Ionization-Induced Ultrarapid Response Behavior of Fibrous and Porous Electrospun Hydrogels Containing Carboxyl Groups

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ABSTRACT: Fibrous porous membranes composed of poly(*N*-isopropylacrylamide-*co*-acrylic acid) and poly(*N*-isopropylacrylamide-*co*-hydroxyethyl methacrylate) were prepared by electrospinning. The membranes behaved like hydrogels in water after being crosslinked at elevated temperatures. Investigations of the swelling and deswelling behavior indicated that the response rates significantly increased after the carboxyl and/or anhydride groups in the hydrogel membranes were ionized or neutralized with NaOH. It took them less than 60 s to reach equilibrium swelling and about 90 s to reach equilibrium deswelling. The response rates were much higher than those of the parent un-ionized membranes; this indicated that ionization played an important role in the ultrarapid response behavior. The response rate was also higher than that of most hydrogel materials previously reported and was even comparable to superporous hydrogels with high moisture contents. The mechanism of the ultrarapid response behavior of the ionized membranes was qualitatively analyzed. We believe that the fine fiber diameter, high porosity, and improved wettability with water contributed to the ultrarapid response behavior. This study presents a new and facile method for improving the response rate of hydrogel materials made by electrospinning. © 2009 Wiley Periodicals, Inc. J Appl Polym Sci 115: 2485–2492, 2010

Key words: fibers; hydrogels; swelling

INTRODUCTION

Temperature-responsive poly(*N*-isopropylacrylamide) (PNIPAm) hydrogel materials are well known for their dramatic volume-phase transition from a swollen, hydrated state to a shrunken, dehydrated state when the temperature is increased from below to above the lower critical transition temperature (LCST) at about 32°C. PNIPAm hydrogels have attracted great attention because of their potential and demonstrated applications, which range from superabsorbents, drug-controlled release systems, enzyme and cell immobilization, bioseparation, and on–off switches in microfluid systems.[1–6]

A high response rate is crucial for the applications of PNIPAm hydrogels. However, conventional PNIPAm hydrogels directly synthesized in aqueous solutions show low response rates, especially deswelling rates, because a dense skin layer that prevents the diffusion of water forms during dehydration.[7–9]

Therefore, many strategies have been developed in the last decade to improve the response rates of PNIPAm hydrogels.[10–22] For example, freely mobile and grafted chains[10,11] and pendent micellar structures[12] have been introduced into the network of PNIPAm hydrogels. A heterogeneous phase-separated structure was incorporated by the synthesis of PNIPAm hydrogels in mixed solvents of water and tetrahydrofuran.[13] Some macroporous and microporous PNIPAm hydrogels[14–19] with greatly increased response rates were reported. Superporous hydrogels, synthesized by crosslinking polymerization of monomers in the presence of gas bubbles formed by the chemical reaction between acid and $NaHCO_3$, exhibited ultrarapid swelling and deswelling rates.[20] Copolymerization with surfactants and water-soluble monomers also enhanced the swelling rates.[21] Zhuo et al.[7] reported poly(vinyl alcohol) (PVA)/PNIPAm hydrogels with a semi-interpenetrating network structure. The hydrogels exhibited both high mechanical properties and significantly enhanced response rates, which underwent full deswelling in 1 min. It was believed that the PVA formed water-releasing channels, which gave rise to the increased hydrophilicity of the hydrogel networks. However, the swelling process was not as rapid as the deswelling process: several 10 s of minutes were necessary for the gel to reach maximum swelling.

On the other hand, electrospinning is a facile and versatile method for preparing nonwoven mesh fabrics, membranes, or mats containing ultrafine fibers from polymer solutions. It has recently attracted great research interest, especially for the fabrication of functional and reactive ultrafine fabrics that can be used as sensors, filtration media, biomaterials, and so on.[22–24] The application of electrospinning to prepare hydrogels has also been explored. To our knowledge, Hsieh and coworkers[24–27] were the first to report electrospun hydrogels. Ultrafine hydrogel fibrous membranes from poly(acrylic acid) (PAAc),[24] a mixture of poly (N-isopropylacrylamide-co-acrylic acid) [poly(NIPAm-co-AAc)] and PVA,[25] PVA/PAAc mixtures[26] and poly(acrylamide-co-maleic acid)[27] have been reported.

At the same time, a few previously reported macroporous or superporous hydrogels[20] exhibited ultrarapid swelling and/or deswelling kinetics with a minimum swelling time of about 1 min. Because electrospun membranes are also highly porous and their submicrometer-sized fibers are thinner by one to three orders of magnitude than the cell walls of the previously reported porous hydrogels, it is reasonable to expect that electrospun hydrogels may exhibit response rates surpassing conventional porous hydrogels. However, according to Chen and Hsieh,[25] the swelling rates of PVA-crosslinked electrospun hydrogels was not as high as expected: it took 5 min or even longer to reach maximum swelling.

Zhang et al.[28] found that the ionization of carboxyl groups (—COOH) increased the temperature sensitivity of acrylic acid (AAc) containing hydrogels as a result of the stronger electrostatic repulsion among carboxylate anions (—COO$^-$) and the expanded conformations of polymer chains in the hydrogels. Therefore, it is reasonable to expect that ionization could also enhance the response rates of electrospun hydrogels containing carboxyl groups.

In this study, we used Zhang's approach and investigated the influence of an ionization or neutralization reaction on the response behavior of electrospun hydrogels composed of poly(NIPAm-co-AAc) and poly(N-isopropylacrylamide-co-hydroxyethyl methacrylate) [poly(NIPAm-co-HEMA)]. The samples were crosslinked by an esterification reaction in the fibers. We demonstrated that ionization of the AAc and/or anhydride groups significantly enhanced the swelling and deswelling rates; for example, it took only about 30–60 s for the gel to reach equilibrium swelling and 90–200 s for the gel to reach equilibrium deswelling. The response rates were even comparable to those of superporous hydrogels with very high moisture contents.[20] The ultrarapid response rates of the ionized samples were attributed to the improved wettability or hydrophilicity of the membranes. On the contrary, the response rates of the un-ionized specimens were

much lower: the times for swelling and deswelling equilibriums were about 5 min and 200–300 s, respectively. We believe that this study presents an alternative route for the production of ultrarapid responsive hydrogel materials.

EXPERIMENTAL

Materials

N-Isopropylacrylamide (NIPAm) and hydroxyethyl methacrylate (HEMA) were purchased from Sigma-Aldrich (Shanghai, China). AAc, 2,2′-azobisisobutyronitrile, potassium persulfate, sodium phosphate dibasic (Na_2HPO4), N,N′-dimethylformamide, and tetrahydrofuran were analytical grade. NIPAm was purified by recrystallization in a toluene/n-hexane mixture, and all other chemicals were used as received.

Preparation of the polymer

Poly(NIPAm-co-HEMA) was synthesized by free-radical polymerization in deionized water at 70°C under nitrogen protection with potassium persulfate as an initiator. The feed ratio of NIPAm against HEMA for the preparation of the copolymer was 95 : 5. The potassium persulfate content was 0.2 wt % of the monomers. The product was dried in vacuo at 60°C overnight and washed with a large amount of alcohol to remove the residual monomer and initiator. Poly (NIPAm-co-AAc) was synthesized in tetrahydrofuran at 65°C with 2,2′-azobisisobutyronitrile as an initiator. The feed ratio of NIPAm to AAc for the preparation of poly(NIPAm-co-AAc) was 50 : 50. The product was dried in vacuo at 40°C for 1 week. The polymerization conversions of the two copolymers were both determined to be above 92%. The compositions of the copolymers were estimated by elemental analysis. The actual molar ratios of NIPAm in poly(NIPAm-co-HEMA) and poly(NIPAm-co-AAc) were 86.7 and 43.2 mol %, respectively.

Electrospinning and aftertreatment

The copolymers poly(NIPAm-co-HEMA) and poly(NIPAm-co-AAc) were weighed and added to N,N′-dimethylformamide. The suspension was magnetically stirred until the polymers were completely dissolved. A small amount of a saturated Na_2HPO_4 aqueous solution was added dropwise. The content of Na_2HPO_4 was 0.5 wt % of the polymers. Na_2HPO_4 not only increased the conductivity of the solutions but also worked as a catalyst for the esterification reaction between HEMA and AAc in the electrospun fibers.[25] The weight ratios of the two copolymers were 50 : 50, 70 : 30, and 90 : 10, respectively. Stock solutions with the various polymer contents (from 2 to 20 wt %) were prepared for

electrospinning. We finally found that polymer solutions with solid contents in the range 7–10 wt % showed quite satisfying electrospinnabilities. Electrospinning was carried out on a laboratory-made apparatus similar to one that was reported in the literature.[24] The polymer solution was poured into a 50-mL syringe attached to a syringe pump (WZ-50C6, Medical Instruments Corp. of Zhejiang University, Hangzhou, China) mounted on a vertical mount. The potential was applied to the needle tip with a high-voltage power supply (Qiaofeng Electrostatic Equipment Factory, Hangzhou, China). Electrospinning was conducted at a voltage of 20 kV and an extrusion rate of 1.0 mL/h under ambient conditions. The fibers were collected on grounded aluminum foil as the target. The distance between the target and the needle tip was about 10 cm. After electrospinning, the obtained electrospun mats with a thickness of about 2 mm were dried at 80°C overnight *in vacuo* and then heat-treated at 140°C for 1 h and at 160°C for 0.5 h for crosslinking. Subsequently, the samples were immersed in a 0.05M NaOH aqueous solution for about 10 min to allow the NaOH solution to permeate into the porous membranes. During this process, the nonesterified carboxyl groups were neutralized; also, the anhydride groups were hydrolyzed and ionized. Finally, the samples were purified after they were repeatedly immersed in deionized water and drained to remove the excess NaOH solution. Significantly, when the samples were immersed in the NaOH solution for a long time (e.g., 12 h or longer), they were completely dissolved; this demonstrated the occurrence of the hydrolysis of ester crosslinkages in the fibers.

Determination of the swelling ratios and response rates

Because the swollen hydrogels became quite slippery and somewhat fragile, to measure the equilibrant swelling ratios several pieces of dried hydrogel membranes were placed in a shallow sieve basket with a diameter of 4 cm and a height of 1 cm of stainless steel wires and immersed in deionized water at various temperatures for about 48 h. The sieve basket was taken out to drain free water, and a filter paper was used to remove excess water from underneath the sieve. The weight of the swollen electrospun hydrogel membranes was determined by subtraction of the basket weight from the total weight. The equilibrium swelling ratios were determined by the following equation:

$$\text{Equilibrium swelling ratio} = (W_s - W_d)/W_d$$

where W_s is the weight of the swollen hydrogel membranes at equilibrium and W_d is the weight of the dried hydrogel membranes.

To determine the swelling rates, the dried samples were quickly immersed in deionized water at 25°C, taken out at certain time intervals, and then measured gravimetrically after excess water was removed from underneath the sieve basket with filter paper. The swelling ratio was defined as follows:

$$\text{Swelling ratio} = (W_t - W_d)/W_d$$

where W_t is the weight of the swollen hydrogel membranes at a particular time. The deswelling rate at various temperatures was determined gravimetrically in a similar method after the samples were equilibrated in water at 25°C for 48 h. The definition of deswelling ratio was as follows:

$$\text{Deswelling ratio} = (W_t - W_d)/(W_s - W_d) \times 100\%$$

The values shown in this article are the average of five duplicated experiments.

Characterization

The as-electrospun membranes were sputter-coated with gold and observed on a SIRION-100 field emission scanning electron microscope (FEI, Eindhoven, The Netherlands) at a voltage of 5 kV to shed light on the morphology and fiber diameters. The porosity of the as-electrospun membranes was measured by mercury porosimetry (Autopore IV 9500, Micromeritics, Norcross, GA). The surface area was measured by nitrogen adsorption of the fibers with an Autosorb-1-C volumetric adsorption analyzer (Quantachrome Instruments, Boynton Beach, FL) and calculated with the Brunauer–Emmett–Teller (BET) method.

RESULTS AND DISCUSSION

Morphology of the electrospun fibers

Figure 1 presents representative field emission scanning electron microscopy (FESEM) images at different magnifications of the as-electrospun membranes of the mixture of poly(NIPAm-*co*-HEMA) and poly(NIPAm-*co*-AAc) at a ratio of 50 : 50. The figure shows that the fibers were solid and uniform in both shape and size. Defects frequently observed in electrospun fibers, such as beads or fibers with a so-called beads-on-a-string structure, were not observed; this indicated that the sample solution used in this study had satisfactory electrospinnability. The average fiber diameter was about 200 nm [see the inset of Fig. 1(B)], and the membranes were highly porous. The porosity of the as-electrospun membranes was 96.4%, as determined by mercury porosimetry, and the BET surface
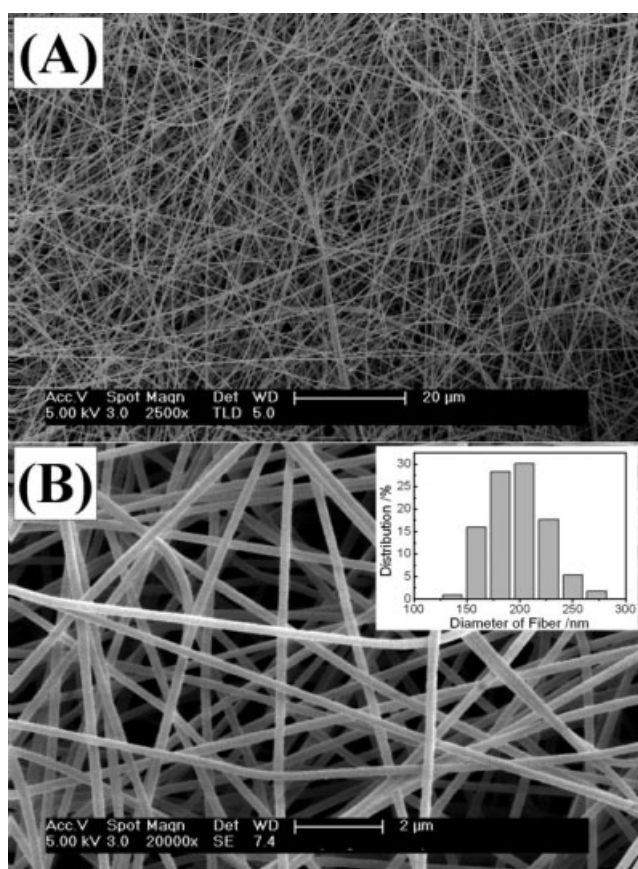
Figure 1 FESEM images of electrospun fibrous membranes of poly(NIPAm-*co*-HEMA)/poly(NIPAm-*co*-AAc) at magnifications of (A) 2500 and (B) 20,000×. The inset shows the histogram of the fiber size distribution. The samples were thermally crosslinked at elevated temperatures but not hydrated in water.

area was 9.11 m^2/g, as determined by nitrogen adsorption (Table I).

The as-electrospun membranes could be easily dissolved in water. Only after crosslinking at elevated temperatures did the membranes become insoluble in water and behave like hydrogels. Upon being immersed in water, the dried membranes adsorbed water rapidly, swelled significantly, and finally formed translucent and slippery hydrogels, as shown in Figure 2(A). As to the microstructure of the dehydrated hydrogel membranes, the FESEM image in Figure 2(B) shows that the membranes remained porous and that the fibers in the membranes still remained fibrous after a cycle of hydration and dehydration (drying). The average fiber diameter was about 220 nm [see the inset of Fig. 2(B)], which was only slightly larger than that of the as-electrospun fibers, as shown in Figure 1(B), and the BET surface-area-to-volume ratio was determined to be 8.24 m^2/g, which was only slightly smaller than that of the as-electrospun membranes (Table I). This further demonstrated that the fibers

TABLE I
Porosity and BET Surface Area of the Hydrogel Membranes

Sample	Porosity	BET surface area (m^2/g)
Before hydration and drying	96.4%	9.11
After hydration and drying	40.2%	8.24

were crosslinked, whereas the fibers were apparently twisted and the packing density was obviously higher. The mercury porosimetry results show that the porosity of the dehydrated hydrogel membranes was 40.2%, which was much smaller than that of the as-electrospun membranes.

The fibers were crosslinked by the esterification reaction between the hydroxyl and carboxyl groups in the fibers under the catalysis of Na$_2$HPO$_4$.[25] Furthermore, because the molar concentration of AAc was higher than that of HEMA in all three samples, the excess carboxyl groups underwent anhydridation at temperatures above 140°C. As reported previously, the intramolecular dehydration upon heating did not contribute to the intermolecular crosslinking
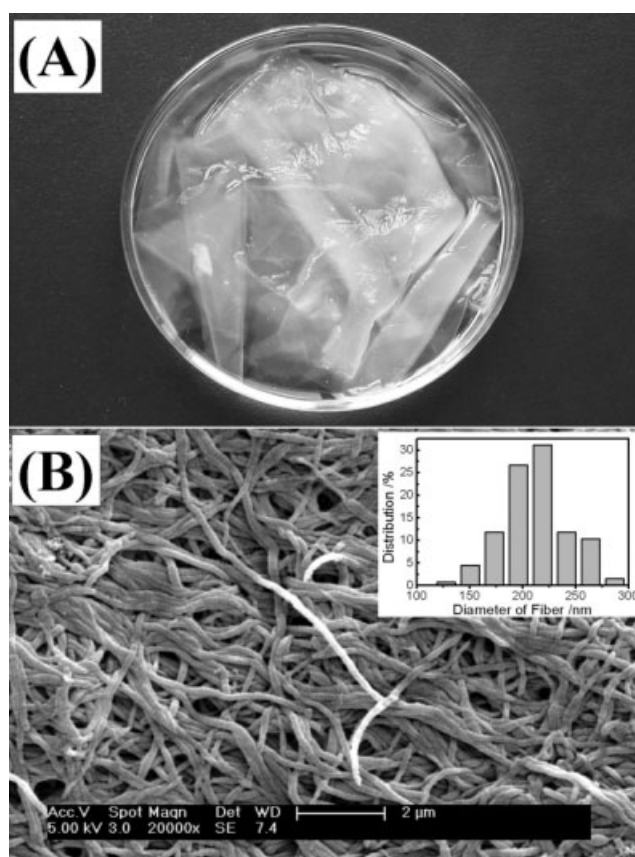

Figure 2 (A) Optical picture of electrospun fibrous membranes of poly(NIPAm-*co*-HEMA)/poly(NIPAm-*co*-AAc) in a swollen state and (B) FESEM image of these membranes after dehydration *in vacuo*. The inset shows the size distribution of the dehydrated fibers.
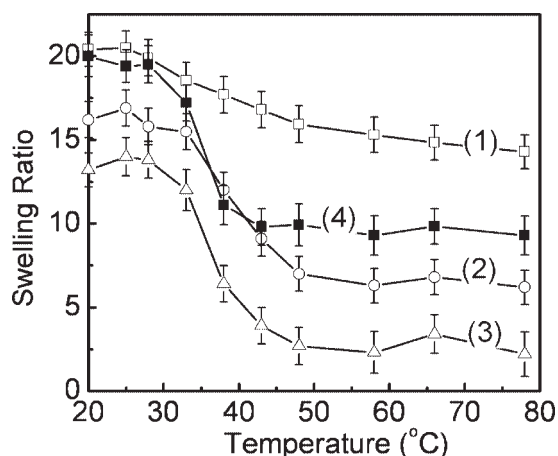
Figure 3 Temperature dependence of the swelling ratios of (1–3) ionized electrospun hydrogel membranes [with poly(NIPAm-*co*-HEMA)/poly(NIPAm-*co*-AAc) weight ratios of (1) 50 : 50, (2) 70 : 30, and (3) 90 : 10] and (4) un-ionized samples (with a weight ratio of 50 : 50).

and insolubility of the electrospun fibers.[25] However, as mentioned in the following section, the carboxyl and/or anhydride groups played a crucial role in determining the properties of the electrospun fibers: upon hydrolysis and neutralization, they significantly improved the hydrophilicity, water-retention properties, and response rate of the electrospun fibers.

Swelling and deswelling behavior

The temperature dependence of the swelling ratios of the ionized and un-ionized electrospun hydrogel membranes is shown in Figure 3. In the un-ionized sample, the weight ratio of poly(NIPAm-*co*-HEMA) to poly(NIPAm-*co*-AAc) was 50 : 50, whereas the weight ratios of the two copolymers in the three ionized samples were 50 : 50, 70 : 30, and 90 : 10, respectively. An apparent decrease in the swelling ratios was observed at temperatures above 33°C for all of the samples. The transition temperature was consistent with the LCST of PNIPAm hydrogels reported in the literature.

The swelling ratios of the un-ionized sample (see curve 4, Fig. 3) were somewhat smaller than those of the ionized sample with a similar composition (see curve 1, Fig. 3) at temperatures below LCST. At temperatures above LCST, the un-ionized sample also exhibited a lower water retention. At the same time, the water retention increased with the increase of poly(NIPAm-*co*-AAc) content in the ionized membranes. Therefore, we concluded that ionization increased the hydrophilicity of the hydrogels and then increased the swelling ratios and water retention.

The influence of ionization and the content of carboxyl groups on the LCST values is also shown in Figure 3. The LCST was about 35°C after ionization, which was higher than that of pure PNIPAm and un-ionized poly(NIPAm-*co*-AAc). It was also obvious that the swelling transition occurred more broadly, which was consistent with the results of nonporous hydrogels of poly(NIPAm-*co*-AAc).[25,29]

The swelling behavior of the ionized hydrogel membranes is presented in Figure 4(A). All of the three ionized samples reached equilibrium swelling in less than 60 s. Because the swelling rates were very high and the time intervals for sample weighing were relatively long, it was not possible to conduct an accurate kinetic analysis in this study. On the contrary, the swelling rate of the un-ionized hydrogel membranes was much lower. As shown in Figure 4(B), it took more than 5 min for the gel to reach equilibrium swelling, which was close to what was previously reported for PVA-crosslinked PAAc electrospun hydrogel membranes.[25] This indicated that the hydrolysis of the anhydride groups and the
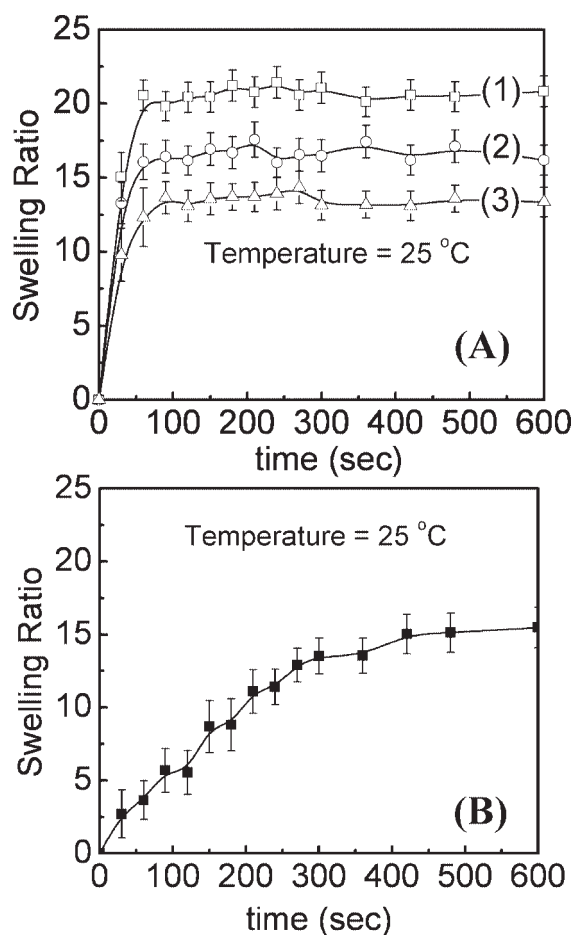

Figure 4 Swelling behavior of (A) ionized samples [with poly(NIPAm-*co*-HEMA)/poly(NIPAm-*co*-AAc) weight ratios of (1) 50 : 50, (2) 70 : 30, and (3) 90 : 10] and (B) an un-ionized sample (with a weight ratio of 50 : 50).

ionization of the carboxyl groups significantly enhanced the swelling rates of the samples.

The deswelling kinetics of the ionized and un-ionized hydrogel membranes at temperatures above LCST are presented in Figure 5(A,B), respectively, in which the weight ratio of the two copolymers was 50 : 50. The deswelling rates of the ionized samples were very high; for example, the samples reached equilibrium deswelling in about 90–200 s for all of the temperatures investigated. Also, the deswelling kinetics of the ionized hydrogel electrospun membranes of other compositions showed similar response rates, but the water retention at equilibrium was much lower. As shown in Figure 5(B), the deswelling rate of the un-ionized sample was also high but was somewhat lower than that of the ionized samples: it took about 200–300 s for the gel to reach deswelling equilibrium. In general, as shown in Figures 4 and 5, the ionized electrospun hydrogel membranes showed both ultrarapid swelling and deswelling rates.

Mechanism of the ultrarapid swelling and deswelling kinetics

It is well known that the swelling and deswelling behaviors of nonporous hydrogels are diffusion-controlled. The kinetics strongly depend on the size of the hydrogels. If there is no convection transport and water sorption is a pure diffusion process, the swelling rate can be determined by the following equation:[30]

$$\frac{W}{W^*} = 4\sqrt{\frac{Dt}{\pi L^2}} \propto t^{0.5} \quad \text{for} \quad W/W^* < 0.8 \qquad (1)$$

where W and W^* are the amounts of water adsorbed at time t and at equilibrium, respectively; D is the effective water diffusion coefficient in the hydrogel; and L is the hydrogel thickness. Similarly, Sato and Tanaka[9] showed that the characteristic times of hydrogel swelling and deswelling (τ) were determined by the characteristic size of the gel (L) and the diffusion coefficient of the polymer network (D) as $\tau = L^2/D$, which can be assumed to be almost the same for hydrogels with the same composition. Therefore, by decreasing the dimension of hydrogels, the swelling and shrinking kinetics can be greatly enhanced. In porous hydrogels, the thickness of cell walls is usually several to several hundred micrometers. Thus, it is understandable that the response rate of porous hydrogels can be greatly decreased. However, the dimension of the hydrogels is not the sole factor affecting the response kinetics. As reported previously,[31] PNIPAm minigels, that is, hydrogel spheres with a particle size of several 10s of micrometers in their swollen state, can reach
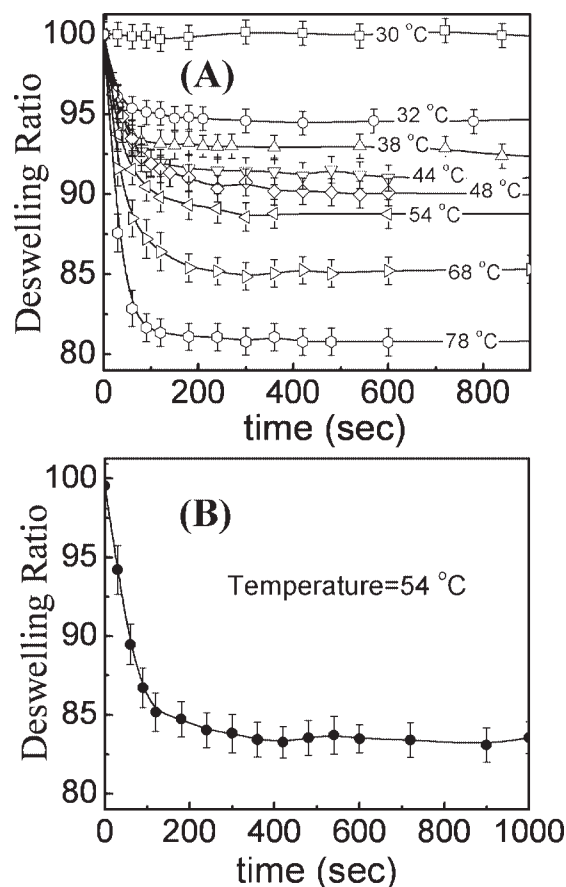

Figure 5 Deswelling kinetics of (A) an ionized sample at various temperatures and (B) an un-ionized sample at 54°C. The weight ratio of the two copolymers in the two samples was 50 : 50.

swelling and deswelling equilibrium within 1 s. This is faster than the rate of porous hydrogels, although the dimensions of the cell walls of the latter are similar to that of the minigels and the polymers of the porous hydrogels are more hydrophilic.

Because the electrospun hydrogel membranes are highly porous, swelling is, in fact, a combination of two simultaneous processes: permeation of water into interfiber pores (capillary flow) and diffusion of water into hydrogel fibers. Similarly, the deswelling process combines together the dehydration of hydrogel fibers and the squeezing of water out of the porous media. Therefore, the final swelling or deswelling rate is determined by the slower one of the two processes. As mentioned previously, PNIPAm minigels that were several 10s of micrometers in size could reach swelling and deswelling equilibrium within 1 s, which was much faster than the rate of electrospun hydrogel membranes containing submicrometer-sized fibers. Thus, we concluded that the capillary flow was the slower process and determined the final response rates of the electrospun porous hydrogels.

We now consider the influence of ionization on the response rates of the electrospun hydrogels. As is well known, the permeation rate of a liquid in porous media can be described by the Washburn equation as follows:

$$h^2 = \frac{t\gamma R\cos\theta}{4\eta} \qquad (2)$$

where h is the height of the liquid front; R is the mean diameter of the pores; γ and η are the surface tension and the viscosity of the solvent, respectively; θ is the contact angle; and t is the time required for the solvent to rise the distance h above the liquid. Obviously, the hydrophilicity or wettability with water of the porous hydrogels plays a crucial role in the swelling and deswelling kinetics because the smaller the contact angle is, the higher the permeation rate is. Moreover, for electrospun hydrogel membranes, the mean diameter of the pores increases with increasing swelling ratio because of the bulk volume expansion, and the contact angle decreases because of the hydration of the fibers. Chen and Park[32] demonstrated that the swelling time of superporous hydrogels decreased from about 9 to 1 min when the moisture content was increased from about 10 to 140 wt %. Also, as mentioned previously, Zhang et al.[28] demonstrated that poly(NIPAm-co-AAc) hydrogels exhibited improved temperature sensitivity because of the dissociation of carboxyl groups (—COOH) of AAc to carboxylate anions (—COO⁻). These studies confirmed that increased hydrophilicity resulted in an enhanced response rate. As to the electrospun membranes, ionization significantly improved their hydrophilicity. According to previous studies,[33] the water contact angle of surfaces coated with polyanhydride decreased from about 100° to about 40° after polyanhydride was hydrolyzed at pH 7.2. The water contact angle values of surfaces coated with carboxyl groups decreased from about 50–60° to about 30° after ionization.[34] The static water contact angle values of the porous electrospun membranes could not be measured because the water droplets were absorbed rapidly when they were placed on the surface of the porous electrospun membranes. Therefore, the hydrophilicity of the electrospun membranes was qualitatively evaluated by observation of the spreading and adsorption behavior of water droplets on the dried surface of the electrospun membranes. I took less than 10 s for a water droplet to completely spread and permeate the dried ionized hydrogel membrane, whereas the time was prolonged to more than 10 min for the un-ionized membranes. This confirmed that ionization of carboxyl and anhydride groups greatly improved the hydrophilicity of the membranes.

CONCLUSIONS

Ultrathin thermoresponsive fibrous porous hydrogel membranes were prepared by the electrospinning of PNIPAm copolymers, followed by heat treatment for crosslinking. The crosslinked membranes behaved like hydrogels, and the fibers in the membranes remained fibrous after they were immersed in water and then dried. Swelling and deswelling measurements showed that the electrospun fibers were thermosensitive and exhibited ultrarapid response rates after the anhydride and carboxyl groups on the fibers were ionized by neutralization with NaOH, whereas the un-ionized fibers exhibited a much lower swelling rate. Both the ultrathin fiber diameters and the enhanced hydrophilicity or wettability of the ionized electrospun membranes contributed to their unusual ultrarapid response rates. We believe such ultrarapid responsive materials can find applications in many fields, such as superabsorbents, biomolecular separation and purification, and drug-controlled release systems.

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