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Surface-Ionized thermosensitive poly(*N*-isopropylacryl amide) hydrogels with faster response

*Xin-Cai Xiao**

School of Life Sciences, South-Central University for Nationalities, Wuhan, 430074, China. Fax: +86-27-6784-2689; xiaoxincai@mail.scuec.edu.cn

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Abstract: Poly(*N*-isopropylacrylamide) hydrogels have been successfully modified by concentrated sulfuric acid for the first time. The modified hydrogels displayed faster, larger magnitude and hydration/dehydration dynamic response to temperature cycling without increasing the lower critical solution temperature (LCST). These contributions were attributed to sulphate ester groups resulting from terminal hydroxyl groups of poly(N-isopropylacrylamide). These results may lead to technological application for temperature-responsive thin film and microgel particles with higher surface-to-volume ratio.

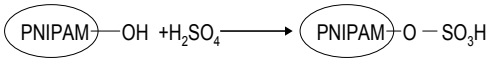
Introduction

Stimuli-sensitive hydrogels, which exhibit volume or phase transitions in response to slight environmental changes, such as temperature, pH, ionic strength, light, electric and magnetic fields, etc., are called intelligent materials [1]. Because there are many cases in which environmental temperature fluctuations occur naturally and in which the environmental temperature stimuli can be easily designed and artificially controlled, in recent years much attention has been focused on thermoresponsive hydrogels [2, 3]. Chemically crosslinked poly(*N*-isopropylacrylamide) (PNIPAM) is a typical temperature-sensitive hydrogel. It has a transition temperature or lower critical solution temperature (LCST) around 32 °C resulting from rather complex polarity of this molecule. Below the LCST, the amide functionality binds water molecules via hydrogen bonding, thus imparting both water solubility and surface activity. However, moving above the transition temperature breaks these hydrogen bonds, and the polymer expels water molecules and undergoes a coil-to-globule transition, thereby precipitating and forming particles [4-5]. This useful property has been used in numerous fields, including drug delivery [6-7], chemical separations [8-9], chemical transducer [10-11], enzyme and cell immobilization [12-13].

It is well known that conventional PNIPAM hydrogels has a slow response rate to temperature changes [14], limiting its applications in many fields such as “smart” actuators and on-off switches. Many investigators have made significant efforts to develop thermal sensitive PNIPAM hydrogels with rapid shrink/swell property. For example, preparing the gels at temperatures above the LCST results in a phase-separated structure and can enhance the shrinking rate greatly [15-16]. The introduction of dangling chains into the PNIPAM hydrogels network improves the shrinking kinetics properties [17-18]. Gas blowing [19] and applying radiation lead to porous structures of the resultant hydrogels [20]. To achieve a high temperature-response rate, Zhuo’s group has utilized different methods to synthesize PNIPAM hydrogels, such as carrying out polymerizations in mixed solutions [21], using

poly(ethylene glycol)s as pore-forming agents [22-23], interpenetrating poly(vinyl alcohol) within the hydrogels network [24], and using aqueous sodium chloride solution as the reaction medium for gel preparation [25]. All approaches can increase the response rate greatly.

Preparing copolymers by incorporating hydrophilic monomer such as acrylic acid or acrylamide to NIPAM is also a method. The final results show the increase of the LCST of hydrogels and the decrease of the rate of the phase transition with the increase of hydrophilic monomer dosage [26-28]. Because these comonomers are composed of hydrophilic and hydrophobic groups, hydrophilic–hydrophobic balance of the polymers plays an important role in thermoresponsive rate and change of the LCST. Guilherme reported that the terminal groups of the hydrogels prepared in their work are hydroxy groups resulting from cleavage of persulfate initiator [29]. In this work, we only considered influence of hydrophilic groups using these results. We modified PNIPAM hydrogels by sulfuric acid and expected that esterification reaction was performed between hydroxyl groups and concentrated sulfuric acid according to the following mechanism:



In other words, sulfonic acid groups, a strong ion, will be introduced to the end of PNIPAM chains and we expected polymer with this new structure had faster sensitive rate.

Results and discussion

Figure 1 shows the equilibrium swelling ratios of hydrogels as a function of the external temperature. At lower temperatures, these hydrogels absorbed water and became swollen. As the temperature increased, all hydrogels exhibited a similar temperature-dependence that lost water and shrank in volume and it was clear that LCSTs of hydrogels lay in the vicinity of 32 °C.

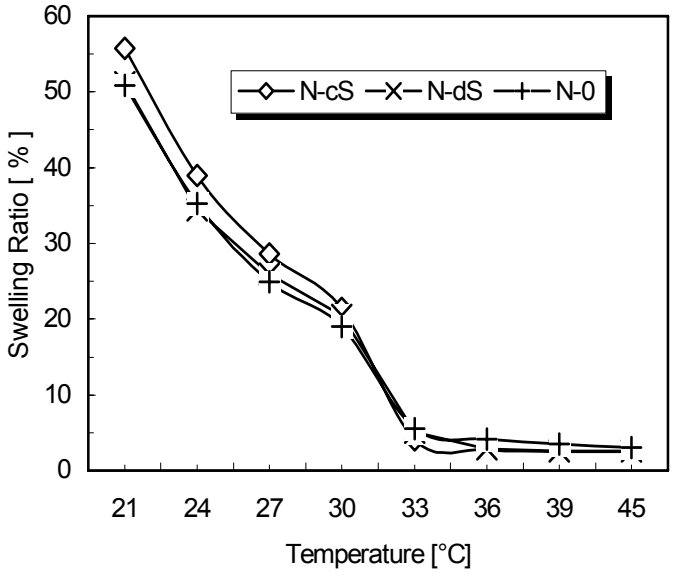
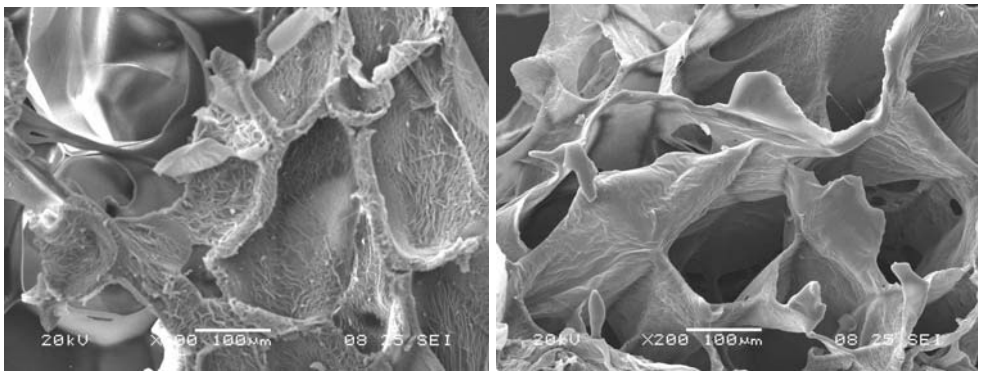


Fig. 1. Equilibrium swelling ratio of the normal hydrogels and the modified hydrogels at different temperatures.

When the temperature increased above the hydrogels' LCSTs, the swelling ratios of hydrogels decreased rapidly and a phase separation occurred. For normal hydrogels and its corresponding modified hydrogels, at lower temperature, the swelling ratio of hydrogels modified at 60 °C was as nearly similar as that of the normal hydrogels, while the swelling ratio of the hydrogels modified at 120 °C was higher than that of the normal hydrogels. This phenomenon is nearly same as previous research which show increasing ion content only increased swelling without impacting the LCST after a certain pH [31].

According to presumption, We investigated the internal morphologies and chemical compositions with SEM and FT-IR spectroscopy methods, respectively, of the hydrogels to test whether sulfonic acid groups incorporate to the end of PNIPAM chains. SEM images (Figure 2) show the internal morphologies hardly changes between the normal hydrogels and the hydrogels modified at 120 °C. We observed that the hydrogels kept shrinking and became stiff under acidic and thermal conditions during the modifying process, so we thought that the internal microstructures were protected by shrinking state of hydrogels.



(a) (b)

Fig. 2. SEM micrographs of (a) the normal PNIPAM hydrogel prepared in dimethyl sulphoxide media and (b) the corresponding hydrogel modified at 120 °C (Scall bar 100µm).

Figure 3 shows the FT-IR spectra of the normal hydrogel (N-0), the hydrogels modified at 120 °C (N-cS) and its interior (N-In) and the hydrogels modified at 60 °C (N-dS). We find that the IR spectra of all hydrogel samples are similar. Every spectrum shows the stretching vibrations of C=O, N-H and CH_3-CH-CH_3 which are the typical groups of PNIPAM at 1657 cm^{-1}, 1547 cm^{-1} and 1366 cm^{-1}, respectively. All samples also show hydroxyl group (O-H, 3436 cm^{-1}) maybe resulting from bond water and/or the cleavage of persulfate initiator. It is interesting that a distinctly different absorption band at 1041 cm^{-1} is observed for the surface of hydrogel modified at 120°C compared with that of N-In and the surface of N-dS. It is this band that is the characteristic adsorption peak of sulfonic acid groups. When the modification temperature is at 120 °C for 8 h, the water evaporation causes sulfuric acid solution to concentrated state from dilute as experiment proceeds and hydrogels keeps shrinking and becomes stiff at this environment; esterification reaction between hydroxyl groups resulting from cleavage of persulfate initiator [29] and concentrated sulfuric acid only happened on the surface of hydrogels, which can explain the sulfonic acid group appear on the surface of N-cS and is incorporated to the end of PNIPAM chains.

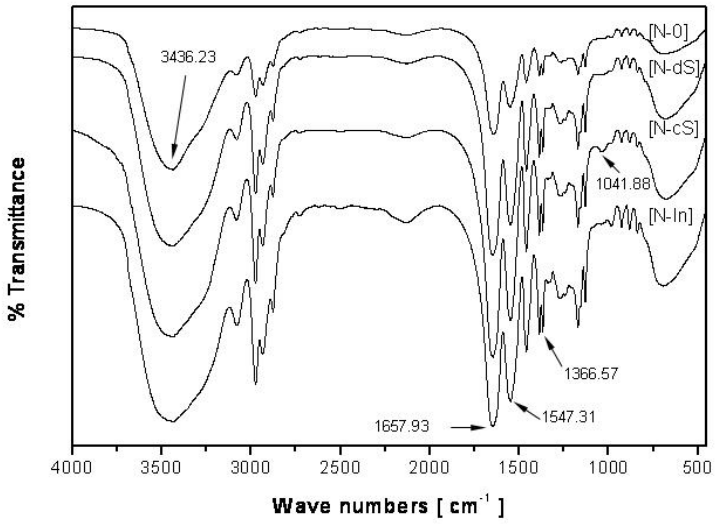


Fig. 3. KBr FT-IR spectra of the normal hydrogel (N-0), hydrogel modified at 120 °C (N-cS) and its interior (N-In), hydrogel modified at 60 °C (N-dS).

Because the sulphate ester groups (-SO_4H) is strongly ionizable and dissociates completely over the whole pH range, and its introduction largely increases hydrophilicity and charge repulsion of hydrogels compared with hydroxyl groups, consequently water uptake increases, which can be used to explain the swelling ratio of hydrogels modified at 120 °C being higher than that of the normal hydrogels. Because hydrogels are bulk gels in this work, so molar ratio of sulphate ester groups on the surface to the total hydroxyl groups can be speculated to be very low, which caused the difference to be not so obvious.

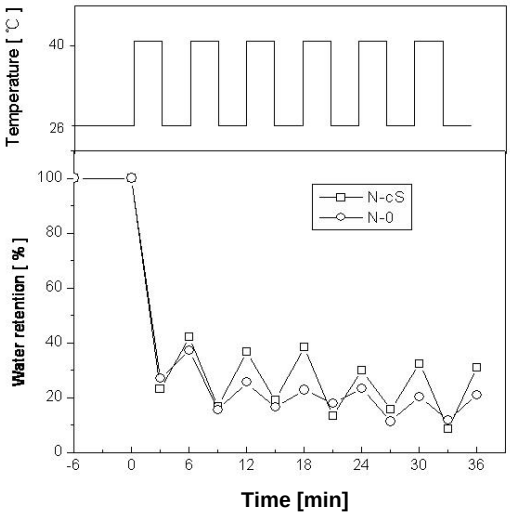


Fig. 4. Oscillatory shrinking–swelling kinetics for the normal hydrogel (N-0) and modified hydrogel (N-cS) over 3 min temperature cycles in double-distilled water between 26 and 40 °C.

Figure 4 displays the oscillatory hydration-dehydration kinetics of the normal hydrogels (N-0) and the corresponding modified hydrogel (N-cS) over the 3 min temperature cycles between 26 (below LCST) and 40 °C (above LCST) in double-distilled water.

This 3 min cycle was continued for a total 6 cycles (36 min) in order to determine response of modified hydrogel to temperature. It is found that, although both hydrogels exhibited an oscillatory hydration/dehydration character upon cycling temperature between 26 and 40 °C and their shrinking-swelling cycles were accompanied by a consecutive reduction in water content, the N-cS exhibited much more rapid, sharp and larger magnitude hydration/dehydration changes compared with N-0.

Conclusions

We have successfully modified poly(*N*-isopropylacrylamide) hydrogels by concentrated sulfuric acid for the first time. The resulting hydrogels presented faster, larger magnitude and hydration/dehydration dynamic response to temperature cycling without increasing the lower critical solution temperature. These contributions were attributed to sulphate ester groups resulting from terminal hydroxyl groups of poly(*N*-isopropylacrylamide). This work may lead to technological application for temperature-responsive thin film and microgel particles with higher surface-to-volume ratio.

Experimental part

Materials

The *N*-isopropylacrylamide (NIPAM) was kindly provided by Kohjin Co., Ltd., Japan, and was used after purifying by recrystallization in hexane and acetone and then drying *in vacuo* at room temperature. The solvent dimethyl sulfoxide (DMSO), the initiator ammonium persulfate (APS), the accelerator *N,N,N',N'*-tetramethylethylenediamine (TEMED), the modificator concentrated sulfuric acid and the crosslinker *N,N'*-methylenebisacrylamide (MBA) were of analytical grade and used as supplied by Shanghai Chemical Co. (Shanghai, China) without any further purification. Double-distilled water was used in all the synthesis processes.

Preparation of the hydrogels

The conventional PNIPAM-based macrogels were prepared by free radical polymerization. In this work, PNIPAM hydrogels were prepared in DMSO and their preparation processes were similar to that published previously [30]. Briefly, 0.4 g of NIPAM monomer, 8.0 mg of MBA and 40.0 mg of APS were dissolved in 4 ml of DMSO to form a monomer solution and the free radical polymerization was carried out in a glass bottle of 30 mm in internal diameter at room temperature.

After mild shaking for a few minutes, 120 µl of TEMED was added into the monomer solution to initiate the radical polymerization. The polymerization was continued for 72 h. After the polymerization, the prepared hydrogels were immersed in double-distilled water at room temperature for at least 48 h and the water was regularly refreshed in order to remove unreacted compounds. The PNIPAM hydrogels thus obtained were designated as the normal hydrogel. After drying in freezer, the hydrogels were cut into disc-like pieces approximately 6 mm in diameter and 4 mm in thickness for the following studies.

Modification of the hydrogels

After two pieces of disc-like hydrogels in respective cups being adequately swollen in double-distilled water, 5 ml of dilute sulfuric acid (10%, V/V) was added into each cup. Then one mixture was heated at 120 °C while another was heated at 60 °C, and both

modification time were 8 h. Finally the products were immersed in double-distilled water at room temperature for at least 48 h and the water was refreshed every few hours. The modified hydrogel obtained were designated as N-cS (at 120 °C) and N-dS (at 60 °C), respectively.

Measurement of swelling ratio of the hydrogels

For the equilibrium swelling ratio study, PNIPAM hydrogels were swollen in double-distilled water in the temperature range from 21 °C to 45 °C, which covers the expected range of LCST of the PNIPAM hydrogels. The gravimetric method was employed to study the hydrogels' swelling ratio. After soaking into distilled water at each testing temperature for at least 8 h, the hydrogel samples were removed and blotted with wet filter paper to remove excess water on the hydrogels surface and weighed. After measurement at one temperature, the hydrogels were re-equilibrated at another predetermined temperature for subsequent swelling ratio measurement. The average values among three measurements were taken for each sample and the equilibrium swelling ratio is calculated as follows [30]:

$$\text{Swelling ratio (SR)} = [W_t\text{-}W_d]/W_d \quad (1)$$

Where W_t is the weight of the hydrogel at each testing temperature and W_d is the dry weight of hydrogels after drying in vacuum.

Morphological analysis

Morphology is a critical factor to analyze final result. In this work, the morphologies of the normal and modified hydrogels were observed by a scanning electron microscope (SEM; Hitachi S-450, Japan) operating at an accelerating voltage of 20 kV. All samples were mounted on a copper stub and sputter-coated with gold to minimize charging.

Compositional analysis

Chemical compositions of hydrogels were analyzed by Fourier transform infrared (FT-IR) spectroscopy using a KBr method (Nicolet MX-1E, USA).

Measurement of the oscillatory hydration-dehydration kinetics of the hydrogels

To detect modified hydrogels with a fast response, the oscillatory hydration-dehydration kinetics of the normal hydrogels and the corresponding modified hydrogels over the 3 min temperature cycles between 26 (below LCST) and 40 °C (above LCST) in double-distilled water were examined gravimetrically. Water retention of wet hydrogel is defined as follows [30]:

$$\text{Water retention} = [W_t\text{-}W_d] / [W_{t0}\text{-}W_d] \times 100 \quad (2)$$

Where W_{t0} is the weight of the swollen hydrogels at a predetermined time at 26 °C and other terms are the same as defined above in the swelling ratio.

Acknowledgements

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