

Triply-Responsive (Thermo/Light/pH) Copolymeric Hydrogel of *N*-Isopropylacrylamide with an Azobenzene-Containing Monomer

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ABSTRACT: A series of triply-responsive copolymer hydrogel was firstly synthesized via free radical polymerization of *N*-isopropylacrylamide, 4-[(4-(acryloyloxy)ethoxy)phenylazo]benzoic acid (AEPZA), a water-soluble azobenzene-containing comonomer, and crosslinker. The properties of the hydrogel were subsequently investigated by UV-Vis absorption spectrometry, differential scanning calorimetry, and gravimetry. UV-Vis spectra showed that the copolymer hydrogel had a reasonable *trans-cis* photoisomerization rate upon UV irradiation and a relatively slow recovery rate in dark. The critical solution temperature (CST) of the copolymer hydrogel decreased with increasing of AEPZA content and subsequently shifted higher value after UV irradiation. Meanwhile, the phase

transitions profile became slower and broader with the incorporation of AEPZA, which could be partly counterbalanced by UV irradiation. The CST could also be affected by the pH value of buffer solution. In addition, equilibrium swelling behavior clearly showed that the swelling ratio could be modulated by temperature, light, and pH. These stimuli-responsive properties should be very important for controlled release delivery system. © 2011 Wiley Periodicals, Inc. *J Appl Polym Sci* 124: 1128–1136, 2012

Key words: stimuli-sensitive polymers; hydrogel; copolymerization; critical solution temperature; photosensitive; pH sensitive; phase transition; azobenzene chromospheres

INTRODUCTION

Stimuli-sensitive polymers have been attached much attention since the end of the last century because of their scientific interest and technological importance,^{1,2} and also have been extensively investigated for various applications, such as controlled drug delivery system, personal care, industrial coatings, oil exploration, biological and membrane science, viscosity modifier, colloid stabilization, and water remediation.^{3,4} Such materials show pronounced property changes reversibly as a response to a small external stimulus such as temperature, added electrolyte, light, and changes in pH, electric field, or a combination of these.⁵ In nature, the change in behavior of a macromolecule is often a result of its response not to a single factor, but to a combination of environmental

changes.⁶ The area of polymers responsive to a single stimulus has been extended to polymers, which show a responsive behavior to multiple stimuli.^{7–9} So fabrication of materials, which can sense specific changes and respond to multiple stimuli in a predictable manner would be of great interest.¹⁰

Thermoresponsive polymers, one of the earliest studied stimuli-sensitive polymers, have been increasingly investigated during the past few decades because of the unique properties of lower critical solution temperature (LCST) or upper critical solution temperature (UCST). Poly *N*-isopropylacrylamide, pNIPAAm, is a well-known thermoresponsive polymer, which undergoes a dramatic swelling transition at its LCST, about 32°C in water. Below this temperature the polymer/gel is swollen, hydrated, and hydrophilic, whereas above the LCST, the polymer/gel shrinks and forms a collapsed, dehydrated, and hydrophobic state due to the breakdown of the dedicated hydrophilic/hydrophobic balance in the network structure. The phase transition collapse is reversible, and the LCST is easy to be controlled over by simple introduction of hydrophobic or hydrophilic moieties into the copolymer, which makes pNIPAAm receive much more attention.^{11–13} Meanwhile, the LCST behavior of pNIPAAm can also be affected by other factors, such as pH, light, solvent, ionic strength, and so forth, and these

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characters can be utilized to make “smart” materials. So there are many scholars have attempted to introduce some other materials into traditional pNIPAAm copolymers to make them dual-stimuli or multistimuli sensitive.^{14–17}

In the above factors, light has been taken into account as an external stimulus to induce the phase separation because of its ready accessibility and chemical purity. Actually, light can offer better spatial and temporal control to trigger the phase transition. Incorporating photochromic chromophores into polymers is intensively used to synthesize photoresponsive polymers or gels. Using this method, various photoresponsive polymers and polymer gels functionalized with azobenzene, leukochromophore, and spirobenzopyran have been being developed and play important roles in many fields. Thereinto, azobenzene and its derivatives are interesting photochromic chromophores because of their environmental stability, easy process-ability, and photosensitive behavior. On UV irradiation, the azobenzene groups undergo a transition of *trans*→*cis* configuration, which increases the solubility of the polymer due to less hydrophobic property. So the LCST of pNIPAAm can be changed by inducing isomerization of the azobenzene side chains. Desponds and Freitag reported the successful synthesis of the copolymer of NIPAAm with a small amount of photoisomerizable azobenzene derivatives, and another carboxylic-containing comonomer, which had been demonstrated to be multistimuli sensitive.¹⁸

Herein, we report a new study of triple-stimuli-responsive copolymer hydrogel, which combines thermo-, photo-, and pH-responsive properties in a single macromolecule. First, we fabricated a photo- and pH-sensitive comonomer, AEPZA, through a series reaction, i.e., diazo-coupling reaction, etherification reaction, and esterification reaction. Then we designed and fabricated copolymeric gels via free radical copolymerization of only two kinds of monomers, NIPAAm and AEPZA, which will obviously less affect the main properties attributed to NIPAAm units of the gels and make its responsive properties more convenience to be adjusted. The properties of the hydrogel were subsequently investigated by UV/Vis absorption spectrometry, differential scanning calorimetry, and gravimetry. We believe this type of copolymer hydrogel will be ideal candidates for various technological applications.

EXPERIMENTAL

Materials

N-isopropylacrylamide (NIPAAm, J and K Chemical Ltd., Shanghai, China) was used after purifying by recrystallization in mixed solution of hexane and

toluene (40/60 vol %) and dried under a vacuum. *N*-methylene-bis(acrylamide) (MBAAm, Sinopharm Chemical Reagent Co. Ltd., Shanghai, China) was used after purifying by recrystallization in methanol and dried under a vacuum. Triethylamine, phenol, tetrahydrofuran (THF), azobisisobutyronitrile (AIBN), and dimethyl sulfoxide (DMSO), were purchased from Shanghai Sinopharm Chemical Reagent Co. Ltd. and used without further purification. Hydrochloric acid (HCl, 36%), starch potassium iodide paper, anhydrous potassium carbonate (K₂CO₃), sodium nitrite (NaNO₂), sodium carbonate (Na₂CO₃), sodium hydroxide (NaOH) and potassium iodide (KI) were purchased from Shanghai Lingfeng Chemical Reagent Co., Ltd. and used without further treatment. Ethylene chlorohydrin and *p*-aminobenzoic acid were purchased from Shanghai Jingchun Reagent Ltd. Acryloyl chloride was synthesized in our lab.

General methods

- The ¹H-NMR spectra was recorded with a FT-NMR 300(300 MHz, bruker) spectrometer, and DMSO-d₆ was used as solvent.
- IR spectrum was measured with a Nicolet IS10 FTIR spectrophotometer.
- The UV/vis absorption spectra were measured by a ZF-1 UV spectrophotometer.
- UV irradiation was carried out with a 12 W ZF7 ultraviolet lamp (254 nm and 365 nm), which was purchased from Nanjing Keer Equipments and Instruments Co. Ltd. The distance between gel sample and irradiation source was about 10 cm.

Synthesis of 4-[(4-(acryloyloxy)ethoxy)phenylazo]benzoic acid (AEPZA)

4-[(4-hydroxy)phenylazo]benzoic acid

p-aminobenzoic acid (1.372 g, 0.01 mol), HCl (36%, 3 mL) were mixed in deionized water (12 mL). The mixture was cooled to 0°C over a salt-ice bath with constant stirring. After the mixture was completely dissolved, 1.035 g (0.015 mol) of NaNO₂ in 5.2 mL deionized water was added dropwise till the starch potassium iodide paper became blue to yield a solution of diazonium salt. The rate of addition was adjusted so that the temperature of the suspension was maintained at <5°C. Another mixture composed of phenol (0.941 g, 0.01 mol), NaOH (1.28 g, 0.032 mol), and deionized water (12 mL) was prepared and cooled in salt-ice bath to 0°C. The diazonium salt solution was then slowly added to the formed phenolate solution with constantly stirring for 60 min. The rate of addition was adjusted so that temperature of the resulting mixture was maintained at <5°C. A brownish-orange slurry mixture formed.

The slurry was stirred over the salt-ice bath for a further 3 h. The slurry was then neutralized by diluted HCl solution to pH = 2–3. The red–orange product that precipitated out was collected by filtration and washed with deionized water several times and dried in a vacuum oven at 37°C. The crude product was recrystallized from aqueous ethanol to produce 2.28 g 4-[(4-hydroxy)phenylazo]benzoic acid (yield 94%). ¹H-NMR(SO(CD₃)₂, TMD): δ = 7.49 (d, 2H), 8.01(t, 4H), 8.13(d, 2H).

4-[(4-hydroxyethoxy)phenylazo]benzoic acid

Exactly 3.42 g of 4-[(4-hydroxy)phenylazo]benzoic acid (0.01 mol), anhydrous K₂CO₃ (3.15 g), KI (0.1 g) and ethylene chlorohydrin (2.4 mL, 0.035 mol) were dissolved in 60 mL of DMSO, resulting in a dark red mixture. The mixture was heated to 110°C over an oil bath and stirred at this temperature for 7 h. After cooling at room temperature, a great deal of water was added and some diluted HCl was added to adjust the mixture to weak acidity, then the precipitate was collected by filtration. The solid obtained was redissolved in 100 mL weak alkaline water and 10 mL ethanol was added. The mixture was heated to reflux for 8 h. The crude product was precipitated by the addition of diluted HCl, collected by filtration, and washed with water till the filtrate neutrality, and dried over a vacuum oven at 37°C. The orange product, 4-[(4-hydroxyethoxy)phenylazo]benzoic acid was obtained. ¹H-NMR (DMSO-d₆): δ 8.12 (d, 2H), 7.93 (t, 4H), 7.17 (d, 2H), 4.12 (t, 2H), 3.75 (t, 2H).

4-[(4-(acryloyloxy)ethoxy)phenylazo]benzoic acid (AEPAZA)

Two grams of 4-[(4-hydroxyethoxy)phenylazo]benzoic acid (0.0049 mol) and triethylamine (2 mL) were dissolved in 39 mL THF. The mixture was cooled to 0°C over a salt-ice bath with constant stirring and a mixture of acryloyl chloride (3 mL) in THF (39 mL) was added dropwise. The rate of the addition was adjusted so that the temperature was maintained at <5°C through out the addition. After the addition, the resultant solution was stirred at room temperature for 24 h. Then, a great deal of water was added and the precipitate was collected by filtration. The solid obtained was redissolved in a little THF and some aqueous solution of NaHCO₃ was added to adjust the mixture to weak alkalinescence. The mixture was laid aside for 8 h. The crude product was precipitated by the addition of diluted HCl, collected by filtration, and washed with water till the filtrate neutrality, and dried over a vacuum oven at 37°C. ¹H-NMR (DMSO-d₆): δ 8.14 (d, 2H), 8.00 (t, 4H), 7.47 (d, 2H), 6.56 (d, 1H), 6.40 (m, 1H), 6.33 (d, 1H), 4.55 (t, 2H), 4.49 (t, 2H).

TABLE I
Feed Composition of Copolymer Gels

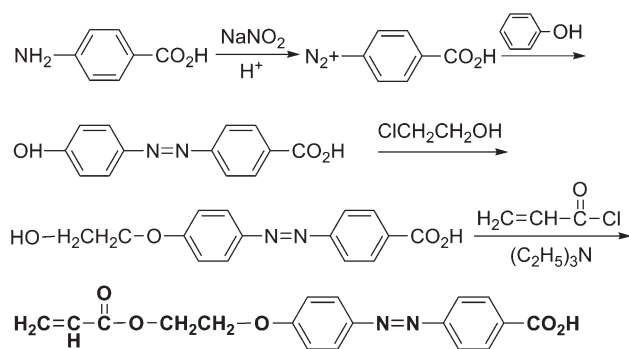
Sample	AEPAZA (g)	NIPAAm (g)	MBAAm (g)	AIBN (g)	DMSO (mL)
GelAEP0	0	0.151	0.004	0.008	0.3
GelAEP0.010	0.005	0.151	0.004	0.008	0.3
GelAEP0.019	0.010	0.151	0.004	0.008	0.3
GelAEP0.029	0.015	0.151	0.004	0.008	0.3
GelAEP0.001	0.003	0.906	0.024	0.046	1.5
GelAEP0 (UV-Vis)	0	0.906	0.024	0.046	1.5

Synthesis of triply-responsive hydrogel

Multiresponsive copolymer hydrogels was prepared via free radical copolymerization using MBAAm crosslinker. NIPAAm, AEPAZA, MBAAm, and AIBN were dissolved in DMSO. After the solids were completely dissolved, the mixture was degassed by bubbling with nitrogen for 15 min and transferred into some glass capillaries with 1 mm inner diameter. These capillaries were then placed in a 50°C oil bath for 12 h. After gelation, the gels were taken out and immersed in deionized water to wash away residual chemicals and unreacted monomers from the polymer networks for 7 d. The water was renewed every day. The feed composition of copolymer gels was showed in Table I. The number in sample name means the AEPAZA feed molar ratio (AEPAZA/(NIPAAm + AEPAZA + MBAAm), mol %). GelAEP0.001 and GelAEP0(UV-Vis) was prepared especially for the measurement of UV-Vis absorption spectra. They were prepared and treated in exactly the same way as the above except that the reactions were carried out in glass tubes with φ8 × 120 mm and the gels immersed for at least half-month. IR (KBr, cm⁻¹): σ = 3290 (m, —NH—, str), 1633(s, C=O, str), 1538, 1457 (s, benzene ring, str), 1171, 1130 (m, C—O—C, str).

Spectroscopic characterization and photoisomerization studies

Because of the less solvency of AEPAZA monomer in water, spectroscopic characterization of it was performed in DMSO solution. The photoisomerization studies of AEPAZA monomer was performed with 1 mg of the monomer in 3.0 mL DMSO. Spectroscopic characterization of copolymer hydrogel was performed in deionized water. Considered the range of the UV spectrophotometer, we prepared GelAEP0.001 and GelAEP0 (UV-Vis), as reference sample. Before measurement, the two hydrogel were chopped into thin slices (25 × 8 × 1.5 mm) respectively, then were put into two quartz cuvettes, and remaining space of the cuvette was filled with deionized water. These measurements were carried out for different ultraviolet light irradiation time from



Scheme 1 Synthetic routes of the azobenzene-containing monomer AEPaza.

0 to some time when the absorption peak no longer change at 25°C. Kinetics of the photoisomerization was analyzed by kinetic eq. (1)

$$\ln \frac{(A_0 - A_{ps})}{(A_t - A_{ps})} = kt \quad (1)$$

where A_0 , A_t , and A_{ps} , are the absorbance of the azobenzene chromophores at their correspondence wavelengths at time 0, t , and at the photostationary stage, respectively; k is the rate constant of the photoisomerization process.

Phase transition temperature studies

Phase transition temperature of copolymer hydrogels before and after UV irradiation were measured by differential scanning calorimeters (DSC, METTLER TOLEDO DSC823e) at a scanning rate of 5°C min⁻¹ from 0 to 50°C in nitrogen, the nitrogen gas flow rate was 30 mL/min. Sample weight was adjusted to within 20 to 23 mg, especially the error of two weights of same kind of hydrogel, the one was prepared for DSC measurement before UV irradiation, the other was for after UV irradiation, was controlled no more than 0.02 mg. The test of every sample was carried out thrice.

Swelling studies

The hydrogel was swollen to equilibrium over a range of temperature (24–40°C), the fluctuation of every temperature was within ±0.2°C, in deionized water. After swelling equilibrium was reached (~30 min each temperature, which was decided according to the swelling kinetics experiment data and Ref. 19), the hydrogel was removed from the deionized water, the excess surface solvent was lightly surface dried with filter paper, then weighted (m_h). The weight of xerogel, m_x , was obtained after drying the hydrogel in a vacuum oven at 40°C for 48 h. The equilibrium swelling ratio (SR) was obtained from eq. (2).

$$SR = m_h/m_x \quad (2)$$

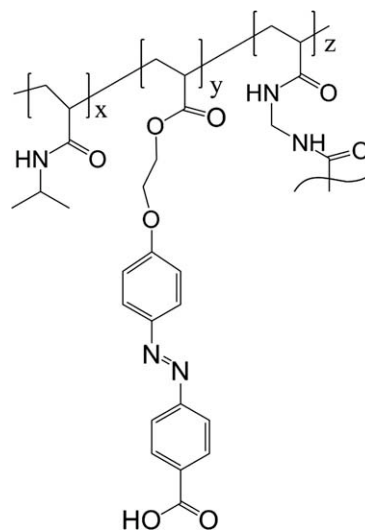
RESULTS AND DISCUSSION

Synthesis of comonomer AEPaza and copolymer gels

In this work, the azobenzene-containing monomer, AEPaza, was developed by a series reaction, i.e., diazo-coupling reaction, etherification reaction, and esterification reaction. The synthetic route was shown in Scheme 1, which was based on two modified literature method.^{20,21} In AEPaza molecule, the azobenzene groups made it hydrophobic, and the carboxyl groups partly counteracted this effect and made it water-soluble. Triply-responsive copolymer gels were prepared by facile free radical copolymerization of NIPAAm, AEPaza, and MBAAm. So the gels contained three types of monomeric units, NIPAAm units, chromophore-bearing units, and little MBAAm units, Scheme 2. The formed gels were transparent yellow colloid in water (Supporting Information, Fig. S1). The ¹H-NMR characterization of AEPaza, the FT-IR, and UV-vis characterizations of the copolymer gels confirmed the successful synthesis of AEPaza and incorporation of it into the cross-linked copolymer gels. Detailed characterization can be found in the supporting information (Supporting Information, Fig. S2, S3).

Spectroscopic characterization of AEPaza and the copolymer hydrogel

Photoisomerization is characteristic of azobenzene-containing monomer AEPaza. Azobenzene groups are mainly in the stable *trans* conformation in nature, and which can be evidenced by a strong absorption peak at about 363 nm connected with the $\pi \rightarrow \pi^*$



Scheme 2 Chemical structure of the triply-responsive gel.

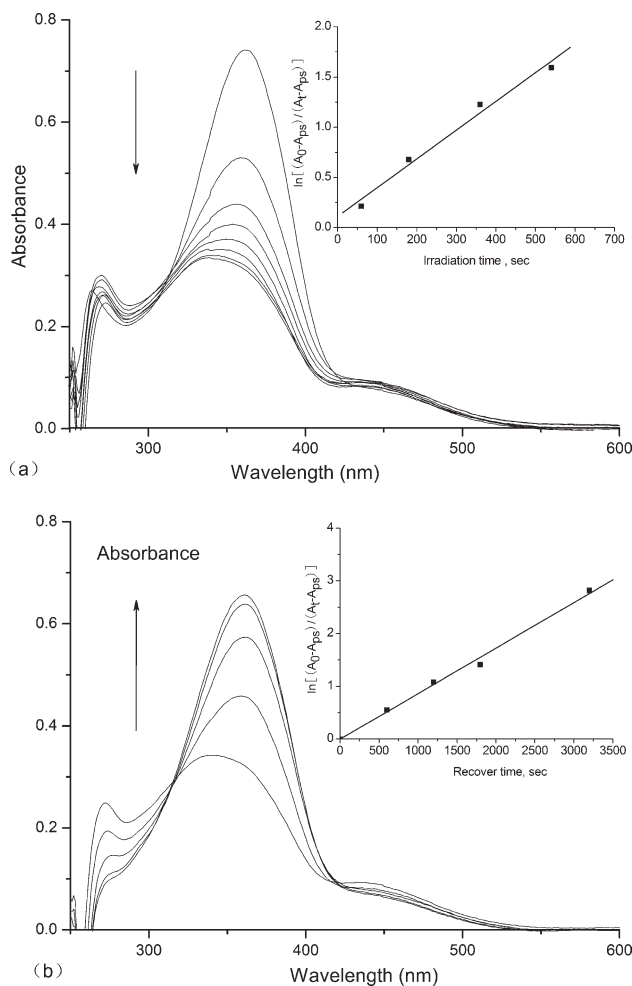


Figure 1 UV-Vis spectral changes upon photoisomerization of AEPZA (0.86 mM) in DMSO: (a) *trans*→*cis* photoisomerization upon UV irradiation; (b) *cis*→*trans* photoisomerization in dark situation. Kinetics of the photoisomerization processes are shown in the insets. Rate constants for the *trans*→*cis* and *cis*→*trans* photoisomerization are measured to be $2.9 \times 10^{-3} \text{ s}^{-1}$ and $9 \times 10^{-4} \text{ s}^{-1}$.

electronic transition in the UV-Vis absorption spectra of AEPZA. Upon UV irradiation, the *trans* conformation switch to *cis* conformation, then the absorption peak aroused by $\pi \rightarrow \pi^*$ electronic transition become smaller and smaller, and at the same time the absorption peak at 440 nm connected with $n \rightarrow \pi^*$ electronic transition become strong a little. Take off the UV light or replaced by visible light irradiation, the *cis* change to *trans*. Figure 1 shows the spectral changes of AEPZA upon UV (a) and visible light (b) irradiation in DMSO. The spectra showed two main bands, a major one at 363 nm and a small one at 440 nm. Upon irradiation, the major band gradually decreased and shifted to slightly shorter wavelength ($\sim 358 \text{ nm}$), the small one increased slightly. The changes, aroused by the transformation from *trans*- to *cis*- in azobenzene groups, became slower and slower with increasing irradiation time till to a

state, in which the change between *trans* and *cis* configuration were dynamic balance. The isomerization rate constants of AEPZA are comparable to other azobenzene chromophores in literature.^{14,22,23} Figure 2 shows the spectral changes of copolymer gels upon UV irradiation in water, which also gave convincing evidence for the successful synthesis of the azobenzene-containing copolymer gel. The photoisomerization behavior was obstructed when AEPZA was incorporated into the crosslinked polyacrylamide hydrogel matrices because the azobenzene groups' mobility was limited by the molecular network, so the *trans*→*cis* photoisomerization rate of the copolymer hydrogel, $1.4 \times 10^{-3} \text{ s}^{-1}$ in Figure 2, was a little less than that of AEPZA monomer, $2.9 \times 10^{-3} \text{ s}^{-1}$ in Figure 1.

Phase transition temperature of the hydrogel

An important and useful feature of pNIPAAm is the possibility of controlling its phase transition temperature by various means, in particular, by varying the monomer composition. In general, incorporation of azobenzene-containing comonomer leads to a lower LCST. And the decrease can be counterbalanced by UV irradiation. Such a tendency was observed in our research work, which agrees with the reported result.^{18,24–26}

Figure 3 shows the phase transition temperature curves of the copolymer hydrogels with different AEPZA content before (solid line) and after (broken line) UV irradiation. From the Figure 3, we know the phase transition occurs not at a single temperature but at a temperature range and it is easy to find the peak temperature, so here we adopt the

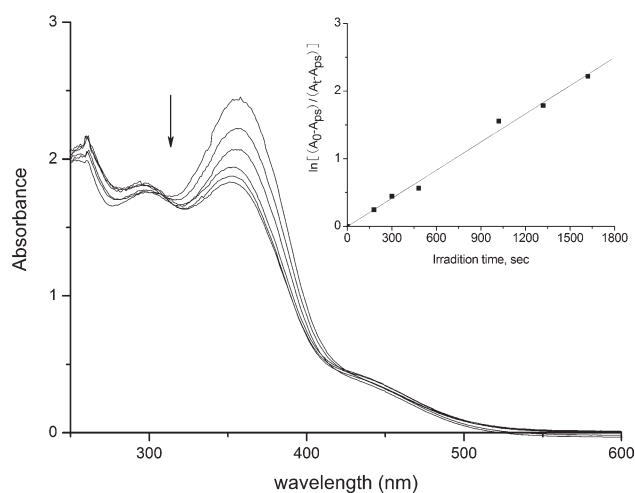


Figure 2 UV-Vis spectral changes upon photoisomerization of GelAEP0.001 in water: *trans*→*cis* photoisomerization upon UV irradiation. Kinetic of the photoisomerization process is shown in the inset. Rate constant for the *trans*→*cis* photoisomerization is measured to be $1.4 \times 10^{-3} \text{ s}^{-1}$.

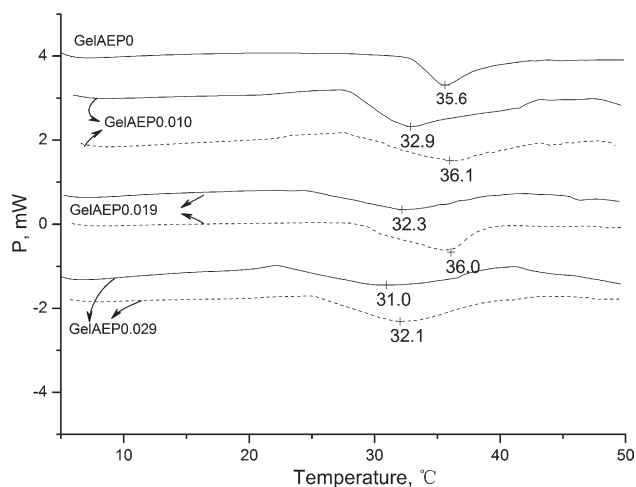


Figure 3 Phase transition of the hydrogels measured by DSC before (solid line) and after (broken line) UV irradiation.

peak temperature as CST to analyze the phase transition of the hydrogels. Compared with the CST of pure pNIPAAm hydrogel, 35.6°C, the phase transition peak temperature of the copolymer hydrogel shifted to lower temperature side. Increasing the amount of incorporated AEPAZA led to a continue decrease in the CST. Indeed, the phase transition temperature depends on the subtle balance between the hydrogen bond formation ability of the polymer with water and the intermolecular hydrophobic forces.²⁷ By introducing the AEPAZA moieties into the copolymer, the intra- and intermolecular hydrophobic interaction is enhanced and the copolymer gel become less hydrophilic to shrink at a lower temperature.²⁸ As a result, the above observations showed that the CST of the copolymer hydrogels strongly depends on the comonomer constitutions. In addition, the incorporation of AEPAZA made the copolymer gel less temperature sensitive and exhibited a slower and broader phase transition curve as shown in Figure 3. The tendency became more and clearer with increasing the AEPAZA content, which also was consistent with the previously reported results.^{9,29,30} Hence, both the shift of the CST and the broader phase transition curve gave evidences that the join of the AEPAZA had a significant impact on the phase transition.

The photoinduced isomerization of azobenzene chromophore may cause large structural changes in the molecules, which are reflected by changes in the physicochemical behavior. In particular, the distance between the para carbon atoms in azobenzene changes from ~ 9 Å in the *trans* to 5.5 Å in the *cis* form. *Trans*-azobenzene has no dipole moment, while the dipole moment of *cis*-azobenzene benzene is 3.0 D,³¹ which induces higher hydrophilicity.³² So a photo-effect on the hydrophilicity is expected as a

result of the *trans* to *cis* isomerization of the azobenzene groups in the side chains of the hydrogel upon UV irradiation. To contrast the phase transition curves of GelAEP0.010, GelAEP0.019, and GelAEP0.029 before UV irradiation with that of after UV irradiation, the CST increased 3.2°C, 3.7°C, and 1°C, respectively, when the azobenzene groups were in the *cis* conformation compared with the same molecule in the *trans* conformation, Figure 3. The onset of the phase transition temperature of each hydrogel upon irradiation also shifted to higher temperature. And a narrow phase transition curve was found upon irradiation. It was noted the CST of GelAEP0.029 increased only 1°C. This was probably due to the deficient optical transparency of GelAEP0.029. With increasing of AEPAZA monomer, the hydrophobicity of the hydrogel increased, the hydrogel shrank, and so the colors of the hydrogels became darker and darker (Supporting Information, Fig. S1), the optical transparency became bad. Overall, the above studies suggested that the temperature-induced phase transition and the hydrophilicity of hydrogels can be efficiently controlled by electromagnetic irradiation.

From Scheme 1, there are carboxyl groups in AEPAZA molecular, which should impart some polyelectrolyte behavior to the copolymer gel. In an electrolyte solution, the phase transition of the copolymer gels is determined by various coexistent intra- and intermolecular forces, such as van der Waals force, hydrogen bonding, hydrophobic interaction, and electrostatic force.³³ These forces can exert counter effects or coeffects on the copolymer gels, and depending upon the conditions, some forces can dominate the behavior of the gels. For example, the hydrophobic interaction that determines the phase transition of the polymer gel could be canceled out by the electrostatic force when the $-\text{COOH}$ groups are highly ionized.^{34,35} Figure 4 depicts the pH influence on the phase transition of GelAEP0.010. It could be perceived, the transition curves shifted as the pH value of buffer solution changed. At pH 6.9, the CST is 32.9°C, which shifted to 31.4°C at pH 2.4, and 34.4°C at pH 12. At pH 12, the $-\text{COOH}$ groups in the AEPAZA units were highly ionized, and the electrostatic repulsion of these negative charges partly canceled out the hydrophobic interaction groups that determine the phase transition of the polymer gel, so prevented GelAEP0.010 from collapse and made the phase transition occur at higher temperature. At the same time, the ionized $-\text{COO}^-$ groups also affected the phase transition curve and made it sharpness. At pH 6.9, the charges were partly diminished, contributions from both hydrophobic interaction and electrostatic force were expected. When the charges were mostly eliminated by the protonation of the $-\text{COO}^-$ groups at pH 2.4,

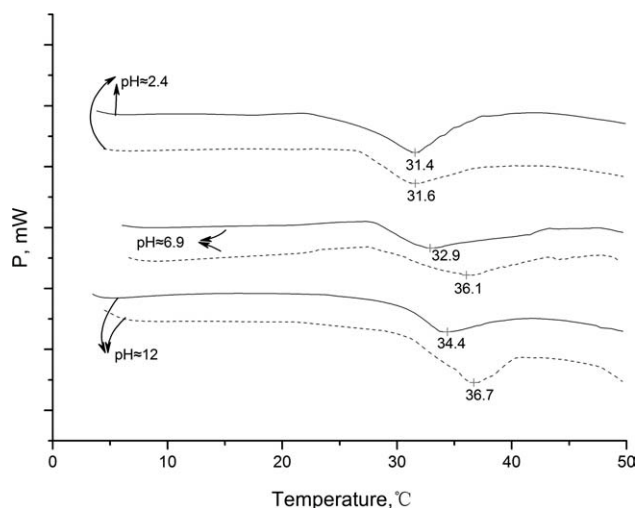


Figure 4 Phase transition of the GelAEP0.010 in different pH buffer solution before (solid line) and after (broken line) UV irradiation.

the “electrostatic repulsion” within the copolymer gels lost, the hydrophilic $-\text{COO}^-$ groups became hydrophobic $-\text{COOH}$ groups, the predominant of hydrophobic interaction recovered, so the gel network collapsed at lower temperature. Such a tendency was also observed in Ref. ¹⁸. In addition, comparing the transition curves of the three samples before and after UV irradiation, the phase transition peak temperature shifted to a higher value after irradiation, which conveyed the temperature-induced phase transition could be efficiently modulated by pH and UV light at the same time. But in particularly, the quantity of the shift was different at different pH buffer solutions, and the CST increased only 0.2°C at pH 2.4. A possible explanation was that in the pH 2.4 media, AEPZA units were in a collapsed status, which limited the isomerization of the azobenzene groups.

According the above studies, it could be concluded that AEPZA incorporated in the copolymer gels contributed to the photo and pH dependence of the CST. Although the rationales behind the present observations of the pH- and photo-effect on the CST of the copolymer gels are more complex and deserve further studies, the regularity of the phase transition shift allows for facile tuning of the CST of the copolymer gels to a desired value, which is very important from an application point of view.

Equilibrium swelling ratio (SR) and swelling kinetics of the hydrogel

Equilibrium swelling ratios of the hydrogels in deionized water measured as a function of temperature, with and without UV irradiation, are shown in Figure 5. As shown in Figure 5, the equilibrium swelling ratios of GelAEP0, GelAEP0.010, and

GelAEP0.029, no matter with and without irradiation, all decreased sharp, underwent a continuous transition when the temperature raised from 24 to 36°C , and tended to accordance value when the temperature above 36°C . Comparing the curves of GelAEP0.010, GelAEP0.029 with GelAEP0, with increase of AEPZA content, the equilibrium swelling ratio became smaller and smaller, e.g., the value was 10 (GelAEP0), 8.2 (GelAEP0.010), and 5.9 (GelAEP0.029), respectively, at 19°C . At the same time, the curves became more and more smoothness, which conveyed that the join of monomer AEPZA could significantly change the swelling ability of the copolymer gel in water below CST. Upon UV irradiation, the hydrophobic *trans*-azobenzene chromophore switched to relatively hydrophilic *cis* configuration, which partly counterbalanced the effect of the azobenzene, and greatly increased the swelling ratio of the copolymer gels in temperature interval from 24 to 32°C . So, it was inferred that the irradiation could also efficiently control the swelling ability of GelAEP0.010 and GelAEP0.029 in water.

The effect of the pH on the equilibrium swelling ratio of GelAEP0.010 at 20°C are shown in Figure 6. The swelling ratio increased with an increase of pH value of the buffer solution. In the pH 10 media, ionization of the carboxyl groups led to an increase of the hydrophilicity and osmotic pressure of the networks. The expansion of electrostatic repulsion between the charged $-\text{COO}^-$ groups destroyed the hydrophobic microdomain formed by the hydrophobic interactions of the side chains.³⁶ On the contrary, in pH 2 media, carboxyl groups were not ionized and existed as $-\text{COOH}$, which increased the hydrophobic interactions and hydrogen bonding between

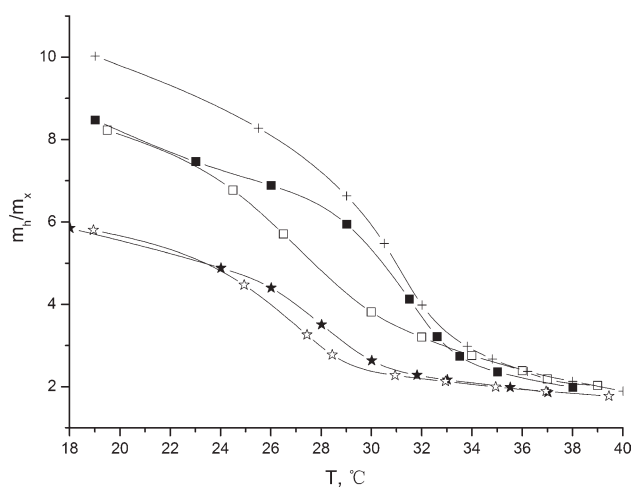


Figure 5 Equilibrium swelling ratios of hydrogels at different temperature without (GelAEP0, +; GelAEP0.010, □, and Gel AEP0.029, ☆) and with (GelAEP0.010, ■ and Gel AEP0.029, ★) UV irradiation.

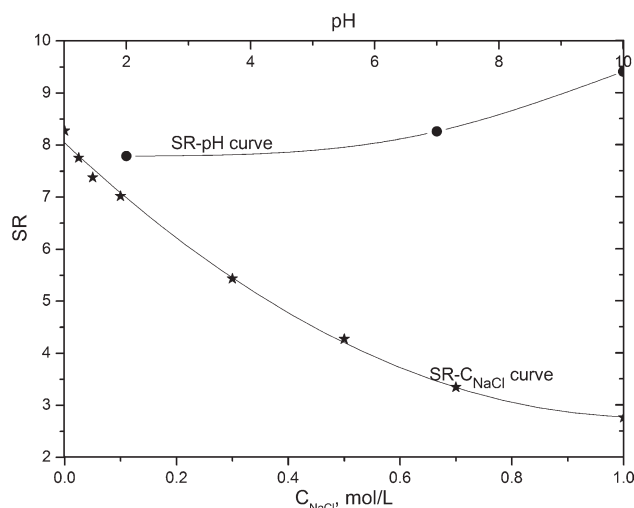


Figure 6 Equilibrium swelling ratio of GelAEP0.010 in different pH aqueous solutions/different NaCl concentration solutions at 20°C.

the carboxylic and amide groups of the copolymer chains, so the hydrophilicity decreased and the equilibrium swelling ratio was lower which is in accord with other reports.³⁷ As a result, the value of swelling ratio was much higher than that of in pH 2.

As aforementioned, the copolymer gels exhibited behavior of weak polyelectrolyte. The pH effect on the phase transition and equilibrium swelling ratio would be confounded with the effect of electrolytes. Figure 6 also shows the equilibrium swelling ratio of GelAEP0.010 as function of NaCl concentration at 20°C. It can be seen that the ionic strength affected them obviously. As the ionic strength increased from 0 to 0.3M, the equilibrium swelling ratio decreased 34.4%. The reasons could be that the addition of NaCl could increase the polarity of the aqueous media thus enhancing the hydrophobic-hydrophobic interactions. The stronger hydrophobic-hydrophobic interaction indicated the stronger tendency for the copolymer gel to self aggregate, a feature that would result in a less hydrophilic of the copolymer in water.²⁹ Here, the curve of equilibrium swelling ratio of GelAEP0.010 in different NaCl concentration solutions was expected to be used to evaluate the effect of ionic strength, especially when the ionic strength of the solution was about or less than that of physiological saline.

CONCLUSIONS

In this work, we reported a facile and reproducible method of preparing the triply-responsive random copolymer gels based on *N*-isopropylacrylamide. The phase transition of copolymer gels in water was tunable. It could be modulated not only by the

amount of the AEPZA in the copolymer network but also by light irradiation because of the photoisomerization of azobenzene groups in the side chain, which undergone *trans*→*cis* photoisomerization on exposure to UV light and therefore led improvement of hydrophilicity of the hydrogel. Moreover, the copolymer hydrogel had a reasonable *trans*-*cis* photoisomerization rate upon UV irradiation and a relatively slow recovery rate in dark. Because there were carboxyl groups in AEPZA moieties, the phase transition of the copolymer gels could also be affected by the pH value of the aqueous buffer. In addition, the equilibrium swelling of the copolymer gels in water could be regulated by temperature, UV irradiation, and pH. Hence, these copolymer gels were triply-responsive, thermo-, photo-, and pH-responsive, which would advantage their application in material science.

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