

Characterization of poly(acrylamide) as temperature-sensitive hydrogel

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In the study hydrogels poly(acrylamide) based with different concentration of N,N'-methylenebis(acrylamide) as a crosslinker agent were prepared using a redox polymerization system. The observations on equilibrium swelling and thermal analysis are related with the thermoresponsive character. This aspect is in relation with the copolymer destination as an inner material for cold therapy packs.

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1. Introduction

It is well known that hydrogels are suitable for biomedical, agricultural and industrial applications. In particular, they have been widely used for the preparation of drug-delivery systems. Hydrogels preformed by chemical or physical crosslinking form three-dimensional, hydrophilic, polymeric networks capable of imbibing large amounts of water [1, 2]. They resemble natural living tissue more than any other class of synthetic biomaterials due to their high water content; furthermore, the high water content of the materials contributes to their bio- and blood-compatibility. Therefore, hydrogels are found in numerous applications in the pharmaceutical, biology and medicine fields [3-10], as electrophoresis materials for biomolecular separation, controlled/sustained drug delivery devices, contact lenses, lubricating surface coatings (used with catheters, drainage tubes and gloves), artificial tendons and cartilages, wound healing dressings, artificial kidney membranes, artificial skin, maxillofacial and sexual organ reconstruction materials, packing materials for liquid chromatography, inner materials for thermosensitive packs. In this regard, the phase-change polymers, which may trigger drug release in response to external stimuli, are the most investigated. Hydrogels providing such 'sensor' properties can undergo reversible volume phase transitions or sol-gel phase transitions upon changes in the environmental condition. These "intelligent" or "smart" polymers play an important role in drug delivery since they may dictate not only where a drug is delivered, but also when and with which interval it is released [11]. The stimuli that induce various responses of the hydrogel systems include physical (temperature, electric fields, light, pressure, sound, magnetic fields), chemical (pH, ions) or biological/ biochemical (biomolecules) ones [12]. Due to their swelling ability, stimulus-sensitive hydrogels have been explored for use in sensors and actuators. In sensors, hydrogels are used as the sensing part for a specific stimulus and in actuators to execute stimulus-driven mechanical work. Hydrogels are

known to have long swelling and shrinking response times due to the fact that the kinetics are controlled by diffusion of ions.

Temperature-sensitive hydrogels are probably the most commonly studied class of environment-sensitive polymer systems [13]. These hydrogels are able to swell or de-swell exhibiting volume phase transition as a result of changing in the temperature of the surrounding fluid, below and above lower critical solution temperature (LCST), respectively. Below LCST the polymer shows full-hydrated and extended conformation, over LCST it extensively dehydrates and changes to compact chain conformation. Such phase transitions is accompanied by the changes in hydrophilic/hydrophobic properties: the gel is hydrophilic in character below LCST, but becomes hydrophobic as the temperature rises above LCST.

The polymer network may be collapsed, i.e. a dramatic diminution of the network volume can be induced by changing temperature. Many scientific works in recent years have been dealing with hydrogels incorporating acrylamide (AAm) monomer used as drug delivery systems. The reason is the lower critical solution temperature (LCST) at about 34° C exhibited as a phase transition in water and going from a swollen to an unswollen state by acrylamide hydrogels, close to human body temperature.

In the present work, were obtained hydrogels based on acrylamide and N, N'-methylene bis(acrylamide) (Bis) as bifunctional crosslinker. The copolymerization, performed in aqueous solution and in the presence of a redox initiation system, undergoes a simultaneous crosslinking process. The aim of this study was to investigate the differences induced on swelling and thermal behaviour dependence by the amount of crosslinking comonomer, as well to relate the swelling properties by the temperature changes.

The gels will be evaluated for some applications, such as inner materials for cold therapy packs, as versatile, practical, therapeutic products helpful for reducing

swelling, inflammation, muscle spasms, aches and pains in sports medicine, surgery, dentistry.

2. Experimental details

Acrylamide (Merck, Darmstadt, Germany) (AAM) as monomer, *N,N'*-methylene-bis(acrylamide) (Sigma, St. Louis, US) (Bis) as crosslinker, potassium peroxydisulphate (Merck, Darmstadt, Germany) (KPS) as initiator, ascorbic acid (Sigma, St. Louis, US) (AAsc) as accelerator, were analytical reagent grade and used as received. Distilled water was used in all the copolymerizations and swelling studies.

The AAM hydrogels were prepared by mixture monomer and crosslinker at a concentration of monomers during gel preparation of 6 wt% in distilled water, with KPS/AAsc redox system of initiation and quantities specified in Table 1. The polymerizations were carried out in glass ampoules with 12 mm diameter and 130 mm length, at room temperature (+24°C) for 24 hrs. The complete synthesis details are given in Table 1.

Table 1. Synthesis of poly(acrylamide) hydrogels

Sample	AAM % ^{x)}	Bis % ^{x)}	10 ⁻² · AAM / Bis molar ratio	10 ³ · KPS/AAsc ^{xx)} molar ratio
1	97.72	2.28	8.5 / 9.1	6 / 0.9
2	98.36	1.62	8.5 / 6.5	6 / 0.9
3	99.00	1.00	8.5 / 3.9	6 / 0.9
4	99.34	0.62	8.5 / 2.6	6 / 0.9
5	99.50	0.50	8.5 / 1.9	6 / 0.9
6	99.60	0.40	8.5 / 1.6	6 / 0.9
7	99.67	0.33	8.5 / 1.3	6 / 0.9
8	99.73	0.27	8.5 / 1.04	6 / 0.9

x) – from the total amount of monomers

xx) - with respect to monomer concentration

The polymer gels obtained in long cylindrical shapes were washed and thoroughly rinsed with large amounts of distilled water to remove any unreacted monomers and initiators physically entrapped within the crosslinked structure, blot dried with filter paper, dried in air and vacuum, and stored for analyses and swelling studies.

The swelling ratio was measured in distilled water in the range of temperature from 25 to 40°C. Preweighed dry hydrogels were immersed in the swelling medium in a thermostatically controlled water bath, at a constant temperature until they swelled to equilibrium. It was confirmed that nearly 72 hrs were enough for the hydrogels to reach maximum equilibrium swelling. After excessive surface water was removed superficially with filter paper, the swollen hydrogels were weighed by a precision electronic balance (A&D Co. Ltd. HR 200).

The percentage swelling (%S) was calculated from the Equation (1) [14]:

$$\%S = \frac{M_t - M_o}{M_o} \times 100 \quad (1)$$

where M_t is the weight of the swollen gel at time t and M_o is the weight of the dry gel at 0 time. The data points shown are averages of at least three separate measurements.

The glass transition temperature T_g was recorded on a Mettler DSC-12E type differential scanning calorimeter at a scanning rate of 15°C/min under a nitrogen atmosphere, and 25°- 400 °C temperature range, under dynamic conditions.

Thermogravimetric analysis (TGA) was performed in air by means of a MOM – Budapest of Paulik, Paulik – Erdelyi type derivatograph, by increasing the temperature from 25 to 700 °C, at a constant heating rate of 12 °C x min⁻¹ and reference material α -Al₂O₃, with simultaneous recording of thermogravimetric TG, derived thermogravimetric DTG, differential thermal DTA, and temperature variation T. The activation energies of decomposition reaction E_a for the obtained gels were calculated from TGA curves using Coats - Redfern and Reich – Levi method [15 - 18].

Coats and Redfern developed a graphical method to determine the kinetic parameters for solid decomposition from non-isothermal data. The Coats-Redfern model can be derived from Equation(2) with rearrangement.

$$\ln\left(\frac{E_a + 2RT}{T^2} \ln \frac{1}{1-x}\right) = \ln\left(\frac{AR}{b}\right) - \frac{E_a}{RT} \quad (2)$$

where:

A – frequency factor (min⁻¹)

E_a – activation energy (J/mol)

x - conversion degree (ratio of the weight loss at time “t” and at the end of the process)

b – dT/dt

T – temperature, °K

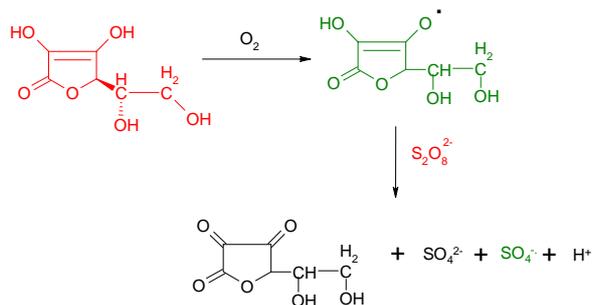
R – gas constant, J/mol x °K

According to this model, a plot of $-\ln[-(\ln(1-x)/T^2)]$ versus $1/T$ should result in a straight line of slope E_a/R .

3. Results and discussion

3.1. Preparation of hydrogel

For the gels preparation by copolymerization of acrylamide with *N,N'*-methylenebisacrylamide it was used the redox initiation system based on potassium persulfate / ascorbic acid. The initiation process has an autocatalytic reaction as follows:



the dehydroascorbic acid catalysed process being at a rate independent of the oxygen presence.

In general aici cred ca e bine de intyrodus varianta care se foloseste cu PSNH₄ si activatorul si avantajul care l confera sistemul nostra ca nu e inhibit de aer ca sa fie justificare la studiu si fapt can u impiedica noul sistem ul;terior in discutie.

In the free-radical crosslinking copolymerization process, the crosslinking reactions considerably enhance the gel effect. This is an autoacceleration reaction. The gel effect starts right from the beginning of the polymerization, that is, even at zero conversion. This copolymerization processes are exothermic in nature; it took an hour to 3 – 4 hrs at any monomeric ratio to obtain the gel form. However, the polymerizations were continued for 24 h to obtain good gelation. In the study there were obtained hydrogels within 1 h through the aqueous solution crosslinking polymerization of AAm and Bis when where used higher concentrations of crosslinker (molar ratio of $8.5 \times 10^2 / 9.1$ AAm / Bis). The gel formation time increased with the crosslinker content decreased.

At the same time, the redox initiation based on potassium persulfate / ascorbic acid used in this study has an independent rate of the oxygen presence [19].

3.2. Dynamic swelling study of the hydrogels

The swelling behaviour is the main characteristic parameter for any hydrogel and is depending on the nature of the polymers (nature of charge, ionic content, crosslinking agent content) and the environmental conditions (pH and temperature of the medium). It appears to be a universal phenomenon which can be observed by choosing appropriate combinations of polymers and solvents. Theoretical considerations also support this view. When a polymer network is in contact with an aqueous solution, the network starts to swell due to the thermodynamic compatibility of the polymer chains and water. The swelling force is counterbalanced by the retractive force induced by the crosslinks of the network. Swelling equilibrium is reached when these two forces are equal.

The extent to which a gel can swell is limited by the presence of crosslinks. As can be expected, the swelling is decreased with increasing of the crosslinking component content. Generally, when crosslinker is added to hydrogel

systems, its molecules are placed between the chains of monomer. Then, the hydrophilic group's number is decreased and swelling ratio is decreased.

The swelling study was conducted on the hydrogels to observe the behaviour as functions of temperature of swelling medium, with the aim of LCST domain establishment as a function of the crosslinker content in the gel structure. Swelling degrees at equilibrium of four selected samples of hydrogels are plotted against temperature of the swelling medium in Fig 1.

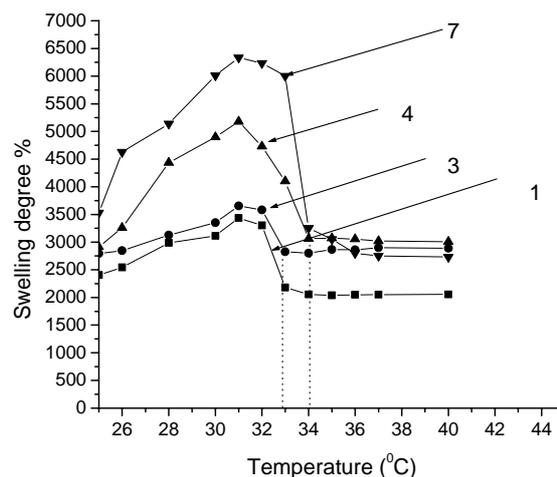


Fig. 1. Swelling degree dependence of the medium temperature of the PAAm hydrogel prepared with different Bis content (samples 1,3,4 and 7 in Table 1).

The polymers can be defined as a hydrogel, because they swell higher than 20% of their mass [20]. The hydrogels show similar swelling behavior in all cases. The swelling curves are similar in shape but differ in size and position.

As can be seen from Fig. 1, swelling capability expressed by the equilibrium value of swelling of the hydrogels increases by temperature until about 31 – 33 °C, when it manifests an abrupt decrease defined as the transition temperature, known as the LCST (the low critical solution temperature). It is clear from this figure that the hydrogel is in the swollen state below 31 - 33 °C. Then, swelling ratio decreases upon increasing the temperature when the hydrogel transforms into a compact – shrunked state above this domain. The swelling ratio of the gel is independent of the temperature above 31 - 33 °C. These results indicate that the collapsed state of the gel is uniquely defined by a swelling ratio of the gel. In contrast, the swollen state of the gel involves many states that correspond to the various swelling ratios of the gel.

The phase transition from the swelling to shrinking state of macromolecules is marked by a discrete weight collapse, too.

Another observation is the swelling of the hydrogels depends on the crosslinker content. The hydrogels produced with lower Bis concentration (samples 4 – 8 in Table 1) exhibited higher both swelling capability and the equilibrium degree of swelling. The LCST domain is also

displaced with 2-3 °C (from 31 °C for sample 1 with higher content of Bis in the study to 33,5 °C for sample 7).

3.3. Thermal behavior of the hydrogels

Table 2 presents some values for thermal characteristics obtained by DSC and DTG analyses of the synthesized hydrogels.

Table 2. Thermal characteristics of the synthesized hydrogels.

Sample	T _g ² (°C)	T _i ³ (°C)	T _{max} ⁴ (°C)	T _f ⁵ (°C)	E _a ⁶ (kJ/mol)
PAAm ¹	179	-	-	-	-
1	188	280	348	417	98
2	190	277	321	415	97.3
3	191	275	330	412	92.8
4	191	273	323	410	78.7
5	191	267	320	402	77.7
6	191	262	318	397	73.5
7	190	256	315	394	68.6
8	190	248	312	394	66.8

¹ PAAm - poly(acrylamide) witness sample

² T_g – glass transition temperature

³ T_i – initial oxidative decomposition temperature

⁴ T_{max} – temperature for maximum weight loss

⁵ T_f – final temperature of the thermal decomposition

⁶ E_a – activation energy

T_g as a characteristic for amorphous phase of poly(acrylamide) dried gels is evidenced in the DSC thermograms shown in Fig. 2.

DSC thermograms were obtained after keeping hydrogels for two weeks in a vacuum oven until constant weights have achieved. Poly(acrylamide) hydrogels containing different content of N, N'-methylenebis(acrylamide) (samples 1–8 in Table 1) have glass transition temperature higher than poly(acrylamide) polymer as a witness sample.

Close observation of DSC thermograms in Fig. 2, indicates the occurrence of endothermic transitions around 179 °C for witness sample – PAAm – and in the temperature range 190 - 191 °C for the crosslinked copolymers AAm – Bis (1, 3, 4 and 7), respectively.

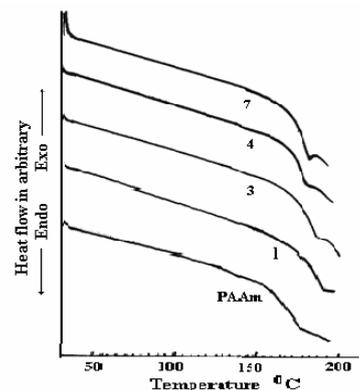


Fig. 2. DSC thermograms of the crosslinked poly(acrylamide) hydrogels.

The increase of T_g indicates the crosslinked nature of polymers as a result of the functional groups in the chemical structure of N, N'-methylenebisacrylamide. This increase is about 7 % comparable with poly(acrylamide), but there are very close values (190 - 191 °C) for the eight synthesized hydrogels, as the differences in their crosslinker content are low.

The TGA analysis underlines the thermo-oxidative behaviour of the synthesized hydrogels. It was investigated the modification of activation energy E_a during the thermal degradation process. By plotting E_a as a function of decomposition conversion degree – x – (ratio of the weight loss at time “t” and at the end of the process), in Figure 3 it is emphasized the decrease of E_a for the studied AAm/Bis molar ratios (samples 1, 4 and 7 in Table 1) used in the synthesis of hydrogels.

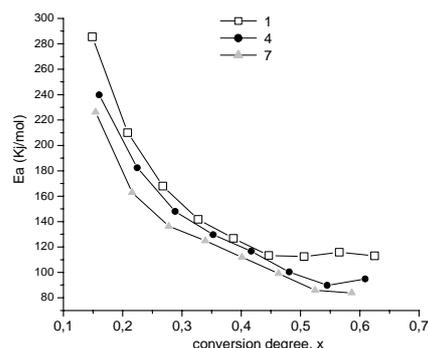


Fig. 3. E_a vs. decomposition conversion degree for the hydrogels (1,4 and 7 in Table 1).

Thus, for a lower AAm/Bis molar ratio of 8.5 / 9.1 x 10² (sample 1 in Table 1) it is necessary a greater gradient of activation energy to induce decomposition, comparatively with sample 7, for example.

Taking into account the content of acrylamide (AAm) and of N, N'-methylenebis(acrylamide) (Bis) as crosslinker in the total amount of monomers, respectively, in Fig. 4 there is plotted the variation of the decomposition

activation energy for the hydrogels with the monomers' feed composition.

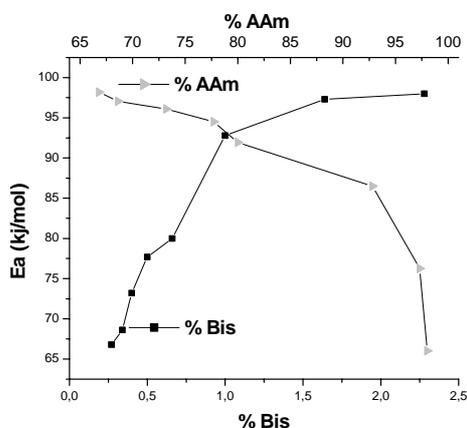


Fig. 4. E_a vs. feed composition in hydrogel synthesis (in Table 1).

It is observed the increase of E_a with the content in Bis in the hydrogel chemical structure, at the same time with a symmetrical E_a decrease as a function of AAm amount.

4. Conclusions

The synthesis of poly(acrylamide) hydrogels crosslinked with different amounts of N, N'-methylenebis(acrylamide) by redox initiated copolymerization it was presented. The synthesized gels thermal characteristics as well their swelling behavior responding to temperature as an external stimulus, provide an unique opportunity to tailoring multifunctional materials for specific applications, as inner material for cold therapy packs.

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