left[-\ln(1-\alpha)^{p}\right] \tag{1}$$

$$\frac{\log[1-(1-\alpha)^{1-n}]}{(1-n)\cdot T^{2}} = \log\left(\frac{AR}{\beta Ea}\right) - 2.303\left(\frac{Ea}{RT}\right) \tag{2}$$

where: α - conversion degree (ratio of the weight loss at time "t" and at the end of the process), A - pre-exponential factor, T - temperature, Ea - activation energy of decomposition, R - gas constant, n - reaction order, m, p - exponents of the conversion function, β - heating rate.

The activation energy presents lower values in the case of crosslinked copolymers with sodium tetraborate/N,N'-methylenebisacrylamide mixture compared to crosslinked copolymers with glutaraldehyde. The low crosslinking efficiency of sodium tetraborate/N,N'-methylenebisacrylamide mixture directs to the obtainment of a copolymer with a raised swelling ratio in water. The variation of activation energy with conversion degree of thermal decomposition reaction (fig. 5) presents a rapid decrease to 0.1 conversion degree, and then its variation is almost linear to the end of the process. The sudden diminution of Ea noticed on the first part of the interval, suggests that on the beginning of degradation process, the decomposition reaction has an autocatalytic behaviour. It can be due to oxygen traces in copolymers that act as catalysts for thermal decomposition processes.

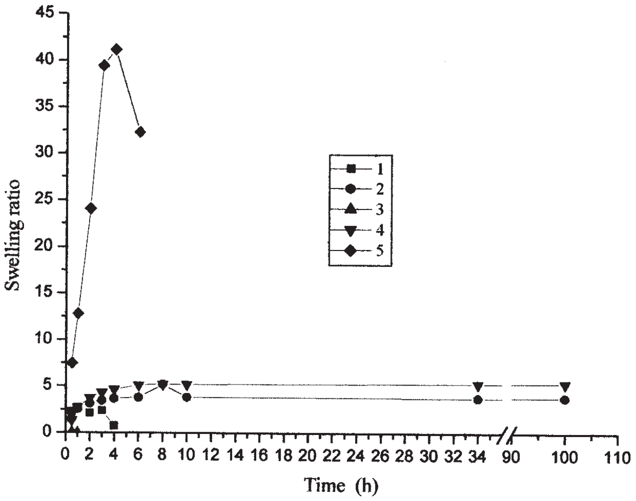


Fig. 6. Swelling ratio in distilled water at 37.5 ^{0}C

The swelling ratios and equilibrium water content values of the crosslinked copolymers are presented in table 4 and figures 6-9.

It can be observed that the highest swelling ratio values record the copolymers 5 and 7 crosslinked with sodium tetraborate/NN-methylenebisacrylamide mixture, the maximum value is reached after approximately four hours.

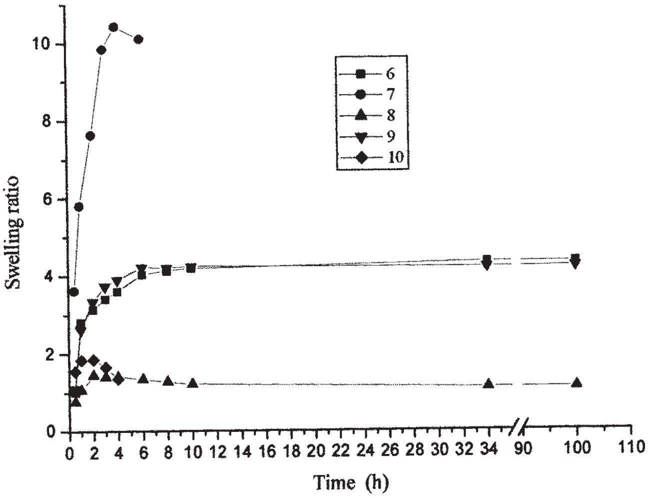


Fig. 7. Swelling ratio in distilled water at 37.5 ^{0}C

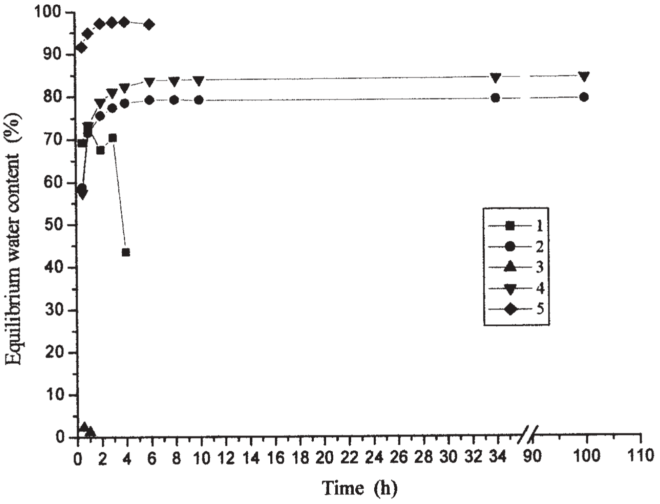


Fig. 8. Equilibrium water content at 37.5 ^{0}C

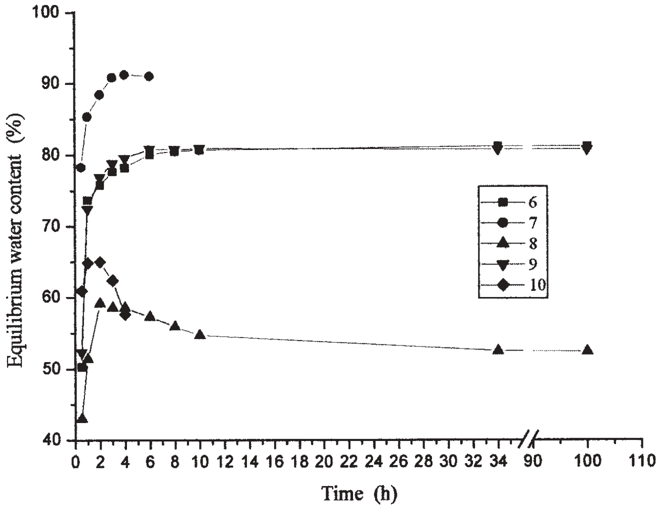


Fig. 9. Equilibrium water content at 37.5 ^{0}C

Quantity of the absorbed water is approximately 41 g water/ g dried copolymer (copolymer 5), and 10.4 g water /g dried copolymer (copolymer 7). The copolymer with higher gravimetric acrylamide ratio (copolymer 5) presents a higher swelling capacity, but in both cases, the equilibrium water content exceeds the value of 90 wt % after 4 h water immersion (97.5 % copolymer 5 and 91.2 % copolymer 7, respectively). Also we notice that at the same PVA/ acrylamide ratio (copolymers 3 and 5), the swelling ratio is influenced by the nature of the initiator and reaction temperature used in the synthesis that direct to copolymers with different properties. Some of the crosslinked copolymers present lower swelling ratio and equilibrium water content values due to more advanced crosslinking reactions. Generally, we can affirm that the copolymers crosslinked with sodium tetraborate/N,N'-methylene-bisacrylamide present a better gel behaviour, comparative to glutaraldehyde or sodium tetraborate crosslinked ones.

Conclusion

To obtain hydrogels based on PVA–acrylamide copolymers different crosslinking agents have been used. IR spectra and thermal behaviour suggest that crosslinking reaction has been achieved. The crosslinked copolymers with sodium tetraborate/N,N'-methylenebisacrylamide mixture present a better behaviour to swelling in distilled water at 37.5^{0}C temperature, comparative to the crosslinked copolymers with glutaraldehyde or only with sodium tetraborate. The equilibrium water content exceeds the value of 90 wt% after 4 h water immersion in the case of sodium tetraborate/N,N'-methylen-ebis-acrylamide crosslinked copolymers. Glutaraldehyde crosslinked copolymers are more thermally stable than crosslinked copolymers with sodium tetraborate/N,N'-methylenebisacrylamide mixture, but swelling behaviour is lower. The hydrogels are synthesized from potential biodegradable and biocompatible raw materials, the thermal characteristics and swelling behaviour in water at 37.5 ^{0}C suggest their potential utilization in systems for sustained release of bioactive principles.

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Manuscript received: 8.04.2008