Effect of the initiator on thermosensitive rate of poly(*N*-isopropylacrylamide) hydrogels

X. C. Xiao*

School of Life Sciences, South-Central University for Nationalities, Wuhan, 430074, China

Received 28 January 2007; accepted in revised form 1 April 2007

Abstract. As the main of thermosensitive polymeric materials, poly(*N*-isopropylacrylamide) (PNIPAM) undergoes volume changes in response to external temperature changes. While in some potential applications, a fast response rate is needed. In this article, effect of the initiator on thermosensitivity of PNIPAM hydrogels was carried out. The characterization of the resulting hydrogels was gravimetrically measured, and the result displays that with increasing the initiator dosage, much faster deswelling rate and much faster shrinking/swelling dynamic response are obtained.

Keywords: polymer gels, fast response, initiator, thermosensitivity

1. Introduction

Environmental stimuli-sensitive polymeric 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., have attracted a widespread interest in the past thirty years due to their potential applications in numerous fields, including drug delivery [1–3], chemical separations [4, 5], sensors [6–8], catalysis [9], enzyme and cell immobilization [10]. 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 thermosensitive gels [11, 12].

As a typical temperature-sensitive hydrogel, poly(*N*-isopropylacrylamide) (PNIPAM) hydrogel undergoes a dramatic reversible volume change at lower critical solution temperature (LCST, about 32°C) [13], which is the result of 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. Its LCST close to physiological temperature makes the polymer an especially good candidate for applications in biotechnology and in medicine [14–16].

In some practical applications, such as “smart” actuators and on-off switches, a fast response is needed, while the normal-type PNIPAM gel cannot successfully satisfy this requirement. To increase the response dynamics, several strategies have been explored [17–22]. In this paper, we wish to present a novel method for the preparation of a fast deswelling PNIPAM hydrogels by changing initiator dosage. The result displays that with increasing the initiator dosage, much faster deswelling rate and much faster shrinking/swelling dynamic response are obtained.

*Corresponding author, e-mail: xcxiao71@yahoo.com.cn
© BME-PT and GTE

2. Experimental

2.1. 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 initiator ammonium persulfate (APS), the accelerator *N,N,N',N'*-tetramethylethylenediamine (TMEDA), and the crosslinker *N,N'*-methylenebisacrylamide (MBA) were of analytical grade and used as received without any further purification. Double-distilled water was used in all the synthesis processes.

2.2. Preparation of the hydrogels

NIPAM, MBA and APS were first dissolved in 4 ml of double-distilled water 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 μ l of TMEDA were added into the monomer solution to initiate the radical polymerization. The polymerizations were continued in water for 4 h. After the polymerization, the prepared hydrogel was 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. After freeze-drying, all hydrogels were cut into disc-like pieces approximately 6 mm in diameter and 4 mm in thickness for the following studies. The feed composition of monomer and other agents are listed in Table 1.

Table 1. Feed composition for the preparation of PNIPAM gels

Sample code	Composition			
	NIPAM [g]	MBA [mg]	Water [ml]	Initiator [g]
A	0.4	8	4	0.08
B	0.4	8	4	0.12
C	0.4	8	4	0.16

2.3. Measurement of swelling ratio of hydrogels

For the equilibrium swelling ratio (SR) 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 hydrogels 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 was calculated as Equation (1):

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

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

2.4. Measurement of the oscillatory shrinking-swelling kinetics of hydrogels

To detect hydrogels with a fast response, the oscillatory shrinking-swelling kinetics of the prepared hydrogels over the 6 min temperature cycles between 26°C (below LCST) and 40°C (above LCST) in double-distilled water were examined gravimetrically. Water retention of wet hydrogel was defined as Equation (2):

$$\text{Water retentio} = \frac{W_t - W_d}{W_{t0} - W_d} \cdot 100 \quad (2)$$

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

3. Results and discussion

3.1. Swelling ratio of PNIPAM hydrogels

Figure 1 shows the equilibrium swelling ratios of hydrogels as a function of the external temperature. As can be seen from Figure 1, when the temperature increased, all hydrogels exhibited a similar temperature-dependence that lost water and shrank in volume and it is clear that LCSTs of hydrogels lie in the vicinity of 32°C. At the temperature below the LCST, these hydrogels absorb water and become swollen. The SRs of the resulting hydrogels increase with increasing the initiator dosage.

Figure 1. Temperature dependence of the SR of PNIPAM gels in the temperature range from 21°C to 45°C. The sample code is defined in Table 1

When transitions occur, the SR of sample C decreases more sharply and the phase-separation degree (changes of SR versus temperature changes around LCST) is the greatest, which demonstrates that the response rate to temperature changes of this PNIPAM hydrogel is the fastest.

3.2. The oscillatory shrinking-swelling kinetics of PNIPAM hydrogels

Figure 2 displays the oscillatory shrinking-swelling kinetics of hydrogels prepared with different the initiator dosages over the 6 min temperature cycles between 26°C (below LCST) and 40°C (above LCST) in double-distilled water. This 6 min cycle was continued for a total 6 cycles (72 min) in order to determine response of hydrogels to temperature. It is found that, although all hydrogels exhibited an

Figure 2. Oscillatory shrinking–swelling kinetics for hydrogels prepared with different initiator dosage over 6 min temperature cycles in double-distilled water between 26 and 40°C. The sample code is defined in Table 1

oscillatory shrinking-swelling character upon cycling temperature between 26°C and 40°C and their shrinking and swelling cycles are accompanied by a consecutive reduction in water content, much more rapid, sharp and larger magnitude shrinking-swelling changes were exhibited with increasing the initiator dosage.

As redox initiator, the system APS/TMEDA can offer free radical, in which TMEDA accelerates a homolytic cleavage on moieties of APS, therefore they play a important role in the vinyl polymerization. The terminal groups of the hydrogels prepared by this polymerization are hydroxy groups (–OH) resulting from cleavage of persulfate initiator [23, 24]. So the content of hydrophilic group (–OH) increases with increasing the initiator dosage. For traditional PNIPAM hydrogels, there is a hydrophilic and hydrophobic balance of polymer side groups, i. e., –CONH– is hydrophilic and –CH(CH₃)₂ is hydrophobic [11]. This balance is broken by the addition of –OH and the final percentages of hydrophilic groups increase with increasing the content of –OH. The resulting polymer chains get more widely expanded in the aqueous media with increasing the initiator dosage. Moreover increasing the initiator concentration affects both the chain length and the crosslinking density of the gels. The dangling chains can increase response rate of hydrogels [17, 18]. Both lead to the larger SR of hydrogels and much faster speed to absorb water at temperature below the LCST. So it is easy to understand hydrogels exhibits faster deswelling rate.

4. Conclusions

To prepare poly(*N*-isopropylacrylamide) hydrogel with fast response rate, effect of the initiator on thermosensitivity of PNIPAM hydrogel was carried out in this article. The characterization of the final hydrogel was gravimetrically measured, and the result displays that much faster deswelling rate and much faster shrinking/swelling dynamic response are obtained with increasing the initiator dosage, owing to increase of –OH that derived from the system APS/TMEDA.

Acknowledgements

This work was financially supported by South-Central University For Nationalities (YZZ06002). The author

gratefully acknowledges the help of the Kohjin Co., Ltd, Japan, for kindly supplying the *N*-isopropylacrylamide.

References

- [1] Kwon I. C., Bae Y. H., Kim S. W.: Electrically credible polymer gel for controlled release of drugs. *Nature*, **354**, 291–293 (1991).
- [2] Jeong B., Bae Y. H., Lee D. S., Kim S. W.: Biodegradable block copolymers as injectable drug-delivery systems. *Nature*, **388**, 860–862 (1997).
- [3] Murthy N., Thng Y. X., Schuck S., Xu M. C., Frechet J. M.: A novel strategy for encapsulation and release of proteins: hydrogels and microgels with acid-labile acetal cross-linkers. *Journal of the American Chemical Society*, **124**, 12398–12399 (2002).
- [4] Kawaguchi H., Fujimoto K.: Smart latexes for bioseparation. *Bioseparation*, **7**, 253–258 (1998).
- [5] Kondo A., Kaneko T., Higashitani K.: Development and application of thermo-sensitive immunomicrospheres for antibody purification. *Biotechnology and Bioengineering*, **44**, 1–6 (1994).
- [6] Hu Z. B., Chen Y. Y., Wang C. J., Zheng Y. D., Li Y.: Polymer gels with engineered environmentally responsive surface patterns. *Nature*, **393**, 149–152 (1998).
- [7] Panchapakesan B., DeVoe D. L., Widmaier M. R., Cavicchi R., Semancik S.: Nanoparticle engineering and control of tin oxide microstructures for chemical microsensor applications. *Nanotechnology*, **12**, 336–349 (2001).
- [8] van der Linden H., Herber S., Olthuis W., Bergveld P.: Development of stimulus-sensitive hydrogels suitable for actuators and sensors in microanalytical devices. *Sensors and Materials*, **14**, 129–139 (2002).
- [9] Bergbreiter D. E., Case B. L., Liu Y. S., Caraway J. W.: Poly(*N*-isopropylacrylamide) soluble polymer supports in catalysis and synthesis. *Macromolecules*, **31**, 6053–6062 (1998).
- [10] Guiseppi-Elie A., Sheppard N. F., Brahim S., Narinesingh D.: Enzyme microgels in packed-bed bioreactors with downstream amperometric detection using microfabricated interdigitated microsensor electrode arrays. *Biotechnology and Bioengineering*, **75**, 475–484 (2001).
- [11] Xiao X. C., Chu L. Y., Chen W. M., Wang S., Li Y.: Positively thermo-sensitive monodisperse core-shell microspheres. *Advanced Functional Materials*, **13**, 847–852 (2003).
- [12] Xiao X. C., Chu L. Y., Chen W. M., Wang S., Xie R.: Preparation of submicrometer-sized monodispersed thermoresponsive core-shell hydrogel microspheres. *Langmuir*, **20**, 5247–5253 (2004).
- [13] Pelton R.: Temperature-sensitive aqueous microgels. *Advances in Colloid and Interface Science*, **85**, 1–33 (2000).
- [14] Jeong B., Kim S. W., Bae Y. H.: Thermosensitive sol-gel reversible hydrogels. *Advanced Drug Delivery Reviews*, **54**, 37–51 (2002).
- [15] Okano T., Yamada N., Okuhara M., Sakai H., Sakurai Y.: Mechanism of cell detachment from temperature-modulated, hydrophilic-hydrophobic polymer surfaces. *Biomaterials*, **16**, 297–303 (1995).
- [16] Liang D., Zhou S., Song L., Zaitsev V. S., Chu B.: Copolymers of poly(*N*-isopropylacrylamide) densely grafted with poly(ethylene oxide) as high-performance separation matrix of DNA. *Macromolecules*, **32**, 6326–6333 (1999).
- [17] Kaneko Y., Sakai K., Kikuchi A., Yoshida R., Sakurai Y., Okano T.: Influence of freely mobile grafted chain length on dynamic properties of comb-type grafted poly(*N*-isopropylacrylamide) hydrogels. *Macromolecules*, **28**, 7717–7723 (1995).
- [18] Yoshida R., Uchida K., Kaneko Y., Sakai K., Kikuchi A., Sakurai Y., Okano T.: Comb-type grafted hydrogels with rapid de-swelling response to temperature change. *Nature*, **374**, 240–242 (1995).
- [19] Nakamoto C., Motonaga T., Shibayama M.: Preparation pressure dependence of structure inhomogeneities and dynamic fluctuations in poly(*N*-isopropylacrylamide) gels. *Macromolecules*, **34**, 911–917 (2001).
- [20] Chen J., Park H., Park K.: Synthesis of superporous hydrogels: hydrogels with fast swelling and superabsorbent properties. *Journal of Biomedical Materials Research*, **44**, 53–62 (1999).
- [21] Zhang X. Z., Zhuo R. X., Yang Y. Y.: Using mixed solvent to synthesize temperature sensitive poly(*N*-isopropylacrylamide) gel with rapid dynamics properties. *Biomaterials*, **23**, 1313–1318 (2002).
- [22] Kabra B. G., Gehrke S. H.: Synthesis of fast response, temperature-sensitive poly(*N*-isopropylacrylamide) gel. *Polymer Communications*, **32**, 322–323 (1991).
- [23] Feng X. D., Guo X. Q., Qiu K. Y.: Study of the initiation mechanism of the vinyl polymerization with the system persulfate/*N,N,N',N'*-tetramethylethylenediamine. *Die Makromolekulare Chemie*, **189**, 77–83 (1988).
- [24] Guilherme M. R., da Silva R., Rubira A. F., Geuskens G., Muniz E. C.: Thermo-sensitive hydrogels membranes from PAAm networks and entangled PNIPAAm: effect of temperature, cross-linking and PNIPAAm contents on the water uptake and permeability. *Reactive & Functional Polymers*, **61**, 233–243 (2004).