Macromolecules

Volume 36, Number 4 February 25, 2003

Communications to the Editor

Wide-Range Control of Deswelling Time for Thermosensitive Poly(*N*-isopropylacrylamide) Gel Treated by Freeze-Drying

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Received September 3, 2002
Revised Manuscript Received December 19, 2002

Stimuli-responsive hydrogels have great potential to construct a variety of systems for drug delivery, absorbents, sensors, and actuators.[1] For these systems to give high performance, the response rate is one of the most important factors. In our previous paper,[2] a treatment of a freeze-drying (FD) and hydration for thermosensitve poly(*N*-isopropylacrylamdei) gel, poly(NIPAAm) gel, was reported as a simple and effective method to accelerate the gel deswelling. After the FD treatment, the honeycomb structure of the gel was formed by hydrophobic bonds between polymer chains. Water in the gel was easily expelled through the honeycomb pores in the deswelling process. According to Gehrke and co-workers, the stimuli-response time of environmentally sensitive gels can be dramatically reduced by decreasing a strut thickness of honeycomb pores as the characteristic diffusional path length.[3] It is considered that pore formation in the gel brings about a decrease of the diffusional path length and an increase of the surface area of the gel. Consequently, some approaches have been reported on the preparation of the porous, fast-responsive gels including γ-irradiation of poly(vinyl methyl ether) solutions to gelate,[4] gel preparation by heating above a lower critical solution temperature (LCST) of the polymer,[5] the incorporation of other hydrophilic polymer into the thermosensitive gel,[6] preparation of the comb-type polymer network,[7] the incorporation of surfactants during gel synthesis,[8] and the incorporation of microparticles into a thermosensitive gel.[9] We have reported the magnetically responsive gel device using the fast-responsive gels after the FD treatment.[10] However, the control of pore sizes or the deswelling time has not been investigated yet.

In the case of our freeze-drying method for pore preparation, water content during the freezing process should be a critical factor to determine the pore size and the rate for expelling water from the gel. The purpose of this research is to demonstrate the relationship between water content and the pore size of gels, and to control the time of gel deswelling as desired. Therefore, the effect of the FD treatment on the pore formation was clarified by images of scanning electron microscopy (SEM), and the deswelling profiles were determined by jumping the temperature from below to above the LCST of the gel.

The gel synthesis and the treatment of the freeze-dry and hydration for the conventional gels were carried out as described in our previous report.[2] Poly(NIPAAm) gel rods were prepared in silicone tubes (2 mm in inner diameter of the mold). Polymerization of the gel cross-linked by *N*,*N*′-methylenebis(acrylamide) (MBA) [NIPAAm/MBA = 99/1−90/10 (mol/mol)] was initiated by ammonium peroxodisulfate, and accelerated by *N*,*N*,*N*′,*N*′-tetramethylethylenediamine. First, the effect of MBA content on gel deswelling was determined as follows. The gel rods equilibrated in water at 295 K were put into flasks and cooled from 295 to 253 K with immersion of the flask in a cool bath. The gel became cold up to 253 K within 3 min, of which the temperature was determined with a thermocouple inserted into the gel. Then the gel was freeze-dried using FD-1 (Tokyo Rikakikai). The gel rods were re-swollen in water at 295 K. The deswelling profiles of gel rods were determined by the temperature jump from 295 to 323 K. The gel length (L) was measured from the pictures recorded by videotape. Time evolution of the gel volume, $(L/L_0)^3$, was

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10.1021/ma0214198 CCC: $25.00

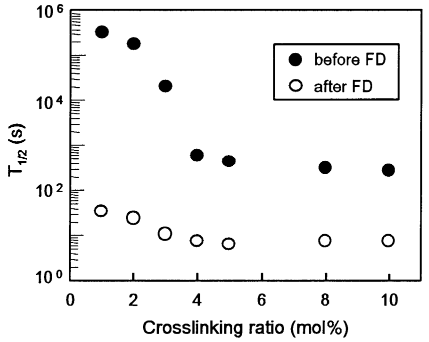

Figure 1. Dependence of the cross-linking ratio of poly(NIPAAm) gel with time for the half deswelling $t_{1/2}$. The conventional gels equilibrated at 295 K were freeze-dried and then re-swollen in water. The times for $t_{1/2}$ were determined just after the temperature was jumped from 295 to 323 K.

given, where L_0 is the initial length of the gel rod ($L_0 =$ 60 mm). We defined the time for half-deswelling of gel ($t_{1/2}$), when $(L/L_0)^3$ passed by 0.5. Second, we prepared 11 kinds of poly(NIPAAm) gels [NIPAAm/MBA = 99/1] equilibrated at different temperatures (276−323 K). The equilibrium swelling degree (Q) for each gel was calculated as the ratio of the swollen weight to the dry weight of the gel. After equilibrating the gel at required temperature, Q was controlled from 23.0 at 276 K to 1.5 at 323 K. Then, the treatment of the freeze-drying and hydration was applied to the 11 kinds of gel rods containing the different amount of water. After re-swelling, the length of each gel at 22 °C returned up to more than 98% of the first length at 22 °C before freezing. Also, the actual volume change of gels was nearly the same even after the FD treatment. To determine the size of pores formed by freezing, the morphology of freeze-dried gel was directly observed with SEM (S-4500, Hitachi) just after freeze-drying. We investigated the cross-sectional morphology of gel rods with altering diameters (1−5 mm). In the case of gel rods for 2 mm in diameter, the gel morphology did not change for the direction of depth. Thus, all of the data were obtained from gel rods of 2 mm. After the gel rods were equilibrated at at 295 K, the temperature was jumped up to 323 K. From the deswelling profile of $(L/L_0)^3$ against time, each $t_{1/2}$ was calculated.

The dependence of the MBA content on $t_{1/2}$ was shown in Figure 1. The $t_{1/2}$ of the poly(NIPAAm) gel was shortened effectively by the FD treatment irrespective of the cross-linking ratio. For the conventional gels, the $t_{1/2}$'s were given between 5 min and 100 h. After the FD treatment, the $t_{1/2}$'s were controlled to be between 8 and 40 s. These results show that the cross-linking ratio is a critical factor, especially for the deswelling time of conventional gels. High content of MBA can cause a decrease in the deswelling time to form rigid networks.[2] On the contrary, the rate of expelling water from the FD treated gel was accelerated at a magnitude of 10^2−10^4 as compared with that of conventional gel. Since the rapid shrinking process can be repeated many times, the microporous structure is probably permanent. However, the swelling of all gels remained slow and was not affected by the microporous structure.

The relationship between pore size of the gel and Q was examined. The gel rods equilibrated at various temperatures gave respective Q's. The representative values of Q were obtained to be 23.0, 16.5, 14.0, 6.7, 5.0, 1.6, and 1.5 at 3, 22, 26, 31.5, 32, 40, and 50 °C, respectively. Figure 2 shows the SEM microphotographs of the FD treated gels frozen at different Q's ($Q = 23.0$−1.5). The pore size was observed to decrease with decreasing Q, and the macropores disappeared in the case of $Q = 1.5$. According to the previous paper, the poly(NIPAAm) gels in the deswelling state above the LCST have only bound water surrounding the polymer chains, except free bulk water.[11] Since the bound water was considered not to freeze at 253 K,[12] the FD treatment could not cause significantly to change the structure of polymer network at $Q = 1.5$. From these consideration, we deduced that water content in the process of freezing gel was an important factor to control the pore size. In our previous report,[2] no pores in the range of micrometer size were shown in the SEM microphotograph on poly(NIPAAm) gel, which was prepared by vacuum-drying instead of the freeze-drying at $Q = 14.5$. This result supports our deduction that the pores are probably formed in the freezing process.

The deswelling profiles were determined for the conventional and the FD treated gel rods due to the temperature jump from 295 to 323 K (Figure 3). The rate of gel deswelling was accelerated with increasing Q on the FD treatment as shown in Figure 3. The deswelling profile of FD treated gel at $Q = 1.5$ was superposed on that of conventional gel. This result led

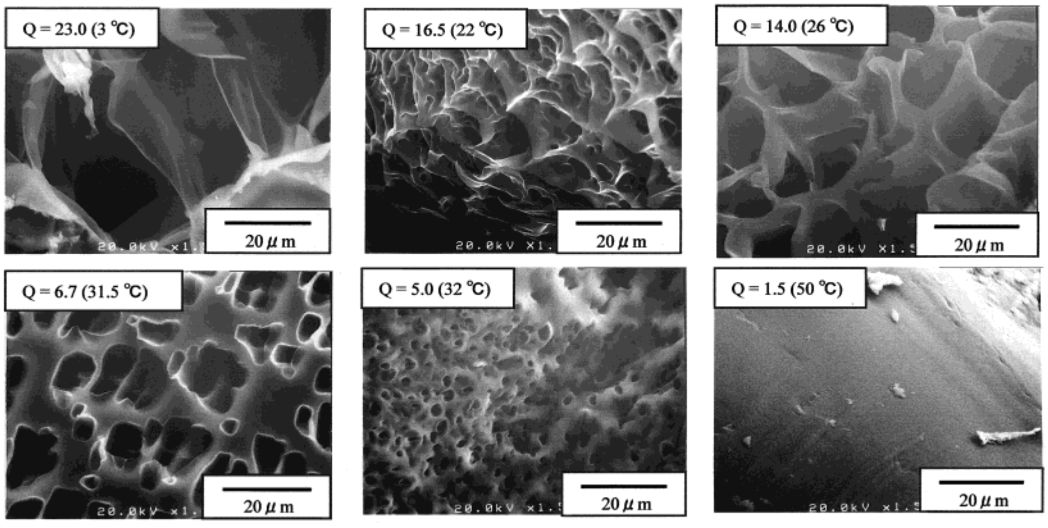

Figure 2. SEM images of the freeze-dried poly(NIPAAm) gels. The gels contained different amounts of water ($Q = 23.0$−1.5), were frozen at 253 K, and then were freeze-dried.

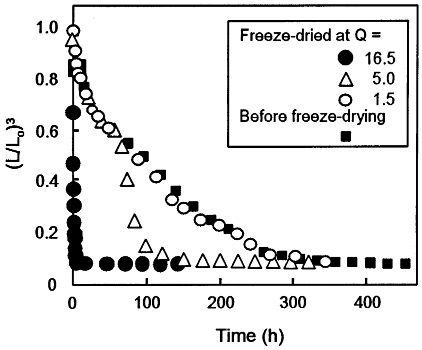

Figure 3. Time dependence of the swelling ratio $(L/L_o)^3$ just after the temperature was jumped from 295 to 323 K.

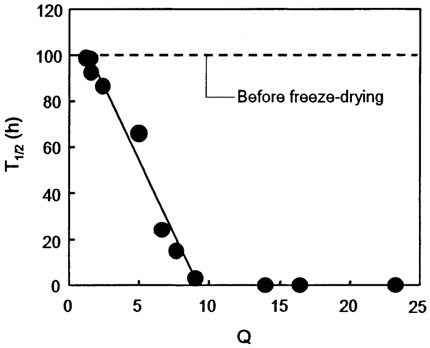

Figure 4. Relationship between the time for half deswelling $t_{1/2}$ and equilibrium swelling degree Q before the freezing. The time for $t_{1/2}$ was determined just after temperature was jumped from 295 to 323 K.

to the same conclusion on the SEM photograph in Figure 2. Note that the gel desweling at $Q = 5.0$ showed the two-stage profiles (stage I, 0−70 h, and stage II, 70−200 h); the gel deswelled as well as the conventional gel during stage I and then turned to fast deswelling after around 70 h.

Figure 4 showed the relationship between $t_{1/2}$ and Q. In the case of $Q > 10$, $t_{1/2}$'s were obtained to be around 30−40 s. The $t_{1/2}$ increased with decreasing Q in less than 10, and reached 100 h at the minimum of Q. This is in accord with the $t_{1/2}$ of conventional gel. It is speculated from the results in Figures 2 and 4 that the decrease of Q causes the smaller pores possessed the thicker struts, the smaller surface area of gels, and the slower gel deswelling. It is considered that the water content is insufficient to form pores in the gel under $Q < 10$. These results suggested that the deswelling rates of poly(NIPAAm) gel were easily controlled by adjusting the water content in the gel before the FD treatment. The $t_{1/2}$ covers from 30 s to 100 h.

Concerning the fast-shrinkable gels, the control of deswelling rate was reported using the incorporation of microparticle within the gel, of which the deswelling time was reduced to 1/80th by adding silica as the mold.[9] As compared with this method, the FD treatment has the advantage of controlling the deswelling time in the extensive range. The $t_{1/2}$ for the FD treated gel came to approximately $1/10^4$th in magnitude as compared with that for the conventional gel.

It was demonstrated in conclusion that the porous structure of the polymer gel could be altered with controlling the equilibrium swelling degree of gels before the FD treatment and deswelling time was shortened by the FD treatment.

Acknowledgment. This work was partly supported by a Grant-in-Aid (No.14750613) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

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MA0214198