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# Synthesis and characterization of thermo-sensitive poly (*N*-isopropylacrylamide) hydrogel with fast response rate

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**Abstract** Thermo-sensitive poly (*N*-isopropylacrylamide) (PNIPA) hydrogel with fast response rate was prepared by polymerizing *N*-isopropylacrylamide (NIPA) in an aqueous hydroxyl-propyl-methyl cellulose solution. The volume phase transition temperature of PNIPA hydrogels was characterized by differential scanning calorimetry (DSC), and the surface morphology was observed by scanning electron microscopy (SEM). The swelling ratios of the hydrogels at different temperatures were measured. Furthermore, the deswelling kinetics of the hydrogels was also studied by measuring their water retention capacity. In comparison with a conventional PNIPA hydrogel prepared in water, the hydrogel synthesized in aqueous hydroxyl-propyl-methyl cellulose solution has higher swelling ratios at temperatures below the lower critical solution temperature and exhibits a much faster response rate to temperature changes. For example, the hydrogel made in aqueous hydroxyl-propyl-methyl cellulose solution lost 89% water within 1 min and about 93% water in 4 min, whereas the conventional hydrogel lost only about 66% water in 15 min from the deswelling measurement in similar conditions.

**Keywords** *N*-isopropylacrylamide, hydrogel, thermo-sensitive, fast response

## 1 Introduction

Poly(*N*-isopropylacrylamide) (PNIPA) is a typical thermo-sensitive polymer and exhibits a lower critical solution temperature (LCST) of about 33°C [1,2]. Below the LCST,

PNIPA hydrogel is well swollen in water. As the temperature increases above the LCST, it shrinks abruptly and loses majority of the water absorbed, displaying phase separation. The special swelling property of the PNIPA hydrogel has been applied in many fields, such as controlled drug release and the immobilization of enzymes [3,4]. However, the response rate of the conventional PNIPA hydrogel is very slow, and greatly limits its applications in some specific fields, such as artificial muscles and on-off switches, in which a high response rate is required. Therefore, it is important to enhance the response rate of the PNIPA hydrogel. Several strategies to increase their response dynamics have been reported [5–18]. Gehrke et al. [5] and Hoffman et al. [6] synthesized a fast responding PNIPA hydrogel with heterogeneous structure using phase separation technique. Okano et al. [7,8] prepared a PNIPA hydrogel with fast deswelling rate by introducing PNIPA chains grafted on the backbone PNIPA network. Zhuo et al. obtained a PNIPA hydrogel that responds rapidly by cold-treatment of the gel network [9], cold polymerization/crosslinking [10,11] or using a pore-forming agent during polymerization [12]. Zhuo et al. also acquired PNIPA hydrogels, the response rates of which were remarkably increased by utilizing different reaction media such as mixed solvents [13–15], aqueous NaCl [16] or saccharide [17,18] solution.

Hoffman et al. [6] synthesized macroporous PNIPA hydrogels at a temperature above the LCST of NIPA and hydroxyl-propyl cellulose (HPC, the LCST of which is 50°C) by evacuation of the reactor near the end of polymerization, making use of the gel effect of the HPC precipitating above its LCST during polymerization. We have prepared a new type of thermo-sensitive PNIPA hydrogel in aqueous hydroxyl-propyl-methyl cellulose (HPMC) solution at a low temperature (15°C) by polymerization/crosslinking. The volume phase transition temperature of PNIPA hydrogels was characterized by differential scanning calorimetry (DSC), and the swelling ratios were measured at different temperatures. We also studied the surface morphology of the PNIPA hydrogels by scanning electron microscopy (SEM), and the deswelling kinetics of the hydrogels by measuring their water retention.

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## 2 Experimental

### 2.1 Materials and instruments

*N*-isopropylacrylamide (NIPA) was recrystallized in benzene/*n*-hexane mixed solvent; *N,N'*-methylenebisacrylamide (BIS, biochemical reagent), *N,N,N',N'*-tetramethylethylenediamine (TEMED, biochemical reagent), ammonium persulfate (APS, analytical reagent) and HPMC (60SH-4000, the content of methoxy group is 28%–30%, and hydroxypropyloxy is 7%–12%) were used without further purification.

### 2.2 Synthesis of the PNIPA hydrogels

To prepare the fast response PNIPA hydrogel, NIPA as the monomer, BIS as a cross-linker, and HPMC were dissolved in de-ionized water and stirred in N<sub>2</sub> atmosphere for 20 min. After the addition of APS as an initiator, nitrogen gas was bubbled. Then TEMED as an accelerator was added into the solution. The polymerization of hydrogel was carried out at 15°C for 24 h. The hydrogel thus obtained was designated as hydrogel HF. The conventional hydrogel (designated as hydrogel HN) was synthesized in pure water, and the other synthesis condition was the same as hydrogel HF. The hydrogels were immersed in de-ionized water at room temperature for 7 d, and the water was refreshed everyday to leach out the unreacted monomer and initiator. The resulting hydrogels were cut into discs (10 mm in diameter, 5 mm in thickness), then put into water at about 60°C for them to shrink naturally. The shrunk hydrogels were dried in a vacuum oven until their weight remained constant. The gels were stored in a desiccator. The hydrogels' designations and the feed compositions are listed in Table 1.

**Table 1** Feed composition for PNIPA hydrogels

Composition	<i>m</i> (composition) / mg				<i>V</i> (composition) / mL		Conversion / % <sup>a)</sup>
	NIPA	HPMC	BIS	APS	H <sub>2</sub> O	TEMED	
Sample HN	100	0	5	4	1.2	0.01	91.3
Code HF	100	3	5	4	1.2	0.01	85.6

a) Conversion (%) =  $m(\text{dried hydrogel})/m(\text{monomer}) \times 100\%$

### 2.3 Measurement of the properties

The hydrogel samples were analyzed by Fourier transform infrared (FT-IR) spectroscopy (Bruker's Vector 33). Before the measurement, the originally swollen hydrogel samples were immersed in de-ionized water for a week, swelled and deswelled for several times, then were dried and levigated.

The LCST of the well-swollen hydrogel samples was determined using DSC (Perkin-Elmer's PYRIS DIAMOND TA LAB SYSTEM). All samples were kept in de-ionized water at 15°C and allowed to swell for at least 24 h to reach the equilibrium state. The thermal analyses were performed from 20 to 45°C (heating rate, 5°C/min) on the swollen

hydrogels under a dry nitrogen atmosphere with a flow rate of 10 mL/min.

The surface morphology of the hydrogels was studied using SEM (Hitachi's S-520). The hydrogel samples were dried in vacuum and coated with gold.

The swelling ratios (SR) of the hydrogels were measured gravimetrically after wiping off the excess water on the surface with moistened filter paper at the temperature ranging from 20 to 50°C. The hydrogel samples were incubated in de-ionized water for at least 24 h at each particular temperature. The swelling ratio was defined and calculated from the following formula:  $SR = m_s/m_d$ . Where  $m_s$  is the weight of water in the swollen hydrogels at the particular temperature and  $m_d$  is the dry weight of the hydrogel.

The deswelling of the hydrogels after a temperature jump from the equilibrated swollen state at 15°C to the hot de-ionized water at 50°C was measured after wiping off the excess water on the surface with moistened filter paper. The weight changes were recorded during the shrinking course at regular time intervals until the weight remained invariant. Water retention (WR) was calculated from the following formula:  $WR = 100(m_t - m_d)/m_s$ , where  $m_t$  is the weight of the wet hydrogel at regular time intervals and the other symbols are the same as defined above. The deswelling kinetics of the hydrogels at 50°C would be obtained by the relation curve of WR and time.

## 3 Results and discussion

### 3.1 The synthesis of the hydrogels

The phase separation during the formation of the hydrogel is the basic condition of synthesizing porous materials [19]. Hydrogel HF and hydrogel HN were prepared respectively in aqueous HPMC solution and pure water. From the experiment, it was found that hydrogel HF is opaque at room temperature, whereas hydrogel HN is transparent, which indicated that the phase separation resulting in a porous structure takes place during the formation of hydrogel HF [5,16,17]. It is a standard procedure to synthesize both conventional hydrogel HN and hydrogel HF, but the existence of HPMC affects the rate of conversion. It is clear from Table 1 that the conversion of hydrogel HN is 91.3%, while the conversion of hydrogel HF decreases to 85.6%. The decrease in the conversion of hydrogel HF was attributed to the steric hindrance of HPMC during the polymerization.

### 3.2 Structure characterization of the PNIPA hydrogels

The FT-IR spectra of hydrogel HN and hydrogel HF are given in Fig. 1. The FT-IR spectra of both gels are similar. There exists a broad band in the range from 3 600 to 3 200, which is –NH– absorption; the band near 3075 cm<sup>-1</sup> belongs to the octave frequency stretch of amide; the peaks of methyl and methylene are at 2 974, 2 933, 2 876 cm<sup>-1</sup>, a typical amide I band at 1 654 cm<sup>-1</sup> is the C = O stretch of PNIPA and the

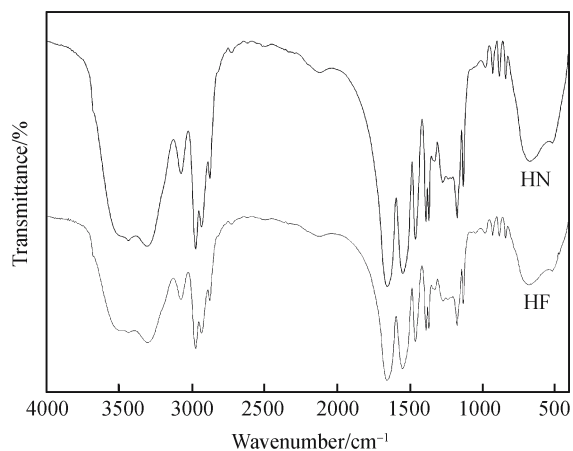


Fig. 1 IR spectra of the PNIPA hydrogels

amide II band at  $1548\text{ cm}^{-1}$  is the  $\text{CN}^-$  stretch of amide; the band near  $1460\text{ cm}^{-1}$  shows the asymmetric twist of methyl; two typical bands of  $\text{CH}^-$  vibration with nearly the same intensity at  $1386$  and  $1368\text{ cm}^{-1}$  belong to the divided bands of the symmetric  $\text{CH}(\text{CH}_3)_2^-$  group; the band at  $1173\text{ cm}^{-1}$  is the  $\text{C}-\text{C}$  stretch of  $\text{CH}(\text{CH}_3)_2^-$  group; the band near  $980, 928\text{ cm}^{-1}$  concerns terminal ethenyl. It is obvious that the functional groups of the PNIPA hydrogel consist of the  $-\text{CONH}$  hydrophilic groups and the  $-\text{CH}(\text{CH}_3)_2$  hydrophobic groups. If there were HPMC in hydrogel HF, a typical and strong peak positioned at around  $1054\text{ cm}^{-1}$ , which belongs to the  $\text{C}-\text{O}$  stretch of HPMC, would appear. From Fig. 1, there is no obvious peak appearing around  $1054\text{ cm}^{-1}$  in the spectra of hydrogel HF. Therefore we suggested that hydrogel HF has the same chemical composition with hydrogel HN from these findings. The HPMC does not exist in hydrogel HF after extensively being washed.

### 3.3 DSC behavior of the PNIPA hydrogels

Essentially, the phase transition of thermo-sensitive hydrogel occurring with the change of the environmental temperature

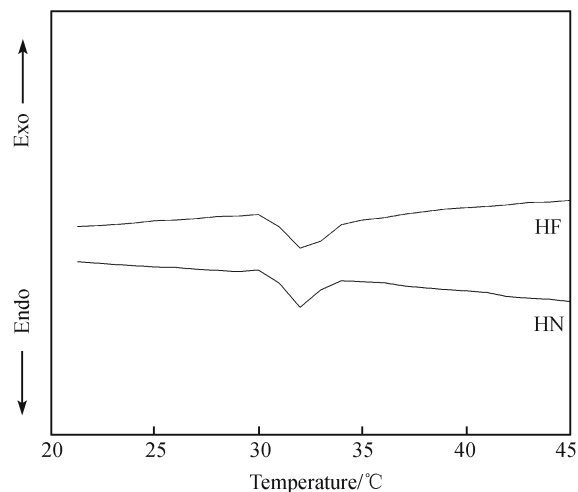


Fig. 2 DSC curves of the PNIPA hydrogels

is a phase separation process therefore it is accompanied with a special critical heat of phase transition. Figure 2 exhibits the DSC thermograms of hydrogel HN and hydrogel HF. Clearly, both the PNIPA hydrogels show a similar LCST around  $31^\circ\text{C}$ . There is no obvious difference between hydrogel HF and hydrogel HN because the phase transition of the hydrogel is affected by both hydrophilic and hydrophobic groups in the network. The addition of HPMC in hydrogel HF will not change the ratio of the two types of groups in the gel structure. In other words, both hydrogels have the same chemical compositions. That is why hydrogel HF has approximately the same LCST as hydrogel HN.

### 3.4 The surface morphology of the PNIPA hydrogels

Scanning Electron Microscope can observe the surface morphology of PNIPA hydrogels directly. Figure 3 shows the SEM of hydrogel HF and hydrogel HN. It is clear that hydrogel HF has a porous structure while hydrogel HN has a tight and smooth surface, and no porous structure in hydrogel HN

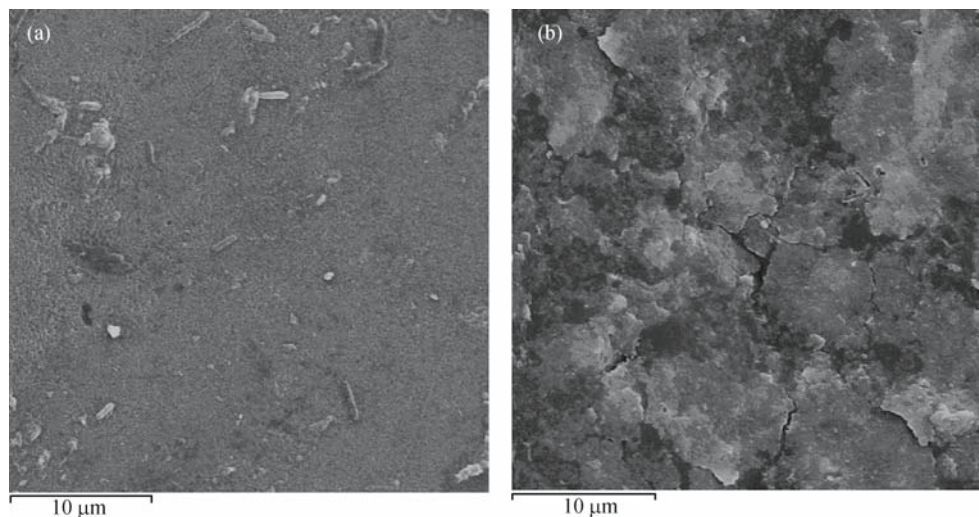


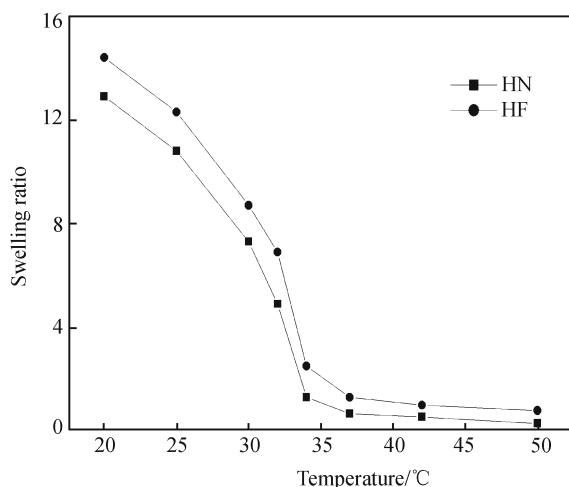
Fig. 3 SEM photograph of the PNIPA hydrogels in dry state: (a) HN; (b) HF

is observed at the magnification times shown in the figure. It indicates that the porous structure provides the channels allowing the entrapped water to be squeezed out so that hydrogel HF has a rapid shrinking rate.

### 3.5 The swelling ratios of the PNIPA hydrogels

A hydrophilic/hydrophobic balance exists in the networks of the PNIPA hydrogel because of the existence of the  $-\text{CONH}$  hydrophilic groups and the  $-\text{CH}(\text{CH}_3)_2$  hydrophobic groups in the side chains. Water interacts with the side chains through the hydrogen bonds between the water molecules and the hydrophilic parts. These hydrogen bonds behave cooperatively to form a stable shell around the hydrophobic groups. All of these interactions lead the hydrogel to be well swollen at a temperature lower than the LCST; when the temperature increases above the LCST, the conventional hydrogel displays a phase separation, those H-bond interactions are destroyed and the associated water is released.

The equilibrium SR is one of the most important parameters for evaluating hydrogels. Figure 4 depicts the temperature-dependent SRs of the hydrogel HF prepared in aqueous HPMC solution and the conventional hydrogel HN prepared in water. It can be seen from Fig. 4 that hydrogel HF and hydrogel HN had a similar transition temperature but exhibited different SRs when the temperature was lower than the LCST. The SRs of hydrogel HF were higher than those of hydrogel HN. When the phase transition occurred, the SRs of hydrogel HF decreased faster than those of hydrogel HN. We considered that the improvement of these properties is attributed to the porous structure of the hydrogel [5,6,16,17], as the network of hydrogel with a porous structure can absorb more water [5,6].

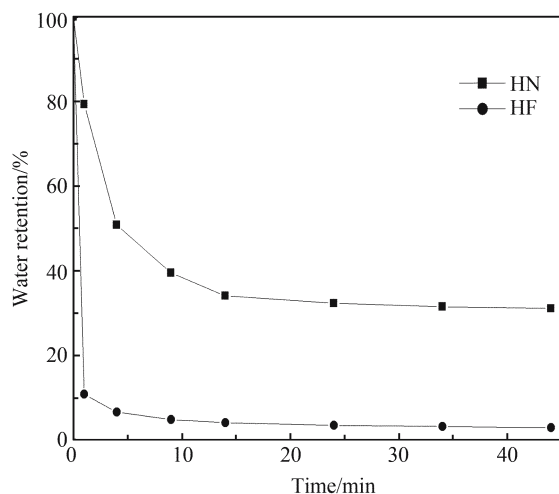


**Fig. 4** Temperature dependence of equilibrium swelling ratio of the PNIPA hydrogels

### 3.6 The deswelling kinetics of the PNIPA hydrogels

For deswelling measurement, the hydrogels were transferred quickly from de-ionized water of 15°C to de-ionized water

of 50°C. The deswelling kinetics of hydrogels is shown in Fig. 5, from which it can be seen that the response rate of hydrogel HF is significantly faster than that of hydrogel HN. For example, hydrogel HF lost 89% water within 1 min and about 93% water in 4 min, whereas hydrogel HN lost only about 66% water in 15 min.



**Fig. 5** Deswelling kinetics of the PNIPA hydrogels

The shrinking rate of hydrogel HF is faster than that of hydrogel HN, which can be explained as follows: when the hydrogel was in the water at the temperature higher than the transition temperature, the interactions on the surface region was destroyed first, the hydrogel began to shrink and the associated water was released quickly. As the temperature increased above the LCST, the hydrophobic interactions between hydrophobic groups on the surface region reinforced and formed a thick hydrophobic tight layer that prevented the inner water in the hydrogel to be diffused out further, thereby bubbles appeared on the surface of the hydrogel to make up for the increased internal pressure [8,20]. However, the existence of the pores destroyed the formation of the hydrophobic tight layer, so water was released quickly. Bubbles were observed on the surface of hydrogel HN during the shrinking process owing to the hydrophobic tight layer that prevented water to effuse out; whereas no bubbles were observed during the shrinking process of hydrogel HF due to the porous structure that made the water absorbed be released easily and quickly. Therefore, the deswelling rate of hydrogel HF is significantly faster than that of hydrogel HN.

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