



Fabrication of Poly (*N*-isopropylacrylamide-*co*-ita- conic Acid) Hydrogels in DMSO/Water Mixtures and their Characterization

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A B S T R A C T

In this article, pH and temperature double responsive poly (*N*-isopropylacrylamide-*co*-IA) hydrogels were prepared by copolymerization in mixed solvents of water and dimethylsulphoxide (DMSO) above zero. The freshly fabricated P(NIPAAm-*co*-IA) hydrogels were characterized by Fourier transform infrared spectroscopy (FTIR), thermogravimetric analysis (TGA) and scanning electron microscopy (SEM) techniques to investigate their chemical compositions, structures, and morphologies. The results showed that all of these gels have similar chemical compositions and structures but differ in surface morphologies. The hydrogels prepared with highest DMSO/water ratios have porous surfaces, while the other gels exhibit smooth and dense surfaces. Temperature and pH sensitivities of the resultant hydrogels were examined through swelling ratios and deswelling/reswelling kinetics experiments, as well. The results indicated that only hydrogels prepared in the highest DMSO/water ratio media exhibited improved properties such as higher swelling ratios, faster deswelling and reswelling kinetics compared with traditional P(NIPAAm-*co*-IA) hydrogels, as the other hydrogels possessed lower swelling ratios and slower deswelling and reswelling dynamics. We have proposed that there maybe an energy barrier existed for conformation transitions in the process of removal of DMSO by water. Only the gels which could overcome the energy barrier exhibited expanded network structures and improved properties while, the other gels maintained their contracted network structures and poor properties.

Key Words:

hydrogels;
DMSO;
phase separation;
energy barrier;
chain conformations.

INTRODUCTION

Over the past 20 years, a considerable amount of research has been focused on polymer hydrogels, especially stimuli-responsive hydrogels, which cannot only preserve a lot of water as conventional gels do, but also exhibit great sensitivity to environment stimuli, such as temperature [1,2], pH [3,4], electric field [5], light [6] and antigens [7]. These hydrogels have been developed for a wide variety

of applications, for example, devices for drug delivery systems [8,9], selective absorption of water [10,11] and bleed stopping [12].

Poly(*N*-isopropylacrylamide) (PNIPAAm) hydrogel is a representative temperature sensitive polymeric network which demonstrates a volume phase transition at lower critical solution temperature (LCST) around 33°C.

Below the LCST, the PNIPAAm

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gel is in the water-swollen state. As the temperature is increased above LCST, it becomes hydrophobic and shrinks quickly [13].

Besides, the PNIPAAm and its copolymers or hybrid gels are also sensitive to many solvents, such as methanol [14], dioxane [15], acetone [16], tetrahydrofuran (THF) [17], dimethylformamide (DMF) [18] and DMSO [19]. Usually, they are all, good solvents for the PNIPAAm and its copolymers, however when each one of them is mixed with water in certain ratios, these solvents become co-nonsolvents and the re-entrant phenomenon takes place.

Contrary to the above observations, PNIPAAm hydrogels prepared in the mixed solvents, such as acetone (or THF)/water mixtures, demonstrate surprisingly responsive properties, as extensively reported by Zhang et al. [20-24]. However, there are only a few reports on the preparation of PNIPAAm hydrogels from DMSO/water mixed solvents at subzero temperatures [25,26]. So far, to our knowledge, there has not been any report on the effect of DMSO/water ratios on the preparation and properties of the PNIPAAm hydrogels above 0°C.

Thus, in this article, an attempt is made to synthesize hydrogels using DMSO and water as mixed solvents at 15°C (far above zero) with the purpose of disclosing the reasons behind the secret that why there has not been any report on the preparation of the PNIPAAm hydrogels in the DMSO/water mixtures above zero. Itaconic acid, however, has been adopted to impart pH sensitivity by replacing the often-used acrylic acid due to its high hydrophilicity and biodegradability [27]. The resulting hydrogels were characterized by swelling ratios and deswelling and reswelling kinetics at various temperatures and pH

media. Fourier transform infrared spectroscopy (FTIR), scanning electron microscopy (SEM) and thermogravimetric analysis (TGA) techniques were applied to analyze their chemical compositions, structural, and morphological characteristics as well.

EXPERIMENTAL

Materials

N-Isopropylacrylamide (NIPAAm, Acros), purified by recrystallization from a mixture of toluene and *n*-hexane(v:v=3:2) and itaconic acid (IA, purity>99%) purchased from Aldrich were used as monomers. *N,N'*-Methylenebisacrylamide (BIS) was purified by recrystallization from methanol and used as a cross-linking agent. Potassium persulphate(KPS), *N,N,N',N'*-tetramethylethylenediamine (TEMED) were used as polymerization initiator and accelerator, respectively. Dimethylsulphoxide (DMSO) was analytical grade and used as received without further purification.

Potassium tetroxalate dehydrate ($\text{KH}_3(\text{C}_2\text{O}_4)_2 \cdot 2\text{H}_2\text{O}$), potassium hydrogen tartrate ($\text{KHC}_4\text{H}_4\text{O}_6$), potassium hydrogen phthalate ($\text{C}_6\text{H}_4\text{CO}_2\text{HCO}_2\text{K}$), disodium hydrogenorthophosphate (Na_2HPO_4), potassium dihydrogen phosphate (KH_2PO_4), sodium tetraborate decahydrate ($\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$) and sodium chloride (NaCl) were all analytical grades and used to prepare pH buffer solutions.

Preparation of Hydrogel

Monomers of NIPAAm and IA were put into a glass tube, and dissolved with the DMSO/water mixed solvents in the presence of the cross-linker BIS. KPS was

Table 1. Feed composition of P(NIPAAm-co-IA) hydrogels (G8000-G4040) synthesized in DMSO and water mixed solvents initiated at 15°C.

Run	Sample ID	NIPAAm (g)	IA (g)	BIS (g)	KPS (g)	H ₂ O (mL)	DMSO (mL)	M _t (g)
1	G8000	0.5000	0.0150	0.0250	0.0125	8.0	0.0	0.5447
2	G7505	0.5000	0.0150	0.0250	0.0125	7.5	0.5	0.5376
3	G7010	0.5000	0.0150	0.0250	0.0125	7.0	1.0	0.5357
4	G6515	0.5000	0.0150	0.0250	0.0125	6.5	1.5	0.5345
5	G6020	0.5000	0.0150	0.0250	0.0125	6.0	2.0	0.5326
6	G5030	0.5000	0.0150	0.0250	0.0125	5.0	3.0	0.5302
7	G4040	0.5000	0.0150	0.0250	0.0125	4.0	4.0	0.5191

M_t: the weight of the resultant dry gel

Table 2. The standard pH buffer solutions with different molarities (C) and ionic strengths (I) and the compounding ways.

Number	pH	C (mol/L)	I (mol/kg)	Compounding way
1	1.68	0.050	0.050	12.71 g $\text{KH}_3(\text{C}_2\text{O}_4)_2 \cdot 2\text{H}_2\text{O}$ in 1000 mL H_2O
2	3.56	0.034	0.034	7 g $\text{KHC}_4\text{H}_4\text{O}_6$ in 1000mL H_2O overnight , filtrated (saturated)
3	4.01	0.050	0.050	10.21 g $\text{C}_6\text{H}_4\text{CO}_2\text{HCO}_2\text{K}$ in 1000 mL H_2O
4	6.86	0.025	0.010	3.53 g Na_2HPO_4 and 3.39 g KH_2PO_4 in 1000 mL H_2O
5	9.18	0.010	0.030	3.80 g $\text{Na}_2\text{B}_4\text{O}_7 \cdot 10\text{H}_2\text{O}$ in 1000 mL H_2O

used as an initiator, and TEMED was added as an accelerator; then degassed and sealed off under nitrogen. Polymerization was conducted at 15°C for 24 h and the produced hydrogels were cut into discs (10 mm in diameter, 2 mm in thickness). The hydrogel discs were immersed in distilled water at 0°C for a week. During this period, the deionized water was replaced everyday to leach out the DMSO, unreacted monomers and linear polymers. The feed compositions of the monomers, cross-linker and mixed solvents compositions are listed in Table 1. The resulting hydrogels were designated as G8000, G7505, G7010, G6515, G6020, G5030 and G4040, respectively.

Preparation of pH Buffer Solutions

Standard pH buffer solutions were prepared according to IUPAC standards and procedures [28]. The pH and compounding materials are listed in Table 2. The ionic strength of the pH buffer solutions were adjusted to be uniform ($I=0.05$ mol/kg) by using NaCl.

Instrumentation

Optical Images

All the optical images were recorded using Canon A510 camera.

FTIR

An RFX-65A FTIR spectrometer (Analect, USA) was used for spectral measurements. The hydrogel samples were dried in vacuum at 50°C for 48 h till reaching constant weights. The dried samples were embedded in KBr discs after being grinded into powder. The scanning wavenumber ranged from 4000 to 500 cm^{-1} .

TGA

The TGA thermograms were recorded on a

PerkinElmer-7 instrument at a heating rate of 10°C/min under N_2 protection over a temperature range between room temperature and 500°C.

Surface Morphology Observation

Scanning electron microscopy (SEM, JSM-5910, Japan) was used to study the surface morphologies of the PNIPAAm hydrogels. To prepare samples for SEM, the swollen hydrogels were freeze-dried and then sputter coated with gold.

Temperature Dependence of the Swelling Ratio

The temperature dependence of swelling ratio of hydrogels was measured gravimetrically after carefully blotting surface water with moist filter paper in the temperature range of 25 and 60°C. Hydrogel samples were immersed in distilled water for at least 24 h at each predetermined temperature. The average value of three measurements was taken for each sample and the swelling ratio (SR_T) was determined according to the following equation:

$$\text{Swelling ratio } (\text{SR}_T) = (W_s - W_d) / W_d$$

where W_s is the weight of swollen hydrogel at the particular temperature and W_d is the dry weight of the hydrogel.

The Equilibrium Swelling Ratio in pH Buffer Solutions

The swelling ratio of hydrogels was measured gravimetrically after carefully blotting surface water with moist filter paper at ambient temperature (25°C). Hydrogel samples were immersed in various pH buffer solutions for at least 24 h. The average value of three measurements was taken for each sample and

the swelling ratio (SR_{pH}) is calculated as follows:

$$\text{Swelling ratio (} SR_{pH} \text{)} = (W_s - W_d) / W_d$$

Where, W_s is the weight of swollen hydrogel at ambient temperature and W_d is the dry weight of the hydrogel.

Measurement of Deswelling Kinetics

The deswelling kinetics of hydrogels were measured gravimetrically at 60°C. The hydrogel samples were first immersed in distilled water at 25°C until equilibrium was reached. Then, the equilibrated hydrogels were quickly transferred to distilled water or pH buffer solution of 60°C. At specified time intervals, the samples were removed from the hot water and weighed after wiping off the excess surface water with moist filter paper. The average value of three measurements was taken for each sample and the swelling ratio (SR_d) is calculated by the following equation:

$$\text{Swelling ratio (} SR_d \text{)} = (W_t - W_d) / W_d$$

where, W_t is the weight of hydrogel at regular time intervals, W_d is the weight of the dry gel

Measurement of Reswelling Kinetics

The kinetics of reswelling of the gels was measured gravimetrically at 25°C. Before the measurement, the hydrogel samples were freeze-dried for 24 h. The weight changes of gels were recorded during the course of reswelling in distilled water after blotting the excess surface water at regular time intervals. The swelling ratio (SR_r) is determined by the following equation:

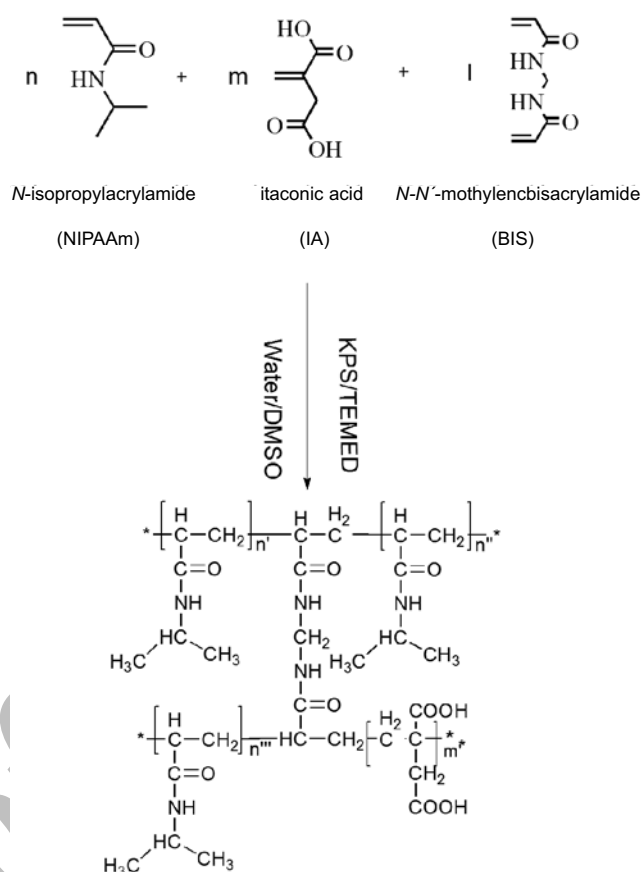
$$\text{Swelling ratio (} SR_r \text{)} = (W_t - W_d) / W_d$$

where, W_t is the weight of hydrogel at regular time intervals, W_d is the weight of the dry gel.

RESULTS AND DISCUSSION

Preparation of Hydrogel

The chemical structures and the polymerization



Scheme I. The molecular structures of the monomers, cross-linker, and synthetic procedure of P(NIPAAm-co-IA) hydrogels.

process of the hybrid hydrogels are shown in Scheme I. It is worth noting that during the mixing procedure the tubes were kept at 0°C with the aid of ice/water to preclude the possibility of pre-polymerization because when DMSO and water are mixed together strong exothermic effect would initiate the polymerization of NIPAAm. For the same cautionary reason, the accelerator TEMED was added at the final step [29]. Otherwise, the obtained hydrogels would be opaque and very soft.

Physical appearances of the formed hydrogels are shown in Figure 1. As it is noticed, gels from G8000 to G6515 are transparent, while G6020 shows slight phase-separation. Both G5030 and G4040 are opaque in the tubes. However, after purification, G5030 turns to be transparent due to its high hydrophilicity, as revealed in Figure 2, while G4040 breaks into pieces due to its poor strength.

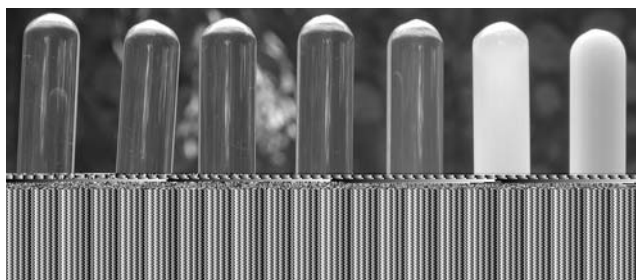


Figure 1. P(NIPAAm-*co*-IA) hydrogels (before disposal) prepared at 15°C (from left to right: G8000, G7505, G7010, G6515, G6020, G5030, and G4040, respectively).

The exact nature of the co-nonsolvency behaviour of linear chains and the corresponding re-entrant phenomenon observed with hydrogels are still puzzling [30]. It has been proposed that when DMSO is mixed with water, different water/DMSO complexes may be formed which behave as poor solvents for PNIPAAm and its copolymers. During the growth of P(NIPAAm-*co*-IA) chains, competitive interactions may exist between DMSO, water, and P(NIPAAm-*co*-IA) chains.

First, the attractive interactions between polymer chains and water molecules have dominating role over the attractions between the polymer chains. With the increase of DMSO, attractive interactions between the two solvents become predominant, resulting in an increase in the free energy for polymer-polymer contact. Finally, the increasing affinity among polymer segments can induce the collapse of the polymer network [31] leading to phase separation and physical appearances of gels which change from transparent to translucent, or even to opaque gels.

The appearances and shapes of the swollen hydrogels are shown in Figure 2. It is surprising to find out that except G5030, the water absorption of the other gels samples is even lower than the conventional gel, G8000. Besides, in these series of gels, the water

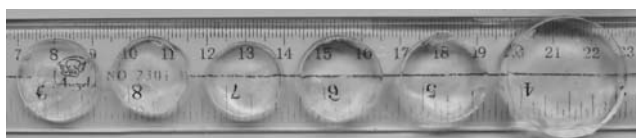


Figure 2. P(NIPAAm-*co*-IA) hydrogels at swollen equilibrium (from left to right: G8000, G7505, G7010, G6515, G6020, and G5030, respectively).



Figure 3. Freeze-dried P(NIPAAm-*co*-IA) hydrogels (from left to right: G8000, G7505, G7010, G6515, G6020, and G5030, respectively).

absorption increases in the order: G7505 < G7010 < G6515 < G6020. During the course of copolymerization in the mixed solvents, the polymer chains are often curled, intertwist with each other, and these interactions are fixed by cross-linking. After purification, DMSO is extracted and replaced by water, and polymer chains tend to take conformational transitions to relaxation state. However, they need to break the bondage of the cross-linkers and conquer the corresponding energy barriers. As known, with the amount of DMSO increased in the gelation, the ionization of carboxyl of itaconic acid becomes gradually weaker.

When the final gel is purified in water, the itaconic acid is ionized and the electrostatic repulsion takes over. Thus, the higher the DMSO content, the greater the forces, and more water can be absorbed in to the hydrogel. Finally, sufficient forces are produced and succeed in intriguing the polymer chains to extend and relax, and so lead to the formation of the honeycomb porous structures. Thus, it is reasonable to assume that when DMSO is used in the gelation, the swelling ratios of the hydrogels are increased in the above order and only G5030 is higher than G8000 which has been prepared in pure water. Figure 3 shows the images of freeze-dried samples, in which it is easier to notice that the volume relationship (G7505 < G7010 < G6515 < G6020 < G8000 < G5030 still remains.

The conversion of monomers has been traced by gravimetric determination. In most cases, nearly quantitative conversion values and complete incorporation of itaconic acid into the thermoresponsive gel matrix are achieved. Furthermore, the hydrogels were subjected to acid-base titration analysis after extraction [27]. The results have revealed that the percentage of PIA in gels changes very little from G8000 to G5030. Hence, the copolymer composition can be approximated very well to the initial feed composition.

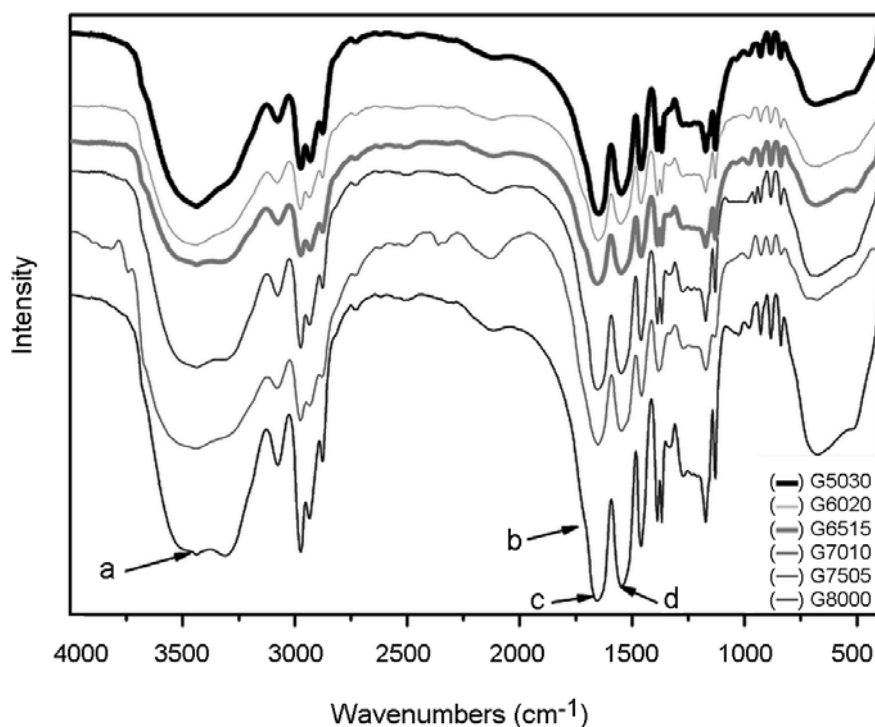


Figure 4. The FT-IR spectra of the resulting hydrogels.

FTIR

Figure 4 shows the FTIR spectra of the P(NIPAAm-co-IA) hydrogels. It can be observed that the IR spectra of all hydrogels are almost the same which is reasonable due to the fixed feed ratio of NIPAAm to IA and the high conversion efficiency. This means that all the gels have similar chemical compositions and structures. The result can be further confirmed by the TGA measurements which are shown in Figure 5. All the gels exhibit a typical broad band in the range of 3700-3100 cm^{-1} (band a) due to the evidence of the OH stretching vibrations of carboxylic acid groups of IA and NH stretching vibration of NIPAAm. The peak at approx. 1730 cm^{-1} (band b) can be attributed to the typical carbonyl vibration in IA. The typical amide-I band and amide-II band of NIPAAm are obvious at 1650 cm^{-1} (band c) and 1550 cm^{-1} (band d), respectively.

TGA

The TGA curves are shown in Figure 5. It is clear that the weight loss curves of the five dried hydrogel samples from G8000 to G5030 are almost the same while G4040 is slightly different. It means the chemical composition and structure of dried gels from G8000

to G5030 change little which is consistent with the IR results while G4040 is somehow different. This is easily understood when taking the initial feed ratios and the process of copolymerization into account. From G8000 to G5030, the initial feed compositions are the same and the reaction process is similar, thus the similar chemical compositions and structures could be expected. As for G4040, even though the initial feed composition is the same, however it is polymerized in

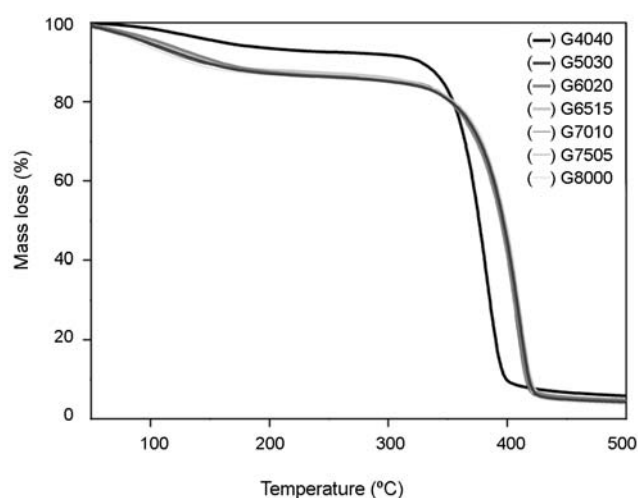
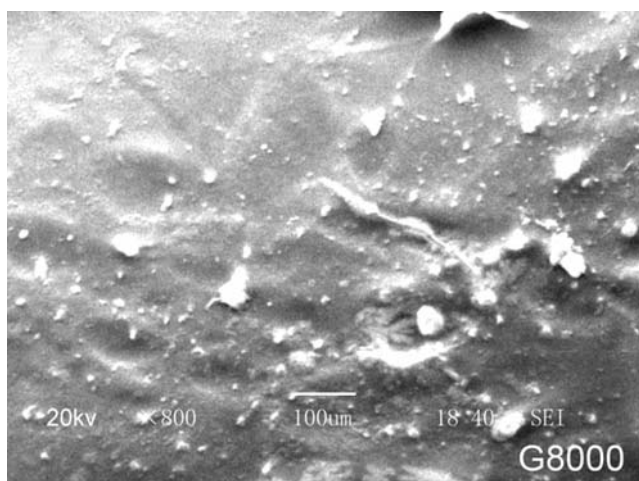
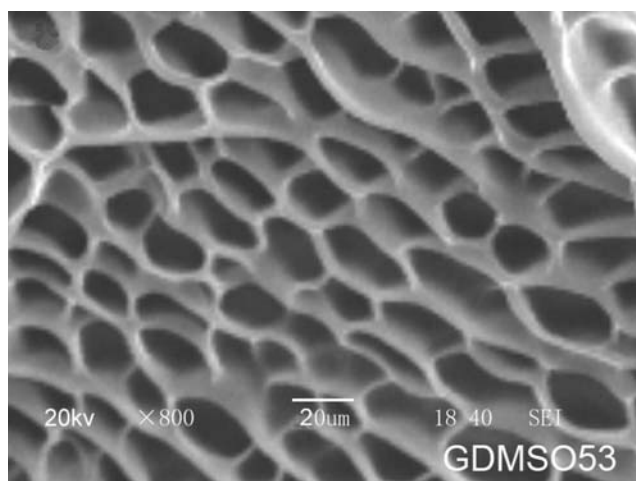


Figure 5. The TGA curves of the resulted hydrogels.



(a)



(b)

Figure 6. The SEM images of the hydrogels (a) G8000 and (b) GDMSO530 (i.e., G5030).

the form of precipitation polymerization likewise, so the cross-link density has been somewhat low and for IA it has been hard to enter copolymerization with the chains of PNIPAAm. The former lead to the low thermal stabilities and the latter induces the low hydrophilicity. Both of them can be reflected in the TGA curves. The initial thermal event occurs in the temperature range 50-150°C which is exhibited in the form of a shoulder in each curve, where G4040 shows a mass loss about 7% whereas others lose about 15%. This is attributed to the evaporation of residual water restrained by different amounts of hydrophilic bonds in the hydrogels. Although the decomposition temperature of G4040 is slightly lower than those of the others, all the hydrogels decompose beyond 350°C show

good thermal stabilities.

SEM

The morphologies of P(NIPAAm-*co*-IA) gels are shown in Figure 6. Only the G5030 exhibits porous structures after being freeze-dried, the surface morphologies of all the other hydrogels are dense, smooth, and homogeneous. This is consistent with the results in Figure 3. As a result of numerous small pores in the hydrogel network, water molecules can be accommodated and easily diffused in and out. Therefore, the swelling ratio of G5030 and its response rate could be greatly enhanced which can be reflected in swelling or deswelling kinetics experiments as described below.

Temperature Dependence of the Swelling Ratio

The equilibrium swelling ratios (ESR) of P(NIPAAm-*co*-IA) hydrogels in distilled water are depicted in Figure 7 as a function of temperature ranged between 25 and 60°C. It is clear that at room temperature, the ESR of the G5030 is much larger than that of the conventional gel sample G8000, whereas those of the other four gels, i.e., G6020, G6515, G7010 and G7505 are smaller than that of G8000. In detail, ESR of G5030 is around 144.8, and that of G8000 is 65.2, while those of G6020, G6515, G7010 and G505 are 37, 40, 43.8 and 57, respectively. As it is mentioned above, due to lack of sufficient energy to break through the constraints of cross-linking, the macromolecular chains of gel samples, e.g., G6020, G6515, G7010, and G7505 undergo relaxation to a lesser extent, discouraging water from entering in to the network. Even though, within them, the swelling ratios still increase with the increase of DMSO content in the preparation of the copolymer gel samples. As DMSO content increases further, the polymer chains acquire sufficient energy to overcome the energy barriers for conformational transitions. The chains are relaxed and expanded, therefore porous structures are formed which can accommodate more water. Thus, the highest plateau value in the equilibrium swelling curve is obtained for G5030 sample.

From Figure 7, it can also be deduced that when the temperature is increased in the region of 40-60°C, ESR of hydrogel decreases gradually. As far as the LCST is concerned, it lies in the vicinity of 45-55°C

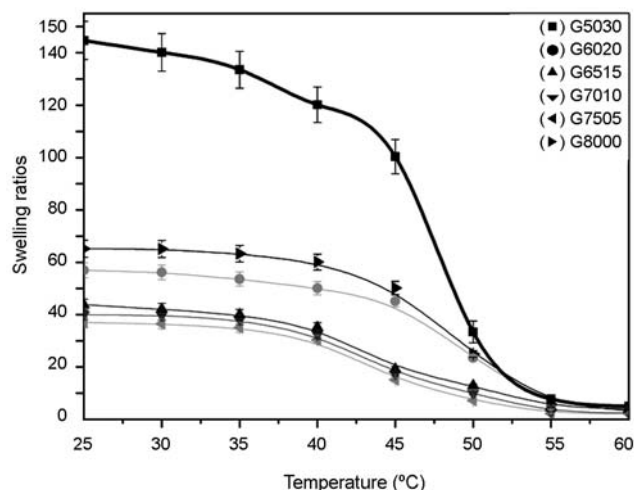


Figure 7. The temperature dependency of equilibrium swelling ratios of the resultant hydrogels in distilled water.

due to the incorporation of the highly hydrophilic monomer, IA. However, the changes of the swelling ratios at LCST seem to be continuous and different from those pure PNIPAAm hydrogels which take a sharp decreasing trend. The differences may associate with the higher hydrophilic nature of the hydrogel network. Since itaconic acid is highly hydrophilic and independent of the surrounding temperature, the conformational transition to the hydrophobic state of the polymer chains may be hindered to some extent and lead to smooth changes.

The magnitude of the swelling ratio reduction (changes of SR vs. temperature, i.e., $\Delta SR = SR_{60^\circ C} - SR_{25^\circ C}$) also depends on the composition ratio of the solvent mixture used for hydrogels prepared. For instance, the SR of G5030 reduces from 145 to around 8.6, with a ΔSR of around 136.4. While in the cases of G6020, G6515, G7010, G7505, and G8000 samples, the ΔSR for each is 49.5, 39.6, 37.57, 34.8 and 61.7, respectively. This result is in agreement with the relationship derived from its initial equilibrium swelling ratios at room temperature. At last, when the temperature reaches 60°C, the hydrophobic interactions become fully dominant in the systems and the difference among the swelling ratios of the hydrogels tends to be less significant.

The Equilibrium Swelling Ratio in pH Buffer Solutions

The pH-responsive character of hydrogels was

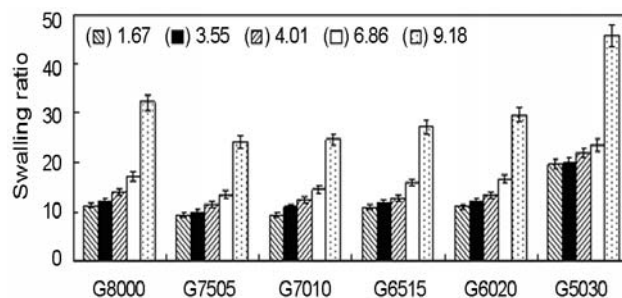


Figure 8. The equilibrium swelling ratio in pH buffer solutions.

investigated by swelling in different buffer solutions of 1.68, 3.56, 4.01, 6.86 and 9.18 at room temperature until the equilibrium was reached, as shown in Figure 8. It can be observed that the swelling ratios of the hydrogels increase as the pH increases. Taken G7010 as an example, in PBS (pH buffer solutions) 1.68, 3.56, 4.01, 6.86 and 9.18 its swelling ratios are 9.38, 11.05, 12.49, 14.51 and 24.7, respectively.

It is known that the carboxylic groups of itaconic acid cannot ionize well and are protonated to form COOH groups in acidic solutions below pK_a values. Thus, the hydrogen bonds between the carboxyl groups (-COOH) in IA and the amide groups (-CONH) in PNIPAAm can restrict the expansion of the network. While under basic conditions, the carboxylic acid groups in IA transform into the ionized form (COO⁻) and the resulting electrostatic repulsion between the ionized groups causes the hydrogels to swell [32]. From Figure 8, it can also be noticed that the composition ratio of DMSO to H₂O in the mixed-solvent mixture used for formulation of hydrogels also has had a significant effect on the pH-dependent swelling ratios and the tendency is similar to that exhibited in the distilled water below LCST. For example, at pH 9.18, the swelling ratios of G8000, G7505, G7010, G6515, G6020 and G5030 samples are 32.3, 24.2, 24.7, 27.3, 29.7 and 45.8, respectively. This phenomenon can be related to different chain conformation structures formed during the course of network formation and purification treatment.

Finally, it is obvious that these swelling ratios in pH buffer solutions are much smaller compared to the values measured in deionized water which can be attributed to the impact of osmotic pressure and charge screening effect [33].

Deswelling Kinetics

The swelling ratio only demonstrates the equilibrium swelling hydration state of responsive gels and from point of view of practical applications, the temperature and pH response kinetics are more significant. Thus, the deswelling experiments have been conducted in order to simulate the use of the hydrogels.

Figure 9a presents the shrinking kinetics of P(NIPAAm-*co*-IA) hydrogel, after transferring equilibrium swollen hydrogel samples at room temperature to distilled water at 60°C. It can be found that all the samples need approximately 120 min to dehydrate to equilibrium state and the difference among the gel samples not being obvious. Usually, expanded network structures of pure PNIPAAm hydrogels favour faster deswelling due to existing large pores. Because, during the initial deswelling, the conventional PNIPAAm hydrogels always undergo phase separation and the surface area shrinks. A dense layer forms on the surface and entraps water inside the hydrogel, preventing heat and mass transfer from the aqueous medium to the inner part of the hydrogel. However, in the case of porous PNIPAAm hydrogels, it is possible for the water molecules to rapidly transfer through the macropores into the innermost matrix, even though phase separation is being occurred on the surface which leads to a rapid deswelling.

However, the acceleration effect has not been remarkable in our systems. This may be ascribed to the presence of the P(itaconic acid) linear chains which is effective in facilitating deswelling in distilled water. Presumably due to the ionized COO⁻ the hydrophilicity of the gel matrix increased, which made it difficult to form a skin layer. However, it is worth noticing that the porous hydrogel is superior to the non-porous hydrogel in the magnitude of its water-loss during the deswelling processes. For example, within the 2 h, the swelling ratio of G5030 drops from 145.2 to 2.9, and the corresponding water-loss is 142.3, while those of G6020, G6515, G7010, G7505 and G8000 are 55.7, 41.8, 38.4, 35.7 and 61.8, respectively. This feature is particularly beneficial in controlled drug release applications because gels prepared with larger DMSO content can release much water or drugs. In other words, to achieve the same amount of drug release, less gel would be needed.

The deswelling has been carried out further at

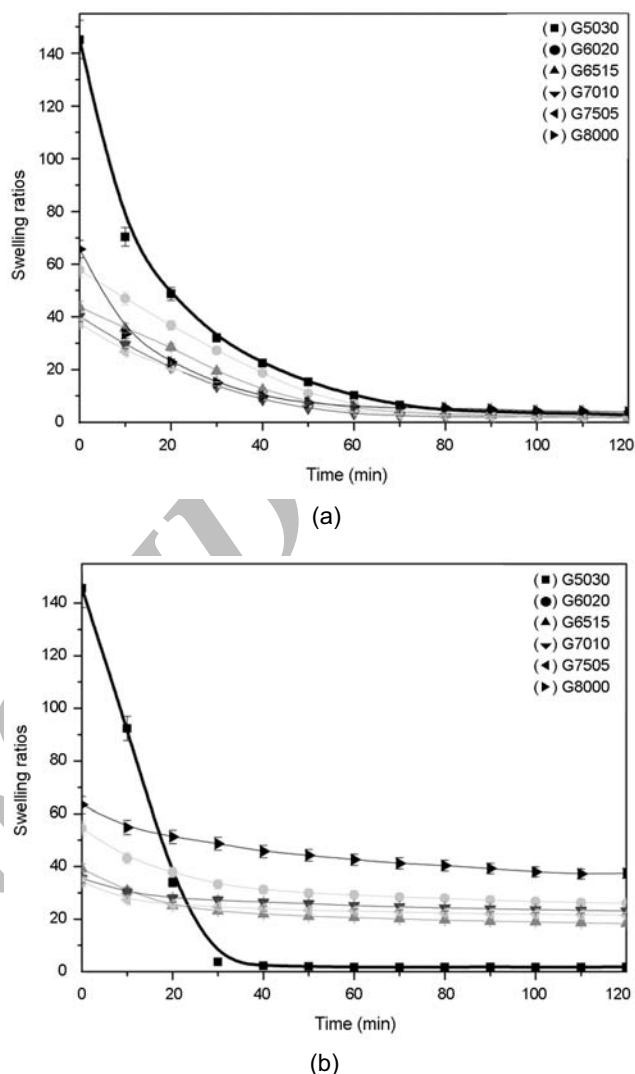


Figure 9. Deswelling kinetics in distilled water or pH buffer solution jumping from 25°C to 60°C: (a) distilled water and (b) pH = 1.68.

1.68, as illustrated in Figure 9b. It is interesting to find out that except G5030 which shrinks to equilibrium in about 30 min, all the hydrogels show rather slow deswelling rates. For instance, after 2 h, the swelling ratios of G6020, G6515, G7010, G7505 and G8000 samples are still 26.1, 24.2, 23.2, 21.5 and 37.5, respectively. It is regarded that, when the hydrogels were transferred from distilled water into the pH=1.68 buffer solutions, the ionized carboxyl became protonated and the hydrogen bonds between polymer chains were generated and a complex was formed which constrained the motion of the network [34]. Besides, the surface region has formed a thick and dense layer which has greatly restricted the outward

permeation of water from interior section of the hydrogel [35]. However, porous hydrogel sample, G5030 which has shown rapid deswelling suggests that the water released from the hydrogel has rapidly excluded through the pores networks, although P(itaconic acid) chains are un-dissociated under the conditions.

Reswelling Kinetics

The reswelling kinetics of P(NIPAAm-*co*-IA) hydrogels in water at 25°C is shown in Figure 10 for six hydrogels. From the curves, we may find out that the water absorption initially rise abruptly and then begin to level off and the reswelling rate is in the order of G5030>G8000>G6020>G6515>G7010>G7505.

In the case of G5030 sample, the absorption of water is faster than that of the conventional hydrogel (G8000). For example, within 30 min, the swelling ratio of G5030 has reached 99.4 and saturated equilibrium has been attained within 1 h. This very rapid reswelling kinetics could be attributed to its heterogeneous porous matrix structures. Generally, three steps have been proposed to determine the swelling rate of hydrophilic networks [36]:

- 1- The diffusion of water molecules into the polymeric system.
- 2- The subsequent relaxation of hydrated polymer chains.
- 3- The polymer network expansion into the aqueous solution.

Owing to the freeze-dried treatment before reswe-

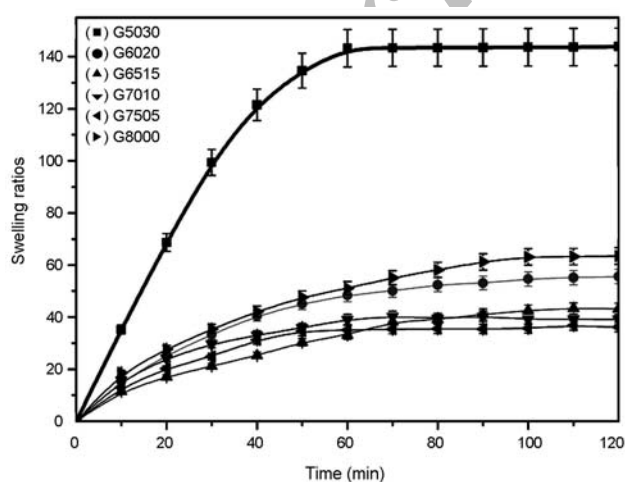


Figure 10. The reswelling kinetics of P(NIPAAm-*co*-IA) hydrogels.

lling, the porous structures, the relaxation conformation, and expanded structures of the matrix can be preserved to some extent.

All these factors have exerted some effects on the reswelling kinetics cooperatively, and thus, G 5030 which has porous structures, relaxed polymer chains, and expanded networks shows the fastest swelling rates. By comparison, all the other mixed-solvents hydrogels absorb water slower than a conventional hydrogel, because their smooth surfaces, strict chains conformations, and compressed structures make it much harder for water molecules to transfer between the hydrogel matrix and the external aqueous phase.

CONCLUSION

In summary, a new series of pH and temperature dual sensitive P(NIPAAm-*co*-IA) hydrogels have been produced in water and DMSO mixed solvents above zero and have been characterized in terms of swelling degree and swelling-deswelling kinetics. The swelling/deswelling behaviour and the respective temperature and pH dependencies of the gels have been found to be dependent on the water/DMSO mole ratio. Only the hydrogels prepared with the largest amount of DMSO exhibit higher swelling ratios and improved response kinetics owing to the extended chain conformations and the macroporous network structures formed. While, the hydrogels prepared with little amount of DMSO exhibit lower swelling ratios and slower deswelling/reswelling kinetics when compared with conventional P(NIPAAm-*co*-IA) hydrogels. It is suggested that there maybe energy barriers built up for the change of polymer chains conformations. These findings may provide some basis for directing the preparation of hydrogels in mixed solvents.

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