

Interaction parameters and volume phase transition of poly(N-isopropylacrylamide-co-N-tertiarybutylacrylamide-co-acrylamide) hydrogels

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In the present study, poly (NIPAM-co-NTBA-co-AAm) terpolymeric hydrogels have been fabricated with different crosslinking ratios. The average molecular mass between crosslinks (M_c), interaction parameter (χ) and crosslinking density of the hydrogels have been determined from stress-strain measurement. The crosslink density of the network increased with an increase in the crosslinking ratio followed by decreases in the value of M_c . The enthalpic interaction parameter (χ_H) was negative whereas larger entropic interaction parameter (χ_S) was found to be positive and responsible for overall increase in total interaction parameter (χ) with temperature. Partial molar enthalpy of dilution (ΔH_1) and partial molar entropy of dilution (ΔS_1) values are found to be negative which are supportive with hydration of gel with hydrogen bonding as well as hydrophobic interaction.

Keywords: NIPAM, Compression modulus, Crosslink density, Interaction parameter, Volume transition

INTRODUCTION

Poly N-isopropylacrylamide (PNIPAM)-based thermoresponsive hydrogels are found to have many applications including biomedical applications such as controlled drug delivery systems, artificial implants, dialysis membrane, burn dressings and cardiovascular devices [1-5]. Since all of these applications primarily depend on swelling capacities of the hydrogels, the fundamental understanding of swelling properties of the hydrogels with water is extremely important [6-10]. The swelling behavior of the hydrogels has been often described not only by equilibrium swelling but also depending on several factors like crosslinking density, network parameter, temperature, and the physical structure of the gels [11-15]. Also, such types of applications need perfect volume phase transition and sharpness.

The total swelling pressure of the non-ionic hydrogels is contributed by mixing polymer and solvent, as well as elasticity. The hydrogels attain the swelling equilibrium at zero osmotic pressure of the hydrogels [16]. The swelling pressure can be determined by the monomer or comonomer type and the effective crosslink density. The effective number of crosslinks consists of both chemical and physical crosslinks playing an important role in controlling the swelling, as well as mechanical behavior of the hydrogels. The physical crosslinking comprises of entanglements of chain, loose chain ends and tied chains [17]. However, due to moisture sensitivity the evaluation of crosslinking density is very tough *via*

instruments like dynamic mechanical analyzer (DMA) and rheology [18].

The volume phase transition of the hydrogels can be discontinuous or continuous depending on the nature of monomer or comonomer present in the hydrogel and stiffness of hydrogel network [13, 19]. The presence of ionized group and stiffness of the polymer network cause an increase in the osmotic pressure required for expansion of the network causing the discontinuous volume change. In the last three decades, the effect of crosslinking density on swelling and mechanical properties of NIPAM-based hydrogels has been reported [14, 15]. Saito and coworkers reported the effect of the amount of the crosslinking agent on the volume phase transition and swelling behavior of PNIPAM [20]. The effect of the concentration of crosslinker on the swelling percentage, interaction parameter etc also reported by Huglin and coworkers [21].

In our earlier study we reported the synthesis of poly (NIPAM-co-NTBA-co-AAm) hydrogels for aqueous protein solution separation process [22]. The purpose of this study is to determine the crosslinking density of poly (NIPAM-co-NTBA-co-AAm) hydrogels by stress-strain experiment and elucidate the effect of crosslinking density on the volume phase transition, as well as the interaction parameter. To our knowledge, no efficient investigations on the effect of crosslinking density on the swelling and phase transition of poly (NIPAM-co-NTBA-co-AAm) hydrogels have been published before.

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In light of this, poly (NIPAM-co-NTBA-co-AAm) hydrogels have been prepared varying the concentration of crosslinking agent and their cross-linking density was determined by using stress-strain measurement. Also, the volume phase transitions and value of interaction parameter of the hydrogels were determined. The novelty of the present study is the literature on NIPAM based terpolymeric hydrogels which have been used for the first time to investigate the effect of the crosslinking density on physicochemical properties.

EXPERIMENTAL

Materials and methods

NIPAM (Acros Organic Chemicals, USA), NTBA (Aldrich, USA) and AAm (Central Drug House Ltd. Co., India) were used without any further purification. The other chemicals N,N-methylene-bisacrylamide (MBA) (Sisco Research Lab, India), ammonium persulfate (APS) (Titan Biotech Ltd. Co., India) and N,N,N,N-tetra-methylene-diamine (TEMED) (Central Drug House Ltd. Co., India) were also used in purchased form. The solvent 1,4-dioxane was purchased from Merck, Germany. Double-distilled water was used to explore the swelling behavior of the hydrogels.

The infrared spectra of the hydrogel samples were recorded on Prestige 21 (Shimadzu, Japan), in DRS mode in the range of 4000–400 cm⁻¹, with 4 cm⁻¹ of resolution. Swelling experiment was performed at different constant temperatures and the swelling percentages were determined by equation (1):

$$\% \text{ Swelling} = \frac{m_t - m_d}{m_d} \times 100 \quad (1)$$

where m_d represents the dry weight of gel and m_t denotes the weight of swollen hydrogel at different time intervals.

The compressive elastic moduli of the equilibrium swollen hydrogels (at 25°C) were determined using a universal tensile machine (UTM, Instron 3360, USA). The compressive stress, (F'/A , force/area) was calculated at constant deformation rate of 1 mm/min. The compression modulus of the hydrogel network can be determined from the slope of the linear plots of compression stress vs strain using equation (2):

$$\frac{F'}{A} = -G(\lambda - \lambda^{-2}) \quad (2)$$

where F' represents applied force, “ A ” cross-sectional area, “ G ” compression elastic modulus and λ denote the ratio of deformed length to initial length of the hydrogel, respectively.

Hydrogel preparation

Free radical polymerization was applied to prepare terpolymeric hydrogels using NIPAM, NTBA, and AAm [22] at room temperature. In the process, the monomers NIPAM, NTBA and AAm were dissolved in (10 ml, 1:2 vol) mixture of 1, 4-dioxane and doubly distilled water followed by addition of MBA. After complete mixing the added initiator APS was dissolved completely. After complete dissolution TEMED (0.25 ml aqueous solution) was added and allowed to complete the polymerization for 24 h. The prepared hydrogels were washed 8-10 times in distilled water and 10-12 cycles by SOXHLET extraction with 1,4-dioxane to eliminate the unreacted monomers, linear homopolymers and other chemicals present in the gel. The washed hydrogels were dried at room temperature for 2-4 days and at about 80°C for 48 h till constant weight. The compositions of the poly (NIPAM-co-NTBA-co-AAm) hydrogels are given below (Table 1):

Table 1. The different proportions of monomers and reagents in copolymer composition

NIPAM/NTBA/ AAm (Molar ratio)	MBA (moles) × 10 ⁻⁸	APS (moles) × 10 ⁻⁴	TEMED (20 vol %)	Nomenclature
25/37.5/37.5	0.00649	1.85	0.25	NTA1
25/37.5/37.5	0.0194	1.85	0.25	NTA2
25/37.5/37.5	0.0779	1.85	0.25	NTA3
25/37.5/37.5	0.155	1.85	0.25	NTA4
25/37.5/37.5	0.233	1.85	0.25	NTA5

RESULTS AND DISCUSSION

Fourier transform infrared spectroscopy

The infrared spectra of the fabricated hydrogels are depicted in Fig. 1. The main features of the spectrum are: (a) the bands associated with the polymer network such as the broad band between 3110 cm⁻¹ & 3567 cm⁻¹, which is attributed to the presence of the N–H stretching frequency of the amide group, (b) the appearance of a peak related to C=O stretching, asymmetric stretching of COO⁻ and symmetric stretching of COO⁻ at 1649 cm⁻¹, 1612 cm⁻¹ and 1448 cm⁻¹, respectively, (c) broad band at 2147 cm⁻¹, is assigned to the presence of –C–N group of MBA, NIPAM, NTBA and AAm. Presence of iso-intensity double peaks at 1394 cm⁻¹ and 1333 cm⁻¹ corresponding to the symmetrical bending vibrations and bimethyl of isopropyl group peak at 1228 cm⁻¹ assigned to –C(CH₃)₃ group.

Network parameters

The theoretical crosslinking density (V_t) of the hydrogels can be expressed in terms of concentration of crosslinking agent (C) and their functionality f :

$$V_t = Cf/2 \quad (3)$$

In the present case the functionality of the methylenebis acrylamide is taken as ‘4’ and the value of C was calculated from their molar concentration in the feed and density of all the dried hydrogels (1.08 kg/dm).

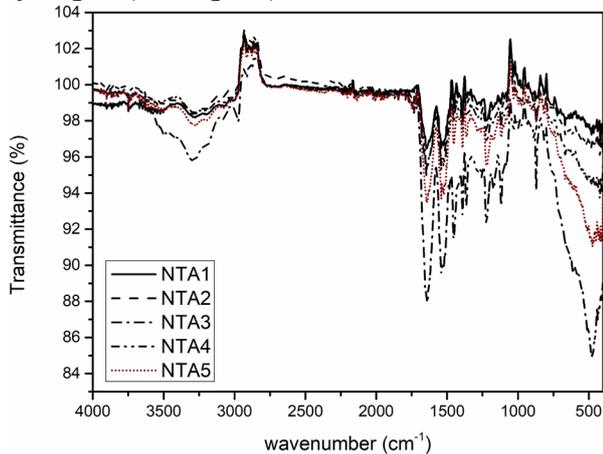


Fig. 1. FTIR spectra of the NTA terpolymer

For compression measurement the cylindrical gels of 1.0 cm in height and 0.8 cm in diameter were swollen in water at 25°C to attain equilibrium. Assuming that the gels swell isotropically, the swelling ratio may be defined as the reciprocal of hydrogel volume fraction was:

$$\frac{V_s}{V_r} = \frac{\vartheta_{2r}}{\vartheta_{2s}} = \left(\frac{d}{d_0}\right)^3 \quad (4)$$

where ϑ_{2s} and ϑ_{2r} represent the volume fractions of the hydrogels in the equilibrium swollen and relaxed state, respectively. ϑ_{2r} and ϑ_{2s} can be calculated using the following relations:

$$\vartheta_{2r} = C_0 \left(\frac{M_0}{\rho_2}\right) \quad (5)$$

$$\vartheta_{2s} = \vartheta_{2r} \left(\frac{d_0}{d}\right)^3 \quad (6)$$

Here, C_0 represents the initial concentration of monomers, ρ_2 is the density of the dry hydrogels and M_0 denotes the molecular weight of repeat unit of the hydrogel network.

Compression (G) moduli were estimated according to:

$$\tau = G(\lambda - \lambda^{-2})$$

where τ denotes the compression stress and the G (modulus) slope of the linear plots of the τ versus $(\lambda - \lambda^{-2})$. The effective crosslinking density, V_e , can be calculated from equation (7):

$$V_e = \frac{G}{RTV_{2s}^3 V_{2r}^3} \quad (7)$$

The interaction parameter, χ , can be determined using Flory–Rehner equation [16, 23, 24]:

$$\chi = \frac{-\left[\ln(1-\vartheta_{2s}) + \vartheta_{2s} + V_e V_t \vartheta_{2r} \left\{ \left(\frac{\vartheta_{2s}}{\vartheta_{2r}}\right)^{1/3} - \left(\frac{\vartheta_{2s}}{\vartheta_{2r}}\right) \left(\frac{1}{2}\right) \right\}\right]}{\vartheta_{2s}^2} \quad (8)$$

In the present study, the value of V_t has been found to be increased with increasing crosslinking agent concentration (Table 2). The effective crosslinking density of hydrogels (V_e) a factor determining the polymer network was evaluated by equation 7 on the basis of the modulus. It is found that the effective crosslinking density get increased with moduli G of hydrogels which indicates the enhancement of mechanical strength of hydrogels. These results indicate that along with the degree of crosslinking, microstructure regularity also affects the mechanical properties. Similar type of results was found in literature [13, 25]. Also, it can be observed that the crosslink density of the hydrogel network, as well as the number of elastically effective chains increase with decrease in the value of M_c .

The value of V_e is related to V_t by equation 9 in which the α represents the value of the effective crosslinking without any crosslinking agent [26]. It may be arisen due to crosslinking in γ –irradiation induced synthesis [26]. The parameter β represents the crosslinking efficiency ($\beta = V_e/V_t$, when $\alpha=0$) and

its magnitude which is generally ≤ 1.0 except some cases where $\beta > 1.0$ is reported [27, 28].

$$V_e = \alpha + \beta V_t \quad (9)$$

Figure 2 shows the plots between V_e and V_t according to equation 9 exhibiting linearity for all hydrogels with $\alpha = 4.16E-05$ and $\beta = 1.62E-05$ which indicates the low crosslinking efficiency of the MBA in the hydrogels. The low crosslinking efficiency of the hydrogels may be attributed to formation of many elastically ineffective hanging chain ends in the hydrogel network [29]. A perfect comparison of the present results cannot be compared with values reported in literatures due to scant value [30] for thermoresponsive hydrogels and nonexistent for the terpolymer considered here. Theoretically the amount of crosslinking agent in the terpolymeric hydrogels calculated at every stage of fractional conversion for each sample is accountable for observed low or high crosslinking efficiency. The relevant reactivity ratios (Q, e) are usually acceptable alternative [26].

Further, the interaction parameter (χ) was found to decrease as MBA content was reduced. Increased crosslinking density decreases the swelling percentage of the hydrogels below the transition temperature. Beyond transition temperature the hydrophobic effect dominates on crosslinking effect on swelling of thermoresponsive hydrogels. χ and T are related in the second-power polynomial: [31]

$$\chi = a_0 + a_1 T + a_2 T^2 \quad (10)$$

where T represents the temperature while the total interaction parameters have enthalpic (χ_H) and entropic (χ_S) contributions [21, 31]. Enthalpic (χ_H) and entropic (χ_S) parameters depend on enthalpy (κ) and entropy (ψ) dilution parameters as $\chi_H = (\kappa)$ and $\chi_S = 0.5 - (\psi)$ [16].

$$\chi_H = -T \frac{d\chi}{dT} = -T(a_1 + 2a_2 T) \quad (11)$$

$$\chi_S = \chi + T \frac{d\chi}{dT} = a_0 + 2a_1 T + 3a_2 T^2 \quad (12)$$

The actual partial molar enthalpy of dilution (H_1) and partial molar entropy of dilution (ΔS_1) can be calculated by:

$$\Delta H_1 = RT\phi^2\kappa \quad (13)$$

$$\Delta S_1 = R\phi\psi \quad (14)$$

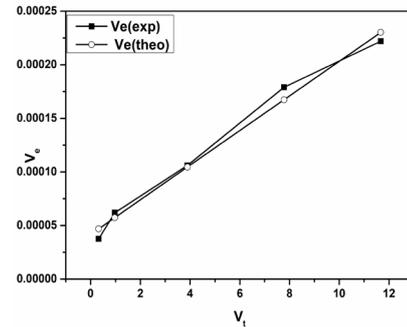


Fig. 2. Plots of theoretical and experimental effective crosslinking density

The plots of χ_H and χ_S versus temperature are depicted in Figure 3. The larger positive value of χ_S and smaller negative value of χ_H gives the overall value of χ .

On the basis of the values of χ_H and χ_S for all samples at various temperatures both ΔH_1 and ΔS_1 values are found to be negative. The plots of ΔH_1 and ΔS_1 versus temperature T are depicted in Fig. 3. The decrease in entropy favors the swelling of hydrogels via hydrophobic hydration and solvation, as well as hydrogen bonding [21]. Also, the reduced enthalpy causes increase in water structuring via enhanced hydrogen bonding and negative ΔH .

Overall total interaction parameter χ are found to be increased with increasing the temperature which may be due to the decrease in mixing of polymer chains upon increase in temperature. The mixing of polymeric chain decreases due to release of absorbed water from the network if the temperature of solution increased. Since the amide groups of NIPAM, NTBA and AAm exhibit hydrogen bonding with water molecules below LCST. It indicates that the water molecules absorbed within the hydrogel network interact with the hydrophilic amide groups on the side chains before the hydrophobic hydration. It results into expelling of absorbed water from collapsed hydrogel network causing the increase in total entropy of the hydrogel.

Table 2. Compression (G) modulus, V_e and M_c for NTA copolymers

	Crosslinking ratio	V_t	V_e (mole/m ³)	M_c (kg/mole)	G (Modulus) MPa	χ (at 25°C)
NTA 1	1.6	0.32	3.75E-05	19.2	0.065	0.49
NTA 2	4.8	0.97	6.19E-05	11.7	0.081	0.52
NTA 3	19.4	3.89	0.000106	6.75	0.101	0.57
NTA 4	38.9	7.78	0.000179	4.02	0.236	0.62
NTA 5	58.4	11.67	0.000222	3.23	0.424	0.69

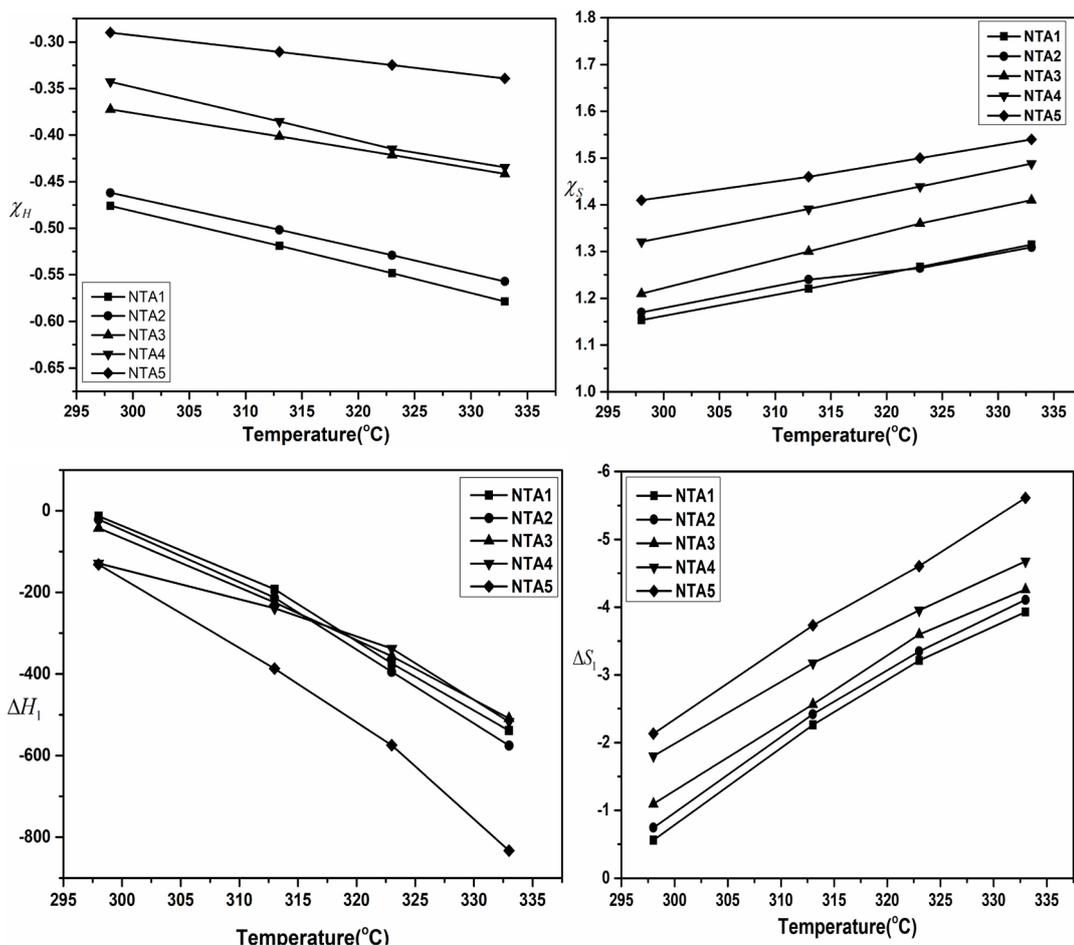


Fig. 3. Plots of χ_H , χ_S , ΔH_1 and ΔS_1 versus $1/T$ for NTH 1, NTH 2, NTH 3, NTH 4 and NTH 5 copolymers

Transition temperature and sharpness of transition

The swelling behavior of the different thermoresponsive hydrogels can be compared with the help of transition temperature and sharpness. Some hydrogels show discontinuous volume transition at specific temperature whereas some shows transition in broad range of temperature [32]. Therefore, it needs to distinguish among broad, gradual and absolute rapid volume change which can be clarified with sharpness. Therefore, the swelling of the hydrogels was normalized with range of temperature used for swelling experiment. The transition temperature of the hydrogel was determined from the inflection point on normalized curve of swelling equilibrium versus temperature (Figure 4) and mentioned in Table 3. The slope of the curve has been used to evaluate the sharpness of transition (Table 3). The transition temperature of

the hydrogels is increased slightly with increasing the crosslinking density of the hydrogel. This may be attributed to the increased stiffness of the hydrogels with increased crosslinking density.

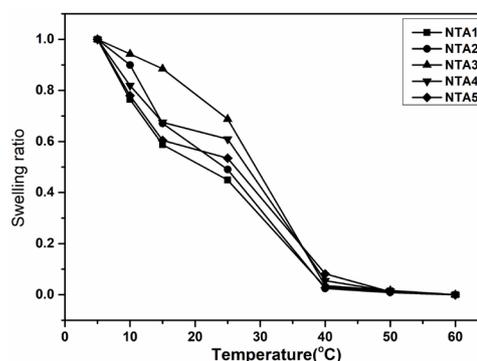


Fig. 4. Normalized swelling equilibrium vs temperature for NTA hydrogels

Table 3. The transition temperature and sharpness of the NTA hydrogels.

Sample	Transition Temperature (°C)	Sharpness (%/°C)
NTA 1	33±1	2 ±0.028
NTA 2	34±1	3 ±0.033
NTA 3	35±2	2 ±0.032
NTA 4	36±2	2 ±0.035
NTA 5	36±2	2 ±0.033

The results of the effect of temperature on the swelling of hydrogel studied in the temperature range 5–60°C in distilled water (Figure 2) clearly suggest that the equilibrium swelling decreased when temperature is raised, which may be due to the hydrophobic interactions of the polymer hydrophobes at higher temperature proving them as thermoresponsive hydrogels. At all temperatures the equilibrium swelling percentages of the hydrogels were found to increase with decreasing the crosslinking ratio.

CONCLUSIONS

The results, from the compression experiments, exploiting mechanical properties, strongly showed a crosslinking density-dependent behavior. The present work on dependence of cross-linking density allowed shedding light on the swelling equilibria, interaction parameter as well as mechanical strength. The volume phase transition of the hydrogels increased with stiffness of the hydrogels. Also, there was not any significant effect of crosslinking density of hydrogels on their thermoresponsive behavior. The current study demonstrates that the swelling and mechanical properties of the poly (NIPAM-co-NTBA-co-AAm) hydrogels can be controlled effectively by varying the amount of MBA.

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