The evaluation of temperature and pH influences on equilibrium swelling of poly(*N*-isopropylacrylamide-*co*-acrylic acid) hydrogels

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Abstract

Hydrogels are synthesized by the method of radical polymerization of monomers: *N*-isopropylacrylamide (NIPAM) and acrylic acid (AA). Characterization of poly(*N*-isopropylacrylamide-*co*-acrylic acid) hydrogels, p(NIPAM/AA), has been performed by Fourier transform infrared spectroscopy (FTIR), X-ray diffraction (XRD) and by determination of the swelling behaviour in aqueous solutions at different temperatures (25, 31 and 37 °C) and pH values (2.2, 4.5, 6 and 6.8). After lyophilisation in the solution at pH 6 and temperature of 25 °C, p(NIPAM/AA) hydrogels have rapidly reached equilibrium degree of swelling, α_e, in comparison to non-lyophilized samples. The mechanism of solvent transport within matrix in lyophilized samples corresponds to less Fickian diffusion, whereas Super case II diffusion is characteristic for non-lyophilized samples. p(NIPAM/AA) hydrogel with 1.5 mol% of ethylene glycol dimethacrylate (EGDM) at the temperature of 25 °C and pH 6.8, has reached the highest swelling equilibrium degree, $\alpha_e = 259.8$. The results of swelling studies have shown that p(NIPAM/AA) hydrogels can be classified as superabsorbent polymers (SAPs). For the evaluation of pH and temperature influences on synthesized hydrogels swelling, a full three-level experimental design has been used. Two-factor interaction model (2FI) is the most optimal model of a full three-level experimental design for representing the swelling equilibrium degree of p(NIPAM/AA) hydrogels as a function of investigated parameters, *i.e.,* temperature and pH.

Keywords: hydrogel, swelling, FTIR, XRD, experimental design.

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Hydrogels are three-dimensional hydrophilic networks connected by chemical or physical bonds that can absorb significant amounts of water or biological fluids (1.1 to 1000 g/$g_{xerogel}$) [1–3]. High degree of water enables a certain degree of flexibility of hydrogels, which is very similar to natural tissues [1,4].

Hydrogels sensitive to external stimuli react to changes in pH, temperature, ionic strength and electromagnetic radiation due to which drastic changes in their swelling degree appear [5]. Regarding the ionization of pendant groups, hydrogels can be classified into neutral and ionic (anionic, cationic and amphiphilic) [5,6]. Temperature-sensitive hydrogels swell or contract as a result of temperature change in the surrounding medium [7]. Characteristics of swelling and contracting of temperature-sensitive hydrogels can be significantly influenced by incorporation of hydrophilic or hydrophobic co-monomers [8]. Polymers with weak ionisable functional groups which can bond and release protons as a response to change in pH in the environment are called pH-sensitive polymers [9,10]. In these polymers, the change in environment pH generates electric charge along the chains among which electrostatic repulsion appears that causes the increase in hydrodynamic volume of polymers [10].

Temperature-sensitive poly(*N*-isopropylacrylamide), p(NIPAM), is one of preferable three-dimensional matrix for bio-medical applications especially for controlled drug delivery [11,12]. Incorporating a hydrophilic monomer like acrylic acid, AA, into the structure of the homopolymer p(NIPAM), hydrogels with higher degree of water absorption and lower critical solution temperature (LCST) are obtained. Furthermore, the LCST is close to the physiological body temperature [13,14].

In the available literature, p(NIPAM/AA) hydrogels are synthesized by emulsion polymerization [15], polymerization in solution, the radical one [16,17], and γ rays polymerization (source ^{60}Co) [18] using *N,N'*-methylene-bis(acrylamide) (BIS) as a cross-linker.

The p(NIPAM/AA) copolymer has been chosen due to its sensitivity to pH and temperature changes in the surrounding medium, which enables its use in drug delivery [19,20], adsorption of heavy metals from sol-

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utions [15] as well as concentration of solutions with different compounds (lignin, polyethylene oxide, blue dextran) etc. [16,17].

The content of AA co-monomer has a significant influence on swelling characteristics of p(NIPAM/AA) [21]. Equilibrium swelling degrees in water of the synthesized copolymer hydrogels with 10 mol% AA in the work of Champ *et al.* [16] range from 16 to 64, whereas in the work of Pei *et al*. [18] the copolymer with 9.59 mol% AA has shown the swelling degree of about 28. According to the other authors' results [16,18], p(NIPAM/AA) copolymers with 10 mol% AA were applicable for potential use in the area of environmental protection and medicine.

Hydrogels based on NIPAM and AA contain weak ionisable groups, carboxyl (COOH) and amino (NH_2) and exhibit changes in chain conformation depending on the pH in the surrounding medium. At higher pH levels (above pK_a AA), carboxyl groups are ionized (COO^-) causing electrostatic repulsion and consequently the increase in the hydrogel swelling degree. At pH values lower than pK_a AA carboxyl groups are protonated (COOH) causing hydrogel contraction. Amino groups at lower pH values in the surrounding medium are protonated (NH_3^+) and the resulting electrostatic repulsive forces increase the network hydrophilicity and hydrogel swelling [11,22–24].

Superabsorbent polymers (SAPs) are weak cross-linked hydrogels which can absorb and retain large amounts of water, up to thousand times greater than their weight in dry state (1000 $g/g_{xerogel}$) [4,25]. The basic pre-condition for the application of hydrogels as superabsorbent materials is the existence of strong repulsive forces between functional groups of the same electric charge in the structure. Characteristics of these polymers are: super-high absorbing capacity, wide pH-independence and easy regeneration and re-use [3]. Hydrogels of high absorbing capacity can be synthesized by co-polymerization of AA with natural polymers (*e.g.*, gelatinized corn starch, carboxymethyl cellulose) [26,27] and synthetic monomers such as potassium acrylate (AK), NIPAM, sulfopropyl methacrylate potassium salt (SPN) [28,29]. SAPs are applied in the production of disposable diapers, pharmaceutical dosage forms, packages, water-swelling rubbers, fire-extinguishing gels, and soil conditioning and water storage in soil as well [30].

Response surface methodology (RSM) represents the group of mathematical and statistical models used for developing and determining dependences between the system responses (*Y*) and variables, *i.e.*, factors (*X*) [31]. In factorial design, the effect of all experimental variables, factors and interaction effects on the system response is being investigated [32]. The simplest experimental design in 3^k system is a full factorial design with two factors where each factor is on three levels [33].

The aim of this work is characterization of synthesized p(NIPAM/AA) hydrogels and investigation of the influences of pH and temperature on hydrogel swelling characteristics by response surface methodology.

EXPERIMENTAL

Material and methods

Monomer *N*-isopropylacrylamide (NIPAM), purity 99% (Acros Organics, New Jersey, USA); co-monomer acrylic acid (AA), purity 98% (Fluka, AG Buchs SG; Chemical Corp, CH); cross-linker ethylene glycol dimethacrylate (EGDM), purity 97% (Fluka, AG Buchs SG; Chemical Corp, CH) and initiator 2,2'-azobis(2--metylpropionitrile) (AZDN), purity 99% (Acros Organics, New Jersey, USA) have been used without further purification.

Aqueous media of different pH values have been prepared by adding hydrochloric acid (Zorka, Šabac, Serbia) or sodium hydroxide (Centrohem, Belgrade, Serbia) in distilled water.

Synthesis of hydrogels

Copolymer p(NIPAM/AA) hydrogels have been obtained by the method of radical polymerization of NIPAM with 10 mol% AA. EGDM has been used as a cross-linker with different molar content, 1.5, 2 and 3 mol% in relation to the amount of NIPAM. The reaction of polymerization has been initiated by adding 2.7 mol% AZDN.

Reaction mixture prepared by homogenization and dissolution of reagents in acetone (Centrohem, Belgrade, Serbia) has been injected into the glass tubes with 5 mm diameter being sealed afterwards. Polymerization has been thermally initiated in the following way: 0.5 h at 75 °C, 2 h at 80 °C and 0.5 h at 85 °C. The removal of unreacted amounts of reagents has been performed by immersion of hydrogels in 30 mL of methanol (Centrohem, Belgrade, Serbia) for 72 h. After rinsing, hydrogels have been dried to the constant mass in a drying oven for 3 h at 40 °C.

Lyophilisation of hydrogels p(NIPAM/AA) in swollen state has been performed in three phases on the device Freeze Dryers Rotational-Vacuum-Concentrator (GAMMA 1-16 ISC, Germany). In the first phase, the hydrogels have been frozen rapidly at –40 °C for 24 h. In the primary drying phase, the amount of the solution has been decreased by the method of sublimation at –30 °C and a pressure of 0.05 hPa for 12 h. In the secondary drying phase, *i.e.*, isothermal desorption, the hydrogels have been heated at 20 °C for 6 h and a pressure of 0.05 hPa, with the removal of the vapour from the drying chamber. Lyophilized hydrogels were packed under vacuum and stored in a refrigerator at 5 °C.

Fourier transform infrared spectroscopy (FTIR)

Hydrogels have been ground into powder on amalgamator (WIG-L-BVG, 31210-3A, USA). Thin transparent pastilles have been prepared from 150 mg of KBr (99%, Merck, Darmstadt, Germany) and 1 mg of p(NIPAM/AA) hydrogels or NIPAM monomer by vacuuming and pressing under the pressure of around 200 MPa. Co-monomer AA has been recorded in the shape of thin film between two plates of zinc selenide (ZnSe). FTIR spectra of samples have been recorded in the area of wavenumbers from 4000 to 400 cm^{-1} on Bomem Hartmann & Braun MB-series FTIR spectrophotometer and the obtained spectra have been analysed using the Win-Bomem Easy software.

X-ray diffraction (XRD)

The samples have been ground into powder and investigated on an automatic diffractometer for powder Phillips PW1030 with monochromatic CuK$_\alpha$ radiation of wavelength λ = 0.154178 nm. Operating voltage of the device has been 40 kV, and the electric current has been 20 mA. Recording of samples has been performed in the range of 3–48° with 0.05° step and time of recording, τ = 5 s.

Swelling behavior

Hydrogels in dried state (xerogels) and after lyophilisation have been immersed into solutions at certain pH values and temperature and the process of swelling has been monitored gravimetrically. The samples have been retrieved from the solution and the surplus from their surface has been removed, and afterwards the mass has been measured in certain periods of time until the equilibrium has been reached i.e. the constant mass. The swelling degree, α, has been calculated according to the following equation:

$$\alpha = \frac{m - m_0}{m_0} \tag{1}$$

where m_0 is the mass of the dry samples, and m is the mass of swollen hydrogels in the moment of time t.

Xerogels swelling has been monitored at different pH values (2.2, 4.5, 6 and 6.8) and different temperatures (25, 31 and 37 °C) with the aim of investigating the pH and temperature sensitivity of p(NIPAM/AA) hydrogels. The ability of hydrogels for contraction has been investigated at the temperature range of 20–80 °C. The hydrogels swelling after lyophilisation has been monitored in the solution of pH 6 at 25 °C.

Certain pH values of solutions have been adjusted by using hydrochloric acid and sodium hydroxide determined using digital pH-meter (HI9318-HI9219, Hanna, Portugal). The influence of temperature on the p(NIPAM/AA) hydrogels swelling characteristics has been investigated in water bath (Sutjeska, Belgrade, Serbia). Accuracies of weight, temperature and pH measurements have been with 5, 2 and 2 decimal places, respectively.

Experimental design

For modelling the process of p(NIPAM/AA) hydrogels swelling the full three-level factorial design has been applied.

In the 3^k design system, when the factor k is quantitative, the levels are signed by coded values, –1 (lower level), 0 (intermediate level) and 1 (higher level).

There has to be an equal distance between coded levels [33]. The full factorial design has enabled investigating combinations of factors, at all levels, and therefore the evaluation of the influence of factors [34].

Factors and levels applied in the three-level factorial design are given in Table 1. The system response is the equilibrium swelling degree, α_e, of p(NIPAM/AA) copolymer hydrogels.

Table 1. Factors and levels for full three-level factorial design

Factor	Level values	
	Coded	Actual
$X_1 - t$ / °C	–1	25
	0	31
	1	37
X_2 – pH	–1	2.2
	0	4.5
	1	6.8

Selection and evaluation of model adequacy and statistically significant factors in the model have been performed by ANOVA test. Factors and interactions, which values of probability levels (p) were lower than 0.05, have been considered to be statistically significant members. Experimental data have been analysed by using Design-Expert software, version 7.0.0 (stat-Ease Inc., Minnesota, USA).

RESULTS AND DISCUSSION

FTIR spectra of NIPAM and AA monomers and synthesized p(NIPAM/AA) copolymer, sample 90/10/1.5, are shown in Figure 1. In sample designation, the first number represents mol% of NIPAM, the second number is mol% of AA, and the third one is mol% of EGDM cross-linker.

In FTIR spectrum of NIPAM monomer (Figure 1A), there has been an absorption band of strong intensity with maximum at 3297 cm^{-1} which has been the result of N–H valence vibrations of the secondary amino group, ν(N–H) [35]. In the area of wavenumbers above

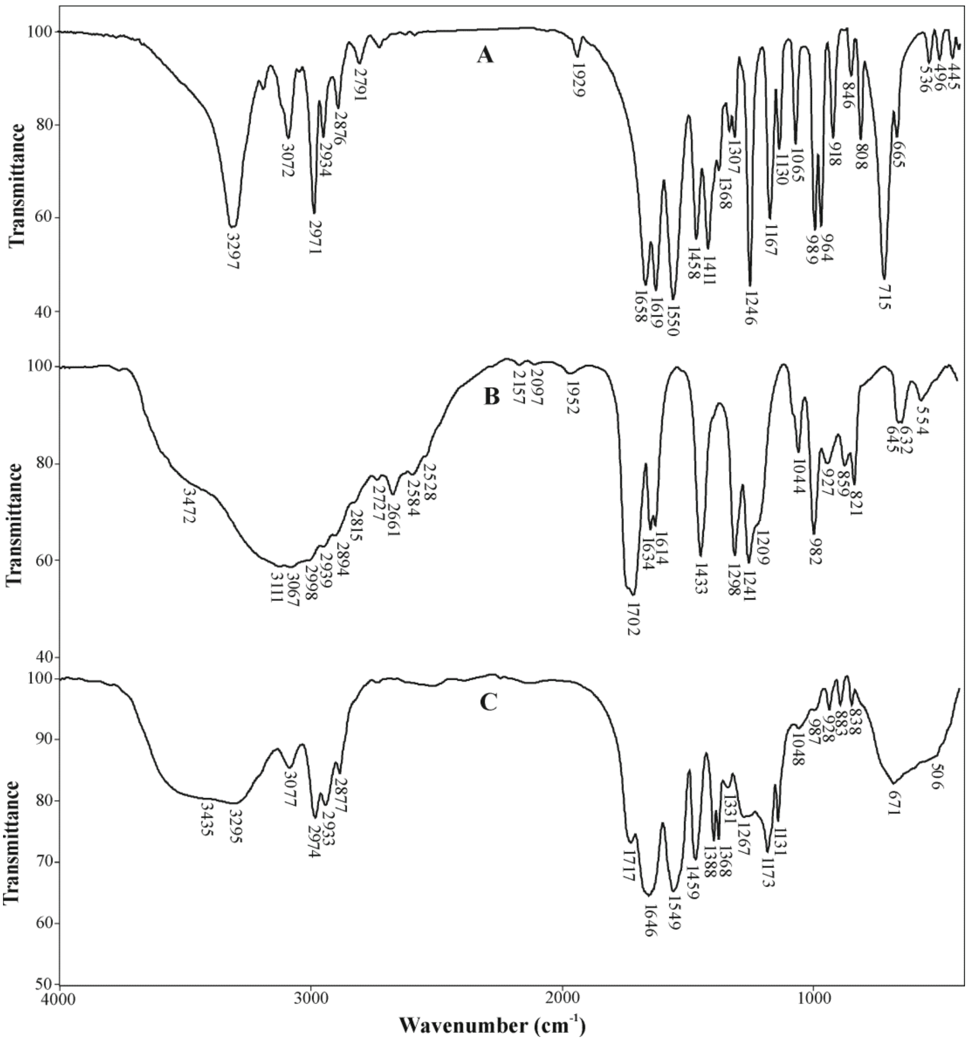

Figure 1. FTIR spectra of NIPAM (A), AA (B) and p(NIPAM/AA), sample 90/10/1.5 (C).

3000 cm^{-1}, the characteristic absorption band has been at 3072 cm^{-1} which has been assigned to asymmetric valence vibrations of C–H bond from the vinyl group ($CH=CH_2$), ν_{as}(=C–H). Asymmetric and symmetric valence vibrations of C–H bond from methyl groups have given the bands with maxima at 2971 and 2876 cm^{-1}, respectively. The result of the amide group vibrating in the structure of NIPAM is absorption band of strong intensity at 1658 (amide band I) and 1550 cm^{-1} (amide band II), which is in accordance with literature data of other authors [36]. Absorption bands of strong intensity with maximum at 1619 cm^{-1} in FTIR spectrum of monomer (Figure 1A) has been assigned to valence vibrations of double bonds, ν(C=C) [37]. In FTIR spectrum of NIPAM only one absorption band has been observed from deformation vibrations of C–H bonds from isopropyl group, $CH(CH_3)_2$, at 1368 cm^{-1}.

In other studies, an absorption band from valence OH vibrations of AA, ν(OH), has appeared in the area of wavenumbers from 3200-2500 cm^{-1} [38], whereas on FTIR spectrum of AA obtained in this work (Figure 1B) there has been an absorption band in the area of wavenumbers 3600–2400 cm^{-1}. Absorption bands of strong intensity with maxima at 3111 and 3067 cm^{-1} have been the result of valence vibrations of vinyl group, ν(=C–H). Asymmetric valence vibrations of CH_2 group have produced the absorption band with maximum at 2939 cm^{-1}, ν_{as}(C–H), whereas valence vibrations of methine group (C–H), ν(C–H), have produced an absorption band with maximum at 2894 cm^{-1}. Absorption bands in the area of wavenumbers 1710–1690 cm^{-1} in aliphatic carboxyl acids have been assigned to valence vibrations of C=O groups, ν(C=O) [39], and in Figure 1B in this area, there has been an absorption band of strong intensity with maximum at 1702 cm^{-1}. Absorption bands with maxima at 1634 and 1614 cm^{-1} have been the results of C=C bond vibrations in the AA structure.

In the FTIR spectrum of synthesized p(NIPAM/AA) copolymer with 1.5 mol% EGDM (Figure 1C), the absence and shifts of certain absorption bands by NIPAM and AA have been observed. Absorption band arising from valence OH vibrations, ν(OH), in the FTIR spectrum of copolymer (Figure 1C) has been shifted towards higher wavenumbers (3700–3100 cm^{-1}) in comparison to the same band in FTIR spectrum of AA (Figure 1B). Absorption band with maximum at 3077 cm^{-1} has represented valence vibrations of C–H bond of the vinyl group of AA and NIPAM [40]. In FTIR spectrum of p(NIPAM/AA) copolymer, the existence of absorption band at 1717 cm^{-1} has been observed as a result of C=O group vibrations of AA. The centroid of this band has been shifted towards higher wavenumbers for 15 units in comparison to the same band in the FTIR spectrum of AA (Figure 1B). The listed shifts of absorption bands from AA indicate that both OH and C=O groups can participate in building of hydrogen bonds in p(NIPAM/AA) copolymer. In the FTIR spectrum of copolymer (Figure 1C), there have been absorption bands from NIPAM at 3295 and 1646 cm^{-1} (amide band I) with shifts of 2 and 12 units towards lower wavenumbers in comparison to the same bands in the FTIR spectrum of NIPAM (Figure 1A), respectively. The results of FTIR analysis have shown that intramolecular hydrogen bonds in p(NIPAM/AA) copolymer were probably accomplished through OH and C=O groups of AA and C=O and N–H groups of NIPAM.

The reaction of polymerization has been performed by breaking the double C=C bonds, which has been shown by the absence of bands from valence C=C bonds, ν(C=C), and deformation vibrations in the plane of the vinyl group, δ(=C–H), of monomers.

XRD difractogram of the powder copolymer based on NIPAM and AA, sample 90/10/1.5, is shown in Figure 2.

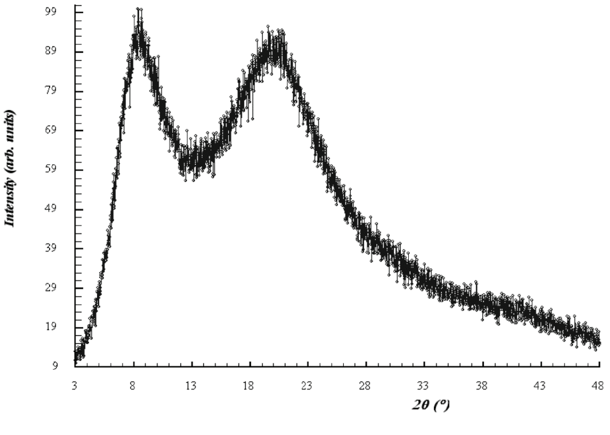

Figure 2. XRD difractogram of p(NIPAM/AA) copolymer, sample 90/10/1.5.

In the XRD difractogram of synthesized p(NIPAM/AA) copolymer, there have been two wide diffraction peaks, secondary at $2\theta = 8.39°$ and fundamental at $2\theta = 19.50°$. Wide diffraction peaks do not have clearly defined reflections and show the lower degree of crystallinity [41], *i.e.*, p(NIPAM/AA) copolymer possesses semi-crystalline structure. Difractogram of p(NIPAM/AA) copolymer in Figure 2 shows considerable similarity with difractogram of p(NIPAM) homopolymer obtained in the works of other authors [41,42].

The process of swelling can be described by three phases: diffusion of water molecules through the matrix, relaxation of polymer chains by hydration and swelling of polymer matrix after the relaxation [43,44].

Water molecules in contact with hydrogel in dried state (xerogel) penetrate into the polymer matrix and hydrate polar hydrophilic groups ("primarily bonded water"). After the hydration, the gel swells leading to the interaction of water molecules with hydrophobic nonpolar groups ("secondary bonded water"). The force of osmotic pressure of the solvent enables further penetration of water molecules into the matrix, which leads to expansion of polymer chains. Hydrogel reaches equilibrium swelling when the forces of osmotic pressure become equal to the elastic force which tends to return the stretched chains into the initial position (elastic retractive forces) [45].

By using the Eq. (2), the mechanism of diffusion of solvent into the hydrogel can be determined (valid for the condition $M_t/M_e \le 0.6$) [46,47]:

$$F = \frac{M_t}{M_e} = kt^n \tag{2}$$

where F is a fractional sorption, M_t the mass of the absorbed solvent at the time t, M_e the mass of the absorbed solvent in the equilibrium state, k constant which is characteristic for a certain type of polymer network and n diffusion exponent.

The swelling of series of p(NIPAM/AA) hydrogels before and after lyophilisation has been monitored in the solution with pH 6 at 25 °C for 72 h, and the results are shown in Figure 3.

By comparative analysis of the obtained graphics in Figure 3, it has been observed that p(NIPAM/AA) copolymers after lyophilisation reached lower equilibrium swelling degree, α_e, (Fig. 3B) in comparison to copolymers which were not subjected to lyophilisation (Fig. 3A). Swelling degree of lyophilized p(NIPAM/AA) hydrogels is in the given interval of 240 min significantly higher than in non-lyophilized samples. Lower value of equilibrium swelling degree of lyophilized p(NIPAM/AA) hydrogels could be the consequence of the repeated second cycle of swelling where polymer network has already reached equilibrium and after lyophilization polymer chains have become less flexible [17]. Lyophilised hydrogels in swollen state significantly more rapidly absorbed the solution, which can be explained by the fact that greater pore size enables better penetration of solution molecules within the polymer matrix. The cross-linking degree also influenced the process

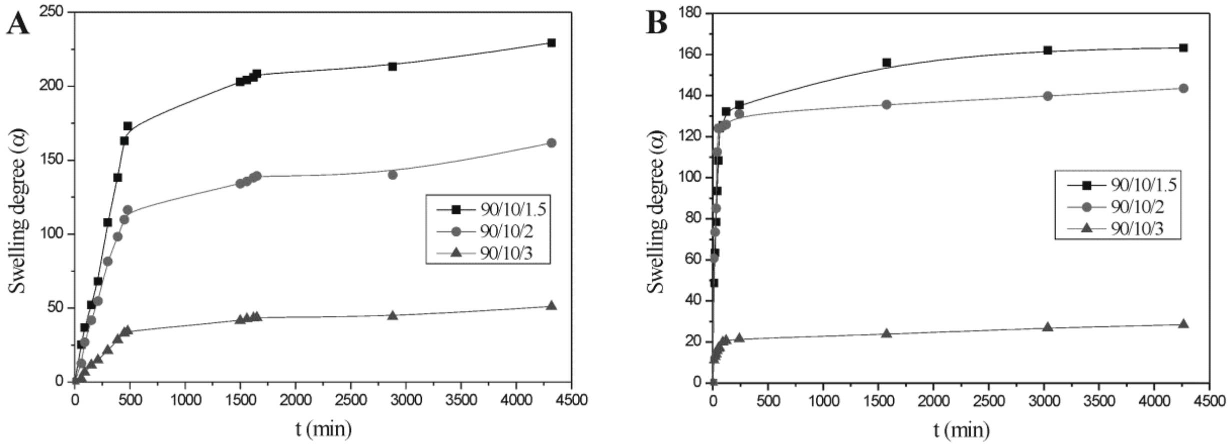

Figure 3. Dependence of the swelling degree, α, of the series of p(NIPAM/AA) hydrogels on time before (A) and after lyophilisation (B) at pH 6 and 25 ℃.

of swelling and with the increase in the amount of the cross-linker EGDM, the swelling degree of hydrogels (α) before and after lyophilisation has decreased (Fig. 3). The highest equilibrium swelling degree at pH 6 of the solution has been obtained for non-lyophilised p(NIPAM/AA) hydrogel with 1.5 mol% EDGM, α_e = = 229.4, which was even 8 times greater than the swelling degree of p(NIPAM/AA) hydrogels in the solution with pH 6 obtained in the work of Pei *et al.* [18].

The results of swelling in the solution of pH 6 and at 25 °C (Fig. 3) have shown that synthesized p(NIPAM/AA) hydrogels in this work can be classified as superabsorbent polymers [4,25].

Values of kinetic parameters (*n* and *k*) obtained by using Eq. (2) for the swelling process of p(NIPAM/AA) hydrogels are presented in Table 2.

Values of diffusion exponent for non-lyophilised p(NIPAM/AA) hydrogels with 2 and 3 mol% EDGM are higher than 1 (Table 2) and mechanism of transport of the solvent within the matrix corresponds to Super case II diffusion, and relaxation of the polymer chains controls the process of swelling [48,49]. The hydrogel 90/10/1.5 before lyophilisation has been characterized by non-Fickian diffusion, the so-called anomalous type of diffusion ($0.5 < n < 1$), where the degree of relaxation of polymer chains is comparable to the degree of diffusion [49,50]. In lyophilised samples of p(NIPAM/AA) hydrogel, *n* is <0.5, which indicates that degree of water penetration into the polymer matrix has been significantly lower in comparison to the degree of relaxation of polymer chains (less Fickian diffusion) [51,52].

Changes in the swelling degree of p(NIPAM/AA) hydrogels with an increase of temperature from 20 to 80 °C in the solution of pH 6.0 are shown in Figure 4.

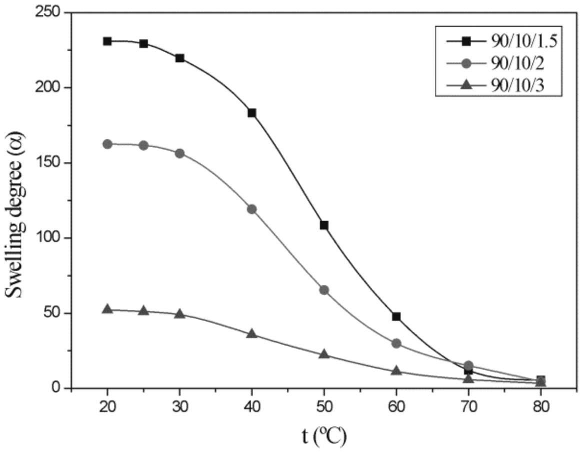

Figure 4. Dependence of the swelling degree, α, for p(NIPAM/AA) hydrogels on temperature.

Temperature sensitivity, *i.e.*, decreasing of the swelling degree with the increase of temperature is observed in p(NIPAM/AA) copolymers (Fig. 4). Sharp decreasing of swelling degree of hydrogels has appeared at 30–60 °C, which classified them into negative temperature-sensitive ones which have lower critical solution temperature (LCST). With the increase in the ionization degree of AA, which has been caused by the change in pH of the environment, the temperature of the phase

Table 2. Kinetic parameters of swelling of p(NIPAM/AA) hydrogels before and after lyophilisation in the solution with pH 6 and at 25 ℃

Hydrogel p(NIPAM/AA)	Before lyophilization			After lyophilization		
	n	k / 10^{-3} min^{-n}	R^2	*n*	k / min^{-n}	R^2
90/10/1.5	0.856	3.296	0.983	0.464	0.100	0.982
90/10/2	1.097	1.007	0.963	0.303	0.210	0.989
90/10/3	1.219	0.424	0.950	0.256	0.215	0.975

transition of p(NIPAM/AA) copolymer was reported to increase [53].

Matrix of the full two-factor three-level experimental design with the obtained results of responses is shown in Table 3.

Table 3. Matrix of the full factorial design with experimental values of the responses

No. of exp.	X_1 t / °C	X_2 pH	Y_{exp} (α_e) 90/10/1.5	90/10/2	90/10/3
1	25	2.2	8.3	8.1	7.9
2	31	2.2	7.9	7.4	7.0
3	37	2.2	2.5	2.3	1.8
4	25	4.5	19.0	16.7	14.8
5	31	4.5	18.7	16.1	13.9
6	37	4.5	15.9	10.2	8.3
7	25	6.8	259.8	175.3	55.0
8	31	6.8	246.6	167.3	49.7
9	37	6.8	31.0	22.3	8.5

From Table 3, it has been observed that the highest equilibrium swelling degree has been shown by p(NIPAM/AA) hydrogel with 1.5 mol% EGDM at pH 6.8 of the solution at room temperature, $\alpha_e = 259.8$.

Two-factor interaction (2FI) model is better and more acceptable in comparison to linear and quadratic model for representing the influence of temperature and values of pH of the solution on equilibrium swelling degree of p(NIPAM/AA) copolymer hydrogels.

Linear interactive, *i.e.*, factorial model of experimental design with two factors has been represented by:

$$Y = \beta_0 + \beta_1 X_1 + \beta_2 X_2 + \beta_{12} X_1 X_2 \qquad (3)$$

where X_1 and X_2 represent factors, Y is the system response, β is the regression coefficient (β_0 is a constant, β_1 and β_2 are linear regression coefficients, β_{12} is the regression coefficient of inter-factorial effects) [54].

Results of analysis of variance (ANOVA) for 2FI model of equilibrium swelling of p(NIPAM/AA) hydrogel, sample 90/10/3 are shown in Table 4.

2FI model obtained for p(NIPAM/AA) hydrogel, sample 90/10/3, has been statistically significant (Table 4), whereas for p(NIPAM/AA) hydrogels with 1.5 and 2 mol% EGDM the model has not been significant, but it can be used for investigation of the dependency between independent variables and system responses. The values of coefficient of determination (R^2) and adjusted coefficient of determination (adj. R^2) for p(NIPAM/AA) hydrogel with 3 mol% EGDM are 0.83 and 0.73, respectively.

Statistically significant members (factors and interactions) have had p values lower than 0.05 and for 2FI model at p(NIPAM/AA) hydrogel, sample 90/10/3, it has been the pH value of the solution (X_2), p = 0.0120 (Table 4). For samples of p(NIPAM/AA) hydrogels with 1.5 and 2 mol% EGDM, pH value has also been a statistically significant factor. It is evident that there is an influence of temperature on equilibrium swelling degree of p(NIPAM/AA) hydrogel with 3 mol% EGDM (Table 3), but in suggested model temperature (X_1) is not a statistically significant factor, p = 0.0650 (Table 4).

Table 4. The results of analysis of variance 2FI model for equilibrium swelling of p(NIPAM/AA) hydrogel, sample 90/10/3

Source	Sum of squares	*df*	Mean square	*F* Value	*p* Value *Prob > F*
Model	2545.05	3	848.35	8.08	0.0231 (significant)
X_1	583.12	1	583.12	5.56	0.0650
X_2	1554.29	1	1554.29	14.81	0.0120
X_1X_2	407.64	1	407.64	3.88	0.1058
Residual	524.78	5	104.96	–	–
Cor Total	3069.83	8	–	–	–

Final equations of the factorial model for equilibrium swelling of p(NIPAM/AA) hydrogels with 1.5, 2 and 3 mol% EGDM as a function of temperature and pH in the form of coded factors are given by Eqs. (4)–(6), respectively:

$$Y = 67.76 - 39.64X_1 + 86.46X_2 - 55.77X_1X_2 \qquad (4)$$

$$Y = 47.32 - 27.54X_1 + 57.86X_2 - 36.80X_1X_2 \qquad (5)$$

$$Y = 18.56 - 9.86X_1 + 16.09X_2 - 10.09X_1X_2 \qquad (6)$$

Equations with coded values have been used for determination of the variables effects on the system response, and the positive sign before certain variable has shown synergistic effect, whereas the negative one has shown antagonistic effect [55,56]. Response surface plots for hydrogels samples, 90/10/1.5, 90/10/2 and 90/10/3, are shown in Figure 5.

From Figure 5 and equations with coded values, it has been observed that pH values have the most significant influence on the equilibrium swelling degree of the series of p(NIPAM/AA) hydrogels. The increase of pH values from 2.2 to 6.8 results in a significant increase of equilibrium swelling degree of hydrogels. This obtained result has been explained by the fact that at higher pH values, electrostatic repulsion appears between dissociated carboxyl groups of AA (COO^-), which causes the swelling of polymer network and higher absorption of the surrounding medium [21]. By the increase of temperature in the investigated range, the equilibrium swelling degree of p(NIPAM/AA) hydrogel has decreased (Eqs. (4)–(6)) which once again has confirmed the fact that hydrogels are negatively temperature-sensitive.

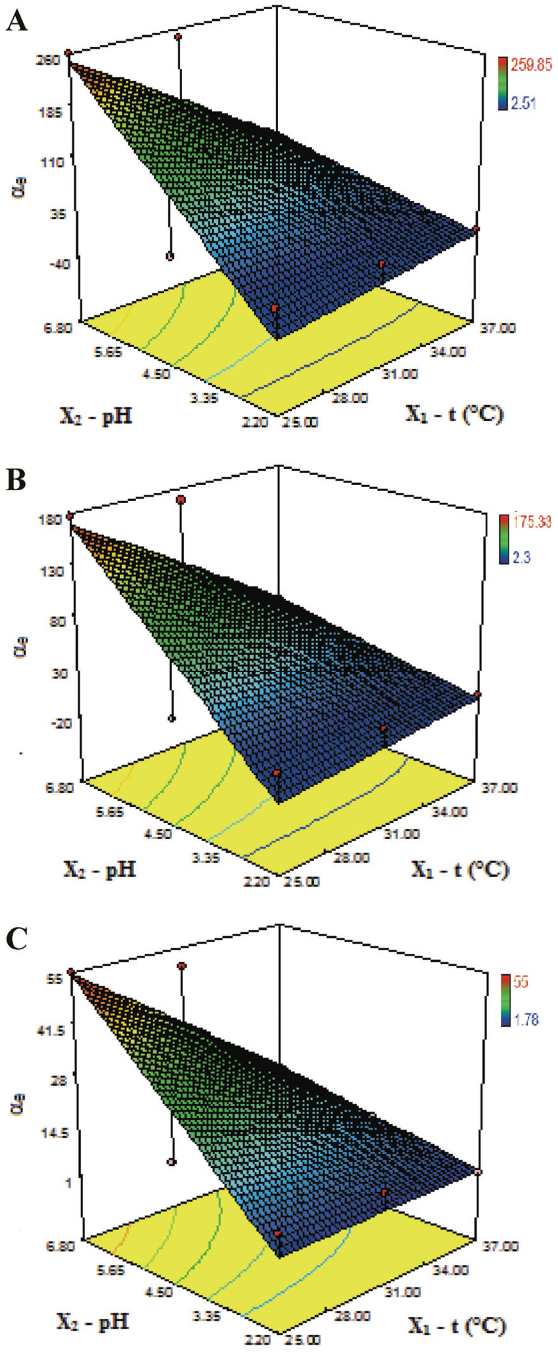

Figure 5. Response surface plot for equilibrium swelling of p(NIPAM/AA) hydrogels as a function of pH and temperature of the medium for samples: 90/10/1.5 (A), 90/10/2 (B) and 90/10/3 (C).

When coded values have been replaced by the actual ones, Eqs. (7)–(9) have been obtained for factorial model of equilibrium swelling degree of the samples of p(NIPAM/AA) hydrogels, 90/10/1.5, 90/10/2 and 90/10/3, respectively.

$$\alpha_e = -460.31 + 11.58t + 162.68\text{pH} - 4.04t\,\text{pH} \tag{7}$$

$$\alpha_e = -295.58 + 7.41t + 107.82\text{pH} - 2.67t\,\text{pH} \tag{8}$$

$$\alpha_e = -64.04 + 1.65t + 29.67\text{pH} - 0.73t\,\text{pH} \tag{9}$$

For the plan of the experiment shown in this work, the most acceptable model for describing the equilibrium swelling of p(NIPAM/AA) hydrogels as a function of two factors, temperature and pH of the solution, is 2FI model. Perhaps with the aim of obtaining even better model, a different plan of the experiment should be adopted, *i.e.*, another type of experimental design should be applied.

CONCLUSION

The results of FTIR analysis have shown that the reaction of polymerization has been carried out by breaking the double bonds, C=C, of monomers and that intramolecular hydrogen bonds in p(NIPAM/AA) copolymer have been probably accomplished through OH and NH groups (proton donor) and C=O groups (proton acceptor) of the monomers. On the basis of XRD diffractogram, it has been concluded that p(NIPAM/AA) copolymer does not possess arranged crystal, but semicrystalline structure. p(NIPAM/AA) copolymers after lyophilisation reach lower equilibrium swelling degree in solution at pH 6 and 25 °C, but in a shorter period of time in comparison to non-lyophilised samples. The swelling of non-lyophilised hydrogels at pH 6 has been controlled by relaxation of polymer chains (Super case II diffusion), whereas in lyophilised samples has been opposite, the swelling has been controlled by the process of diffusion (less Fickian diffusion). Temperature and pH of the environment had the influence on hydrogel swelling, so the highest equilibrium swelling degree has been reached in p(NIPAM/AA) copolymer with 1.5 mol% EGDM in the solution at pH 6.8 and 25 °C, α_e = 259.8. Synthesized hydrogels in this work can be characterized as superabsorbent materials, because they have equilibrium swelling degree higher than 100. In the three-level experimental design, 2FI model has been the most acceptable for describing the dependence of the equilibrium swelling degree on pH and temperature of the surrounding medium. In the suggested model the statistically significant factor, the value of pH, has the highest effect on equilibrium swelling of p(NIPAM/AA) hydrogels.

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IZVOD

EVALUACIJA I OPTIMIZACIJA UTICAJA TEMPERATURE I pH NA RAVNOTEŽNO BUBRENJE HIDROGELOVA POLI(*N*-IZOPROPILAKRILAMID-*KO*-AKRILNA KISELINA)

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(Naučni rad)

Hidrogelovi su sintetisani postupkom radikalne polimerizacije monomera *N*-izopropilakrilamida (NIPAM-a) sa 10 mol% akrilne kiseline (AA) i uz korišćenje umreživača etilenglikoldimetakrilata (EGDM-a) sa različitim molskim sadržajem (1,5, 2 i 3 mol%). Karakterizacija hidrogelova poli(*N*-izopropilakrilamid-*ko*-akrilna kiselina), p(NIPAM/AA), je izvršena infracrvenom spektrofotometrijom sa Furije-ovom transformacijom (FTIR), difrakcijom X-zraka (XRD) i određivanjem ponašanja bubrenja u vodenim rastvorima različitih temperatura (25, 31 i 37 °C) i pH vrednosti (2,2, 4,5, 6 i 6,8). Hidrogelovi p(NIPAM/AA) nakon liofilizacije u rastvoru pH 6 i temperature 25 °C brže dostižu ravnotežne stepene bubrenja, α_e, u poređenju sa ne-liofilizovanim uzorcima. Mehanizam transporta rastvarača unutar matrice kod liofilizovanih uzoraka odgovara manje Fikovoj difuziji, proces bubrenja kontroliše difuzija rastvarača u polimernu matricu. Za ne-liofilizovane uzorke je relaksacija polimernih lanaca ograničavajući faktor prilikom transporta rastvarača unutar hidrogelova ("Super case II" difuzija), izuzev u slučaju kopolimera sa 1,5 mol% EGDM kod koga se javlja anomalni tip difuzije, difuzija i relaksacija polimernih lanaca kontrolišu proces bubrenja. Sintetisani hidrogelovi p(NIPAM/AA) pokazuju pH i temperaturnu osetljivost i svrstavaju se u negativno termoosetljive hidrogelove, sa donjom kritičnom temperaturom rastvora (LCST) ispod koje polimer bubri, a iznad koje se kontrahuje. Pored pH i temperature na stepen bubrenja hidrogelova p(NIPAM/AA) ima uticaj i stepen umreženja, i sa porastom količine umreživača EGDM opada ravnotežni stepen bubrenja. Najveći ravnotežni stepen bubrenja dostiže hidrogel p(NIPAM/AA) sa 1,5 mol% EGDM pri temperaturi 25 °C i pH 6,8, α_e = 259,8. Rezultati bubrenja ukazuju da se hidrogelovi p(NIPAM/AA) mogu klasifikovati kao superapsorbujući polimeri (SAPs). Za procenu uticaja pH i temperature rastvora na bubrenje sintetisanih hidrogelova korišćen je puni eksperimentalni dizajn sa tri nivoa. Najoptimalniji model punog eksperimentalnog dizajna sa tri nivoa za reprezentovanje ravnotežnog stepena bubrenja hidrogelova p(NIPAM/AA) u funkciji faktora, t i pH, je dvo-faktorsko interakcioni model (2FI). Prema modelu pH vrednost je i statistički značajan član (p < 0,05) i ima najveći efekat na ravnotežno bubrenje hidrogelova p(NIPAM/AA). Na osnovu jednačina sa kodiranim vrednostima i dijagramima površine odgovora vidi se da pH rastvora ima sinergistički efekat na ravnotežno bubrenje hidrogelova p(NIPAM/AA), dok temperatura antagonistički efekat.

Ključne reči: Hidrogel • Bubrenje • FTIR • XRD • Eksperimentalni dizajn