Synthesis of Macroporous Poly(*N*-isopropylacrylamide) Hydrogel with Ultrarapid Swelling–Deswelling Properties

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ABSTRACT: A novel technique to synthesize a macroporous poly(*N*-isopropylacrylamide) hydrogel with ultrarapid swelling–deswelling properties by using dodecyl dimethyl benzyl ammonium bromide (DDBAB) during the polymerization/crosslinking reaction at −8°C was proposed. A hydrophobic initiator dodecyl dimethyl benzyl ammonium persulfate (APS) was proved to be produced *in situ* by the reaction of DDBAB and the water-soluble initiator APS and a heterogeneous initiation mechanism was proposed. The scanning electron microscope and environmental scanning electron microscope images showed that the pore size of the hydrogel increased with increase of the amount of DDBAB. The macroporous structure of hydrogel induced a large swelling ratio and rapid swelling–deswelling rate, since the free water could diffuse very quickly through the macroporous network. The time required from equilibrium swollen state to equilibrium shrunken state was only about 1 min and *vice versa*. The oscillating swelling–deswelling measurements showed that this macroporous hydrogel could be used repeatedly. These properties of ultrarapid response and reversibility are advantageous for several technical applications, as a kind of biomaterials, both in medicine and in biotechnology. © 2007 Wiley Periodicals, Inc. J Appl Polym Sci 104: 4080–4087, 2007

Key words: hydrogels; *N*-isopropylacrylamide; temperature sensitive; macroporous; rapid response

INTRODUCTION

Intelligent hydrogels can respond to small external stimuli, such as temperature, pH, light, electric signal, or the presence of certain chemical compounds.[1–5] Great attention has been paid both in fundamental and application aspects to these stimuli-sensitive gels during the past 10 years. Poly (*N*-isopropylacrylamide) (PNIPA) hydrogel is well known as an intelligent temperature-sensitive material and has been studied extensively. A reversible phase transition can be induced around the lower critical solution temperature of PNIPA chain at about 32°C in aqueous media,[1] so the phase transition temperature (PTT) of PNIPA hydrogels was also around 32°C. In water, PNIPA hydrogels are in a highly swollen state below the PTT while the gels are in a shrunken state above the PTT, since the hydrophobic nature of isopropyl groups in the PNIPA plays a dominant role in excluding the water from the gel.[6,7] This sensitive property of PNIPA gel has been utilized in many applications, including chemical sensor,[8] chemical valve,[9] controlled drug release,[10] separation media,[11] immobilization of enzyme,[12] or even color changing pigment.[13]

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However, the response rates of conventional PNIPA gels polymerized in aqueous media at room temperature using ammonium persulfate (APS) as an initiator and *N*,*N*′-methylenebisacrylamide as a crosslinker are too slow to promote new applications such as artificial muscles and rapidly acting actuators. To get over this shortage, several techniques have been proposed. Hoffman and coworkers.[14] synthesized a fast response PNIPA hydrogel at a temperature above its PTT. Okano and coworkers[15–17] suggested that introducing freely mobile and grafted chains into the network of the PNIPA hydrogel could greatly improve its response rate. Akashi and coworkers[18–20] prepared porous PNIPA hydrogels in the presence of nanosized silica particles with subsequent acid treatment. Zhang and Zhuo proposed that the response rate of PNIPA hydrogels could be increased by cold-treating the gel network,[21] cold polymerizing/crosslinking process,[22] utilizing mixed solvent as reaction media,[23–25] or using PEG as a pore-forming agent during the polymerization.[26,27] Recently, Yan et al.[28] prepared a rapid response PNIPA hydrogel by adding a polymeric surfactant to form a semi-interpenetrating network (semi-IPN). All these methods could greatly increase the deswelling rate of hydrogels. But the reswelling rate improved was not so much exciting. The gels required tens of minutes or even longer to reach the swollen state from equilibrium shrunken. It is hard

for the water in exterior environment to diffuse into the gels through the small pores at the shrunken state. The compact interior structure of the gels would prevent the surface pores from enlarging. Another probable reason for the slow reswelling rate is that an irreversible network collapse takes place during the shrinking process before swelling again, although the macroporous structures are formed.[27]

The aim of this article is at synthesizing a macroporous PNIPA hydrogel with ultrarapid response behavior by adding dodecyl dimethyl benzyl ammonium bromide (DDBAB) to form a hydrophobic initiator dodecyl dimethyl benzyl ammonium persulfate (DDBAPS). Element analysis, MS and ^{1}H-NMR were used to prove the presence of DDBAPS. The effects of the amount of DDBAB on morphology, swelling ratio (SR), deswelling and reswelling kinetics, and oscillating response to deswelling–reswelling of the hydrogel were investigated experimentally. The resulted hydrogel was proved to be macroporous by SEM and ESEM observation. The swelling and deswelling kinetics showed that the hydrogel had ultrarapid response behavior, especially in reswelling. The oscillating measurement of deswelling–reswelling showed that the hydrogel could be utilized repeatedly. Although both the hydrogels in our work and Zhang's[22] were prepared in the frozen state, the causes of the rapid responding rates were totally different.

EXPERIMENTAL

Materials

N-isopropylacrylamide (NIPA, 99%, Acros Organics, New Jersy) was used after further recrystallization from *n*-hexane. *N*,*N*′-methylenebisacrylamide (BIS, ≥98%, Fluka Chemika), *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED, 99%, Acros Organics, New Jersy), APS (≥98%, Yixing Second Chemical Reagent Factory, China), and DDBAB (95%, Shanghai Jingwei Chemical, China) were used as received.

Synthesis of DDBAPS

Twenty milliliter aqueous solution of 4 wt % APS was added into 200 mL aqueous solution of 3 wt % DDBAB under magnetic stirring in glass vessel for 1 h at room temperature. Then stop stirring to get the deposit of DDBAPS. The deposit was dissolved in ethanol and then added deionized water to deposit again. The process was repeated for several times to purify the product. The deposit was finally dried (45°C, 0.01 MPa) for 24 h for further measurements. Element analysis ($C_{42}H_{76}N_2S_2O_8$, M_r = 801.17 g mol^{-1}): Calcd: **C** 62.96, **H** 9.56, **N** 3.50, **S** 8.00; Found: **C** 63.35, **H** 9.78, **N** 3.69, **S** 7.70. MS (ESI, CH_3OH, positive ions) signal at 304.5. ^{1}H-NMR (500 MHz, in CDCl3): δ = 0.88 (t, 3H, —CH_3), 1.24–1.32 (m, 18H, —CH_2—), 1.81 (m, 2H, —CH_2—CH_2—N^+), 3.28 (s, 3H + 3H, CH_3—$N^+R^1R^2$—CH_3), 3.53 (t, 2H, —CH_2—N^+), 5.01 (s, 2H, N+—CH2—Φ), 7.40–7.69 (m, 5H, = CH— aryl).

Synthesis of PNIPA hydrogels

NIPA, BIS, and DDBAB were dissolved in deionized water in glass vessel. The glass vessel was cooled in a refrigerator at a temperature of −8°C for 20 min. Then APS and TEMED were added to the glass vessel in which the solution was not frozen. The polymerization was carried out at −8°C for 12 h during which the whole reaction system was frozen. After the reaction, the resulted gel was cut into disks (20 mm in diameter and 5 mm in thickness). The samples were immersed in excessive deionized water at ambient temperature for 72 h. Then the samples were refreshed by deionized water every 4 h to remove the unreacted materials. The hydrogels prepared at various amount of DDBAB were labeled as DB5, DB10, DB20, DB30, and DB100. All these gels are called DB-modified gels. Normal gel (NG) was prepared by the same method, but in the absence of DDBAB. The feed compositions of the monomers and other reactants are summarized in Table I.

Characterization of DDBAPS

^{1}H-NMR spectra were taken with an apparatus Bruker Avanced MX500. Mass spectra were recorded by an apparatus Bruker Esquire-LC. The C, H, N, S element analysis of DDBAPS was carried out by element analyzer (Flash EA112, ThermoFinningan, USA).

FTIR measurement

The hydrogel samples were analyzed by FTIR (Nicolet5700, USA) in the region of 4000–500 cm^{-1}. Before measurements, the originally swollen gel

TABLE I
Feed Compositions of Normal and Modified Pnipa Hydrogels

	Gel samples					
	NG	DB5	DB10	DB20	DB30	DB100
NIPA (mg)	150	150	150	150	150	150
BIS (mg)	5	5	5	5	5	5
4 wt % APS (μL)	100	100	100	100	100	100
TEMED (μL)	10	10	10	10	10	10
DDBAB (mg)	0	5	10	20	30	100
Water (mL)	1.5	1.5	1.5	1.5	1.5	1.5
Conversion (%)[a]	96.2	95.9	98.1	95.7	98.1	96.5

[a] Weight percentage of the gel synthesized from the monomer and crosslinker.

samples were dried (45°C, 0.01 MPa) for at least 48 h and put into KBr pellet.

Morphology observations of PNIPA gels

For SEM observations, the gel samples that reached equilibrium in deionized water were quenched in liquid nitrogen and then freeze-dried for 24 h. Specimens were coated with platinum by a coating equipment (IB-5 ION coater, EIKO, Japan) for 2 min. For ESEM observations, swollen gel samples were observed without further treatment. Both SEM and ESEM morphology were studied using ESEM (XL Series-30, Philips, Netherlands).

Measurement of swelling ratio of PNIPA gels

The gel samples were measured gravimetrically after wiped off the excessive water with filter paper in the temperature range from 10 to 50°C. Before the measurement, the gel samples were immersed in deionized water for at least 24 h at each given measurement temperature. The swelling ratio (SR) is defined as W_s/W_d, where W_s is the weight of water in the swollen sample at a given temperature and W_d is the weight of the sample at dry state.

Measurement of deswelling–reswelling kinetics of PNIPA gels

The equilibrated gel samples at a temperature of 15°C were quickly transferred into hot deionized water of 45°C, and then the deswelling kinetics were measured gravimetrically after removing excessive water from the surface of samples with filter paper. The reswelling kinetics of the shrunk samples that were immersed in the hot water of 45°C for at least 48 h were determined gravimetrically at 15°C.

The deswelling and reswelling kinetics were defined as temporal weight changes for the samples. The change of weight was converted to the normalized swelling degree, which indicated the volume changes of the samples between equilibrium swollen (100%) and equilibrium shrunken (0%) states. The swelling degree is defined as $100 \times (W_t - W_{15})/(W_{45} - W_{15})$, where W_t is the weight of sample at a given time, W_{15} and W_{45} are the weights of samples that reached equilibrium at 15°C and at 45°C, respectively.

RESULTS AND DISCUSSION

Synthesis of DDBAPS

The new compound DDBAPS was synthesized by a simple ion exchange reaction between the water-soluble compounds DDBAB and APS. The reaction

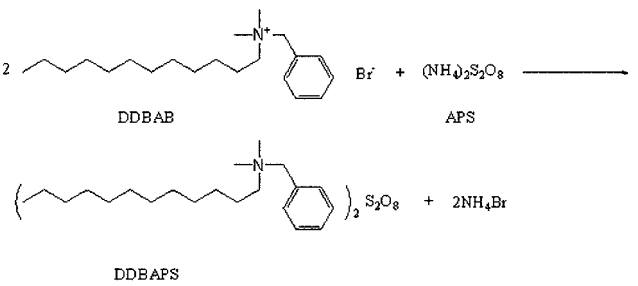


Figure 1 Reaction formula of DDBAB and APS.

formula is shown in Figure 1. The solution of DDBAB became opaque as soon as APS was added. About an hour after, a white wax-looking solid was collected. This white wax-looking solid cannot be dissolved in water, but can be dissolved in organic solvents like ethanol, DMF, and so on. In our further experiment, 150 mg monomer of NIPA, 5 mg cross-linker of BIS, and 10 μm accelerator of TEMED were dissolved in 1.5 mL aqueous solution of 40% DMF as mixed solvent. After adding 10 mg of this white solid, which could be dissolved in the mixed solvent, polymerization/crosslinking reaction took place and PNIPA gel could still be obtained after several hours. This phenomenon implied that this white waxy-looking solid should be persulfate, which could decompose to radicals as an initiator. The result of element analysis indicated that the molecular formula of the white solid should be $C_{42}H_{76}N_2S_2O_8$. The ^{1}H-NMR spectra of pure DDBAPS is shown in Figure 2. The measurements of ^{1}H-NMR and MS confirmed that the cation of the white waxy-looking solid is dodecyl dimethyl benzyl ammonium. All these results proved that the reaction product of DDBAB and APS was a new hydrophobic initiator DDBAPS.

Synthesis of the PNIPA hydrogels

The polymerization was carried out in water when preparing conventional hydrogels. During the reaction, the system was homogeneous. As a result, the conventional hydrogels had a dense structure. In this study, to prevent the hydrophobic initiator DDBAPS that was formed *in situ* in the reaction system from depositing out, polymerization was carried out in the frozen state. The reaction system, which became opaque after adding APS, was in a microphase separation state because of the hydrophobicity of DDBAPS. DDBAPS exited in the reaction medium in the form of tiny agglomeration. In this heterogeneous initiation system, the monomer molecules around the DDBAPS agglomeration could be polymerized but gelation could hardly occur in the areas, which were certain distant from DDBAPS agglomeration, so macroporous hydrogel could be formed because of the microphase separation of the reaction

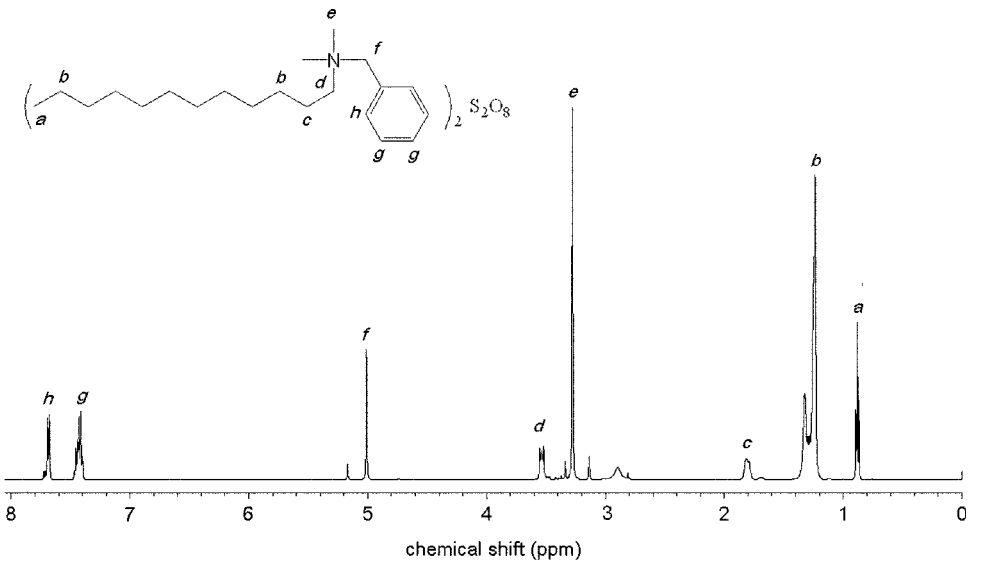


Figure 2 ^{1}H-NMR spectra of DDBAPS in $CDCl_3$.

system. Gel could not be obtained when sufficient amount of DDBAB was added at room temperature because the DDBAPS deposited out from the reaction system. So we suppose that DDBAB neither react as a surfactant nor as a direct pore forming agent. The real function of DDBAB was a reactant to obtain DDBAPS.

DDBAPS was able to initiate the polymerization and crosslinking in the mixed solvent of 40% DMF and 60% deionized water as aforementioned, but because of the hydrophobic property of DDBAPS, it cannot be dissolved in pure water and loses its initiate ability. We used DDBAB and APS as the reactant to obtain DDBAPS *in situ* in pure water, and then, polymerization was carried out in frozen state, which could prevent DDBAPS from depositing out. DDBAPS exited in the reaction medium in the form of tiny agglomeration in our experiments while APS exited in water in the form of ion in most of the previous studies. As a result, the former reaction system was heterogeneous with microphase separation while the latter was homogeneous. The role of DDBAPS was a novel hydrophobic initiator. The hydrophobic nature of DDBAPS, which formed *in situ* caused a heterogeneous initiation system. As a result of this reason, the resulted gels were microphase separation, which was the reason for the rapid responding property of the gels.

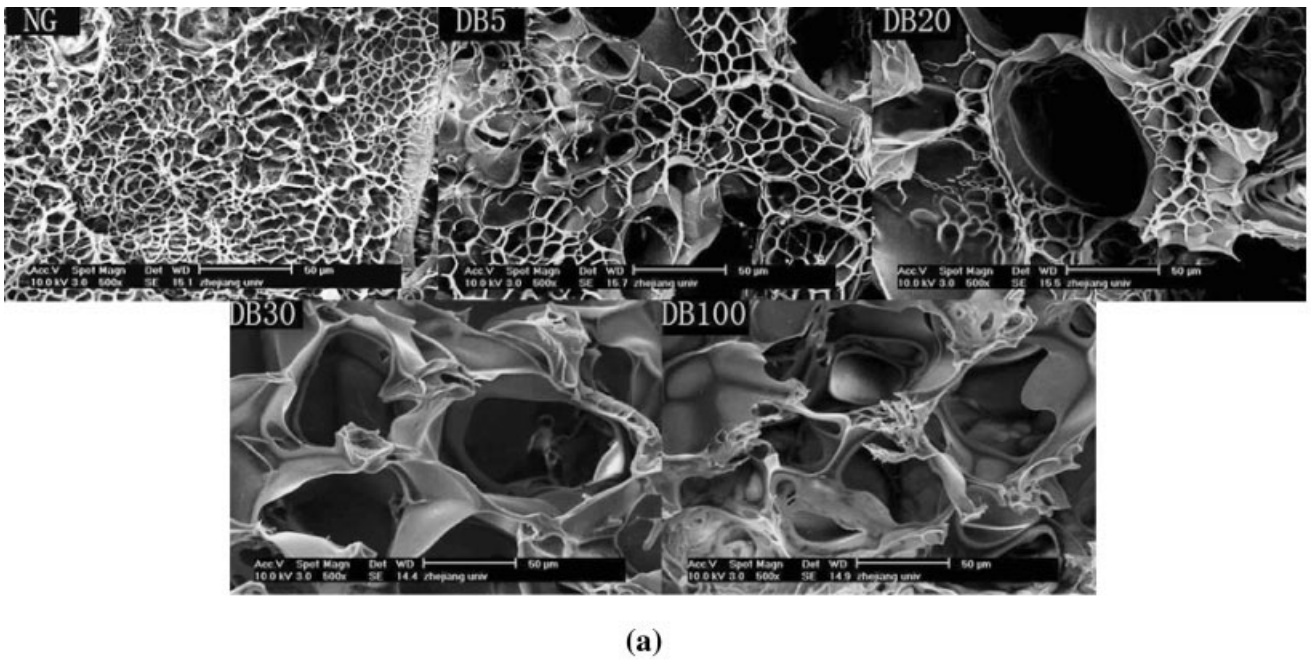
The conversions of the monomers are summarized in Table I. All of the gels had high conversions, indicating that the presence of DDBAB will not prevent the formation of gel. Gel NG was transparent, gels DB5, DB10, and DB20 were translucent while gels DB30 and DB100 were opaque. This difference in appearance should be attributed to microphase separation. Gels DB30 and DB100 were sponge like. A part of water absorbed by the hydrogel could be driven out of the gels, when a certain compressive stress was adding directly towards the gels. For gels NG, DB5, DB10, and DB20, the water in gels could not be driven out of the gels by applications of force even if the gels were brokenly compressed.

FTIR spectra of the gels

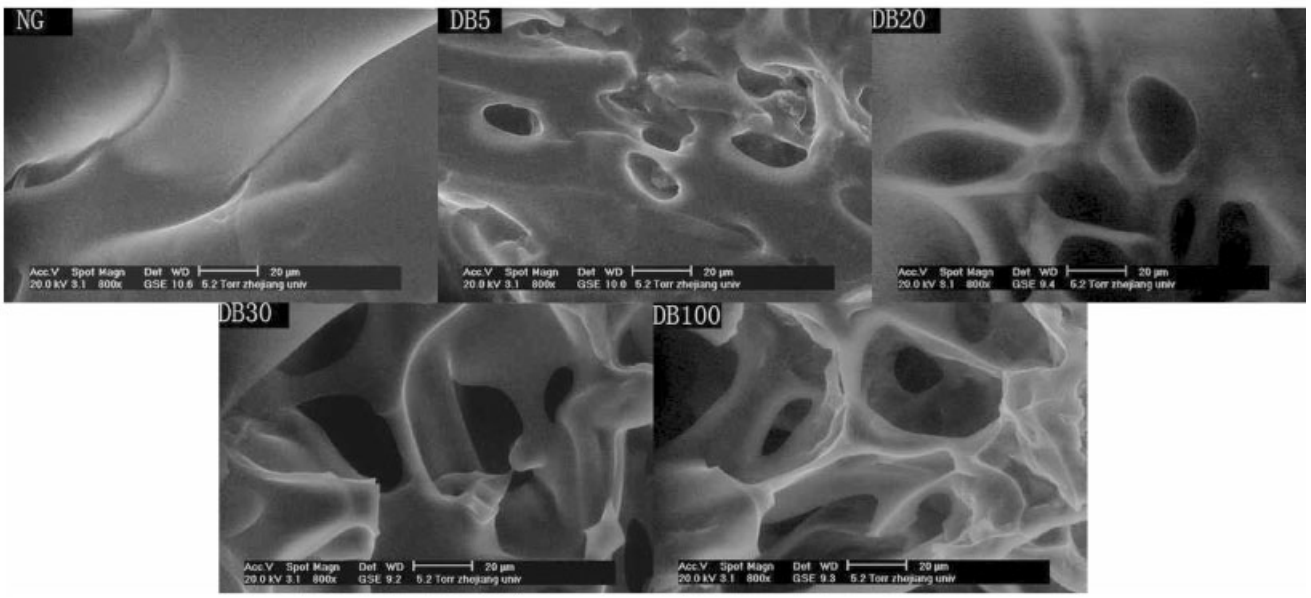
The FTIR spectra of all of the dried gel samples were identical. This indicated that the PNIPA gels synthesized by using DDBAB have the same chemical composition as the conventional PNIPA gel, and after the finish of reaction the redundant DDBAB was washed out completely by excessive deionized water.

Morphology of the gel

The SEM micrographs of the freeze-dried gels are shown in Figure 3(a). It can be seen from Figure 3(a) that gel NG is compact and microporous gel with the pore size of several micron and most of the pores are disconnected. The micropores become larger and a few of macropores can be seen in gel DB5. For gel DB20, the proportion of the macropores increases but some micropores still exist. The morphologies of gels DB30 and DB100 are similar. Both of them are macroporous with the pore size of about tens of times larger than the NG gel. Moreover, none of micropore can be observed and most of the pores are interconnected. The ESEM micrographs of the gels that reached equilibrium swollen state at room temperature are shown in Figure 3(b). It can be seen from Figure 3(b) that the matrix of gel NG is compact and smooth. It indicates that microphase separation did not occur within the gel matrix, so gel NG is homogeneous. The morphologies of gels DB5 and



(a)



(b)

Figure 3 Micrographs of the normal and DB-modified PNIPA hydrogels: (a) SEM micrographs of gels after frozen-dried, ×500 magnification (b) ESEM micrographs of swollen gels, ×800 magnification.

DB20 are similar. In gel DB20, several pores at the size of about 10 μm in diameter can be found. The pores in gel DB20 are larger than that in gel DB5. The pores are not interconnected and most regions of the gel matrices are still compact and smooth just like the gel NG. For gels DB30 and DB100, the gel matrices are full of interconnected macropores with the size of about 50 μm in diameter. These pores were filled with water since the gels were at the equilibrium swollen state. Gels DB30 and DB100 were heterogeneous hydrogels and gels DB5 and DB20, which were at a transition stage between heterogeneous and homogeneous hydrogels, were called semiheterogeneous hydrogels. Heterogeneous hydrogels were opaque and homogeneous hydrogel was transparent in appearance while semiheterogeneous hydrogels were translucent. The interconnected macroporous structure, which makes water to diffuse more easily within the gel matrix, during the deswelling and reswelling processes leads to a rapid response rate.

The difference of morphology of NG and DB-modified gels can be explained as follows, when sufficient amount of DDBAB (for DB30, DB100) was added a heterogeneous initiation system was formed as discussed earlier and no free persurfate anions existed in this system, so heterogeneous hydrogels with macropores were formed. For gel NG, free persurfate anions that ionized by APS led a homogeneous hydrogel without macropores. When comparatively small amount of DDBAB (for DB5, DB10, DB20) was added both free persurfate anions and DDBAPS agglomeration existed and the resulted gels were at a transition stage with disconnected pores.

Zhang and Zhuo[22] reported that fast responsive PNIPA hydrogel could been achieved by decreasing the polymerization reaction temperature below the freezing point (−18°C). They suggested that the network of this hydrogel got to be regularly arranged and exhibited a spiral structure because some crystal nuclei appear and the water molecules start to crystallize and arrange regularly around these nuclei at the beginning of the polymerization reaction at low temperature, which leads to fast responsivity. In our work, however, it is clear from ESEM micrographs of wet hydrogel samples that macroporous structure could not form when DDBAB was not added, although polymerization took place at low temperature, and that pores became larger when more DDBAB was added. So the primary cause of formation of macroporous strcture was adding DDBAB and the effect of ice formation could be neglected.

Swelling ratio

The equilibrium SRs of the NG and DB-modified gels are shown in Figure 4. The SRs of gels NG, DB5, and DB10 are almost the same. The ratio of gel

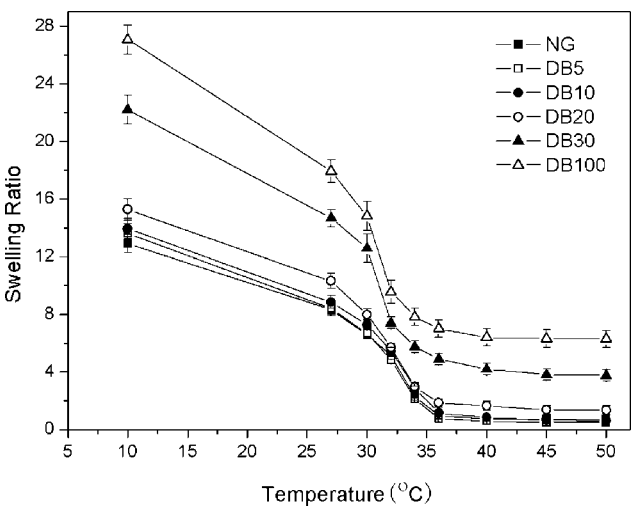


Figure 4 Equilibrium swelling ratio of PNIPA gels as a function of temperature.

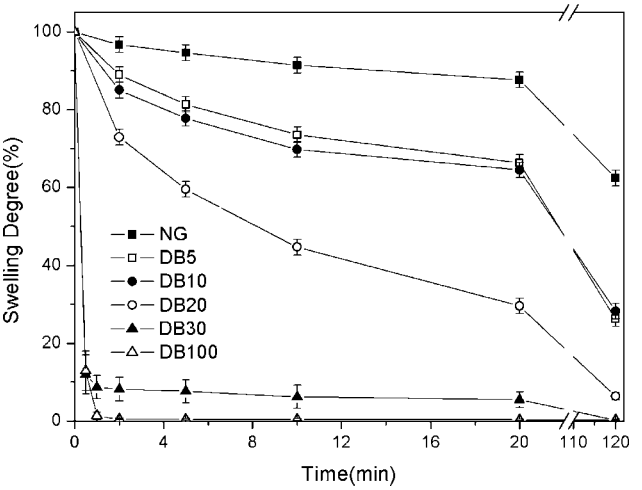


Figure 5 Deswelling kinetics of NG and DB-modified gels at 45°C from the equilibrium swollen state at 15°C.

DB20 is a little higher than them. Great increase of the SR can be seen for DB30 and DB100. It can be seen from Figure 4 that the PTT are around 32°C for gels NG, DB5, DB10, and DB20 while the PTT of gels DB30 and DB100 are around 31°C. The structure of gels DB30 and DB100 were loose. This structure leads the gels to absorb more amount of water at swollen state. At shrunken state above PTT the macropores cannot be occupied entirely by the hydrophobic crosslinked polymer chain as NG gels and the pores of certain size, which can hold a part of water still exist, and so, the SRs of gels DB30 and DB100 are much higher than that of the other gels at shrunken state.

Deswelling kinetics

The deswelling kinetics of gels after a temperature jump from 15°C (below PTT) to 45°C (above PTT) are shown in Figure 5. The deswelling rate increased obviously as increase of the amount of DDBAB. The deswelling rate of gel NG was very slow. It could only loss less than 40% of water even after 2 h. The samples DB5 and DB10 had a similar deswelling kinetics and the rates of them were a little faster than the rate of gel NG. The swelling degrees of the samples DB5 and DB10 were about 30% after 2 h. The deswelling rate of gel DB20 was comparatively fast. The gel DB20 can lost about 70% of water in 20 min and almost reached to its equilibrium shrunken state over 120 min. The deswelling rates of gels DB30 and DB100 were so fast that the time needed for reaching to their equilibrium shrunken states was just 1 min. Here we want to emphasize that we used swelling degrees to describe the swelling and deswelling kinetics because some of the gels had a high SR in the shrunken state to get a normalized

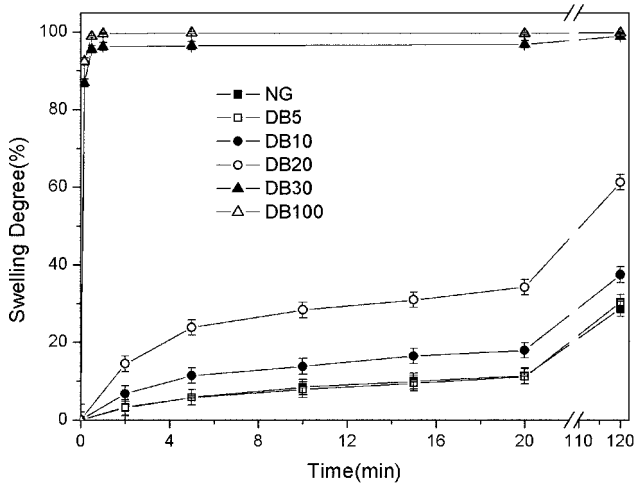


Figure 6 Reswelling kinetics of NG and DB-modified gels at 15°C from the equilibrium shrunken state at 45°C.

result. The swelling degree does not directly indicate the proportion of water in the gel. But the swelling degree indicates the swollen state of the gel between equilibrium swollen (100%) and equilibrium shrunken (0%) states. In Figure 5, the swelling degree of DB100 could reach to nearly zero after a few seconds. This did not denote that almost all absorbed water could be lost, actually, it indicated that the gel reached to an equilibrium shrunken state rapidly and there was still a certain proportion of water in the gel.

The conventional gels form a compact hydrophobic skin layer in the initial stages of the deswelling process, which prevents further water extrusion from interior of the gels. In this study, a heterogeneous structure with interconnected macropores was formed during the synthesis of gels DB30 and DB100 since sufficient amount of DDBAB was added. The pores at the surface of gels was not closed completely and dense hydrophobic skin did not formed, and so, the internal water would be squeezed out of gels directly because of the whole network shrinking.

It has been proven that polymerization of NIPAAm and BIS in the frozen state could result in PNIPA gels with fast deswelling kinetics.[22] However, the deswelling rate of gel NG prepared at −8°C in this study was not such fast. The possible reason for this result was that both the polymer concentration and crosslinking density of gel NG were approximately twice than the gel of Zhang's[22] and the size of gel NG was also much larger, which reduced the deswelling rate of gel NG. In fact, gel NG did deswell faster than the conventional gels, which are prepared at room temperature with both same concentration of NIPAAm and BIS concentration and same size in our additional experiments. The aim of our work is at preparing hydrogels with faster responding property even than that of the gels prepared by frozen polymerization and we think we have found a novel method.

Reswelling kinetics

Figure 6 shows the reswelling kinetics of NG gel and DB-modified gels underwent a temperature jump from the equilibrium shrunken state at 45 to 15°C. An exciting result can be observed from Figure 6 that gels DB30 and DB100 swelled from the equilibrium shrunken state to the equilibrium swollen state in just tens of seconds, the result could rarely be found in most of the former research works. The kinetics of gels NG and DB5 were similar and the rates of DB10 and DB20 were improved. For gels DB20 and DB100, the time needed to reach the equilibrium swollen state was even less than the time to reach the equilibrium shrunken state from the swollen state in the measurement of deswelling kinetics, which never appeared in former works. Because of the incomplete closed porous structure at shrunken state, water molecules could easily diffuse into the interior of the gels. The surface pores enlarged when reswelling, permitting more water molecules to enter into the gels. It was difficult for water molecules to diffuse into the matrix of gel NG, since its pores were closed at equilibrium shrunken state.

Dswelling–reswelling kinetics

The swelling reversibility is also an important property in most of the applications. The deswelling–reswelling kinetics of gels NG, DB20, and DB100 are shown in Figure 7. These gels underwent five deswelling–reswelling cycles in 5 min between 45 and

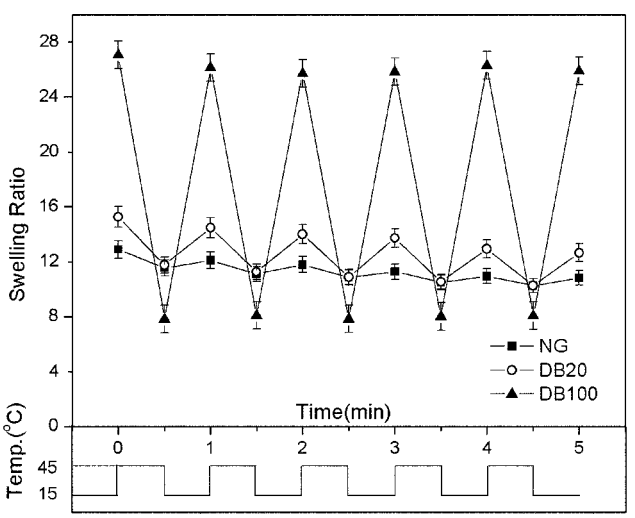


Figure 7 Cycles of deswelling–reswelling processes of PNIPA gels.

15°C in water. The SR of gel DB100 reduced from about 28 to 8 in 30 s when the environmental temperature increased from 15 to 45°C, while the SR increased from about 8 to 28 again during the reswelling, which indicated that gel DB100 underwent a cycle of shrinking to less than third of its equilibrium swollen volume and then came back to nearly equilibrium swollen state again in just 1 min. The changes of gel NG and gel DB20 were not remarkable and the SR appeared downtrend because the reswelling rate was slower than deswelling rate. The wonderful reversible property of gel DB100 was also owing to the macroporous structure.

CONCLUSIONS

This article proposes a novel method to prepare a macroporous PNIPA gel with ultrarapid response properties by adding DDBAB. The insoluble initiator DDBAPS was proved to be prepared by the reaction of DDBAB and APS. Polymerization/crosslink reaction was initiated by the insoluble DDBAPS, which formed a heterogeneous initiation system *in situ* when the solution had been frozen. This initiation system resulted in interconnected macroporous structure, which significantly enhanced the response rate of the hydrogels. The effects of DDBAB amount used on pore size, SR, deswelling and reswelling kinetics, and swelling reversibility of deswelling–reswelling were significant. The optimal amount of DDBAB for obtaining the macroporous structure was about 30 mg per 1.5 mL water containing 0.1 mL 4% APS solution. The method of forming a heterogeneous initiation system *in situ* would be a new way to synthesis macroporous materials. This macroporous PNIPA gel with ultrarapid response and good reversible properties may be useful both in medicine and in biotechnology.

References

1. Hirokawa, Y.; Tanaka, T. J Chem Phys 1984, 81, 6379.
2. Annaka, M.; Tanaka, T. Nature 1992, 355, 430.
3. Suzuki, A.; Tanaka, T. Nature 1990, 346, 345.
4. Tanaka, T.; Nishio, I.; Sun, S. T.; Ueno-Nishio, S. Science 1982, 218, 467.
5. Miyata, T.; Asami, N.; Uragami, T. Nature 1999, 399, 766.
6. Inomato, H.; Goto, S.; Saito, S. Macromolecules 1990, 23, 4887.
7. Tokuhiro, T.; Amiya, T.; Mamada, A.; Tanaka, T. Macromolecules 1991, 24, 2936.
8. Luo, Q. Z.; Mutlu, S.; Yogesh, B. Electrophoresis 2003, 24, 3694.
9. Beebe, D. J.; Moore, J. S.; Bauer, J. M.; Yu, Q.; Liu, R. H.; Devadoss, C.; Jo, B. H. Nature 2000, 404, 588.
10. Bae, Y. H.; Okano, T.; Hsu, R.; Kim, S. W. Makromol Chem Rapid Commun 1987, 8, 481.
11. Annaka, M.; Matsuura, T.; Kasai, M.; Nakahira, T.; Hara, Y.; Okano, T. Biomacromolecules 2003, 4, 395.
12. Ding, Z.; Chen, G.; Hoffman, A. S. J Biomed Mater Res 1998, 39, 498.
13. Hu, Z. B.; Lu, X. H.; Gao, J.; Wang, C. J. Adv Mater 2000, 12, 1173.
14. Wu, X. S.; Hoffman, A. S.; Yager, P. J Polym Sci Part A: Poly Chem 1992, 30, 2121.
15. Yoshida, R.; Uchida, K.; Kaneko, Y.; Sakai, K.; Kikuchi, A.; Sakurai, Y.; Okano, T. Nature 1995, 374, 240.
16. Kaneko, Y.; Sakai, K.; Kikuchi, A.; Yoshida, R.; Sakurai, Y.; Okano, T. Macromolecules 1995, 28, 7717.
17. Kaneko, Y.; Nakamura, S.; Sakai, K.; Aoyagi, T.; Kikuchi, A.; Sakurai, Y.; Okano, T. Macromolecules 1998, 31, 6099.
18. Serizawa, T.; Wakita, K.; Kaneko, T.; Akashi, M. J Polym Sci Part A: Poly Chem 2002, 40, 4228.
19. Serizawa, T.; Uemura, M.; Kaneko, T.; Akashi, M. J Polym Sci Part A: Poly Chem 2002, 40, 3542.
20. Kaneko, T.; Asoh, T.; Akashi, M. Macromol Chem Phys 2005, 206, 566.
21. Zhang, X. Z.; Zhuo, R. X. Macromol Rapid Commun 1999, 4, 229.
22. Zhang, X. Z.; Zhuo, R. X. Macromol Chem Phys 1999, 200, 2602.
23. Zhang, X. Z.; Zhuo, R. X. Eur Polym Mater 2000, 36, 643.
24. Zhang, X. Z.; Zhuo, R. X.; Yang, Y. Y. Biomaterials 2002, 23, 1313.
25. Zhang, X. Z.; Yang, Y. Y.; Chung, T. S. Langmuir 2002, 18, 2538.
26. Zhang, X. Z.; Zhuo, R. X. Eur Polym Mater 2000, 36, 2301.
27. Zhang, X. Z.; Yang, Y. Y.; Chung, T. S.; Ma, K. X. Langmuir 2001, 17, 6094.
28. Yan, H.; Fujiwara, H.; Sasaki, K.; Tsujii, K. Angew Chem Int Ed 2005, 44 1951.