Rapid Deswelling of Porous Poly(*N*-isopropylacrylamide) Hydrogels Prepared by Incorporation of Silica Particles

Takeshi Serizawa, Kazuaki Wakita, and Mitsuru Akashi*

Department of Applied Chemistry and Chemical Engineering, Faculty of Engineering, Kagoshima University, Korimoto 1-21-40, Kagoshima 890-0065, Japan

Received July 30, 2001
Revised Manuscript Received October 19, 2001

Thermoresponsive polymers, which change their physical and/or chemical properties depending on environmental temperature, have gained much attention not only because of their unique properties but also because of their potential for significant technological and biomedical applications. Poly(*N*-isopropylacrylamide) (PNIPAAm) is a well-known thermoresponsive polymer, which shows a coil−globule transition at a lower critical solution temperature (LCST).[1] Many researchers have investigated the thermoresponsive properties of PNIPAAm and the copolymers with other acrylates.[2] PNIPAAm has also been conjugated with various substrates such as polymeric films,[3] silica,[4] proteins,[5] and so on, to regulate certain processes by environmental temperature.

Hydrogels have been prepared from the monomer NIPAAm and suitable cross-linkers, and these hydrogels also exhibit volume phase-transition at the LCST of PNIPAAm and shrink above the LCST with the release of swelled water.[6] Many researchers have studied this phase-transition to analyze its chemical and physical properties.[7] Since the hydrogels can act as a reservoir for various functional molecules, e.g., in biomedical applications, temperature-dependent controlled release of molecules has been demonstrated.[8] In addition, the rapid swelling and deswelling of hydrogels is important for the use of actuators.[9] The deswelling rate of hydrogels is known to be relatively slow compared to that of linear polymer. To refine the hydrogel properties, it is important to enhance and control the shrinking rate by suitable methods.

The formation of a porous structure has been shown to effectively enhance the deswelling rate of PNIPAAm gels. Several reports have described the simple preparation of porous hydrogels including (1) the incorporation of surfactants during hydrogel preparation and their subsequent extraction,[10] (2) hydrogel preparation above its LCST,[11] and (3) hydrogel preparation by a freeze-dry and hydration process.[12] In all cases, the deswelling rate of PNIPAAm hydrogels has been enhanced by the formation of porous structures.

In the present study, porous PNIPAAm hydrogels having a rod shape were prepared by the incorporation of silica microparticles and subsequent acid treatment to remove the silica, and the thermoresponsive properties of these hydrogels were analyzed. The deswelling rate was significantly enhanced compared to conventional hydrogels and was easily controllable by adjustments in the amount of silica. Using the present method, it is simple to control the thermoresponsive properties of the resulting hydrogels. These results are comparable to those of a previous study, in which porous hydrogels were prepared by the polymerization of monomer solutions incorporated into nanoporous silica particles, with a millimeter size range, and subsequent acid treatment was used to remove the silica.[13] Such porous silica−hydrogel composites have been used as a support for the controlled release of model drugs.[14]

PNIPAAm hydrogels were prepared by free radical polymerization of NIPAAm (monomer) and *N*,*N*′-methylenebis(acrylamide) (BIS) (cross-linker) in the presence of ammonium persulfate (APS) (initiator) and *N*,*N*,*N*′,*N*′-tetramethylenediamine (TEMED) (polymerization accelerator) for 8 h at 4 °C in a glass capillary tube with a diameter of 1 mm. For the preparation of porous hydrogels, 0−22% v/v (silica/solvent) of silica particles with a polyhedral shape and a mean size of 3.3 μm was added before the polymerization, and subsequently the silica particles were dissolved in the aqueous 23 wt % HF solution by immersion of the hybrid hydrogels for 24 h at ambient temperature. The resulting cylinder-shaped hydrogel was then cut into 10 mm lengths for the analysis of thermoresponsive properties. Transmission Fourier transformed infrared (FT-IR) spectra were obtained with a Herschel FT/IR-610 (Jasco) under a nitrogen atmosphere at ambient temperature. The hydrogels were freeze-dried and put into a KBr pellet. The interferograms were co-added 10 times and Fourier transformed at a resolution of 4 cm^{-1}. For scanning electron microscopic (SEM) observation, the hydrogels were quick frozen in liquid nitrogen, and then dried under a vacuum. The dried hydrogels were fixed onto a stage for SEM observation. Gold was sputtered onto the sample at a thickness of approximately 20 nm. The surface was then analyzed with a HITACHI S-4100H (Hitachi) at an accelerated voltage of 5 kV. The swelling and deswelling of the hydrogels were observed directly by a Stemi DV4 microscope (Carl Zeiss, Jena, Germany) connected to a digital camera Cyber-shot DSC−F505V (Sony). The swelling ratios were calculated from the weight ratio between the swollen hydrogel (W_s) and the dried one (W_d) (W_s/W_d) and from the ratio between the diameter of the hydrogel at 20 °C (D_0) and the corresponding temperature (D): D/D_0. To analyze the deswelling process quantitatively, a semilogarithmic plot as a first-ordered rate analysis was applied to the time dependence of the deswelling as follows

$$\ln\{(D - D_\infty)\}/\{(D_0 - D_\infty)\} = -kt$$

where D_∞ is the equilibrium-swelling diameter at adequate temperature, k is a constant, and t is time. The greater the slope of the plot of $\ln\{(D - D_\infty)/(D_0 - D_\infty)\}$ against t, the faster the deswelling process.

The preparation conditions and the characterization of porous hydrogels are summarized in Table 1. A monomer, NIPAAm, was polymerized with a cross-linker, BIS, by free radical polymerization in the presence of silica, resulting in the formation of hydrogels with yields between 79 and 82%. The disappearance of a siloxane vibration band for the sequential IR analysis indicated the dissolution of the silica particles incorporated into the hydrogels. The absorption bands corresponding amide groups (amide I and II) were also maintained and the carbonyl vibration band typically assigned to carboxyl acids was not observed. These results indicate that treatment of the hydrogels in an

10.1021/ma011362+ CCC: $22.00
Published on Web 12/06/2001

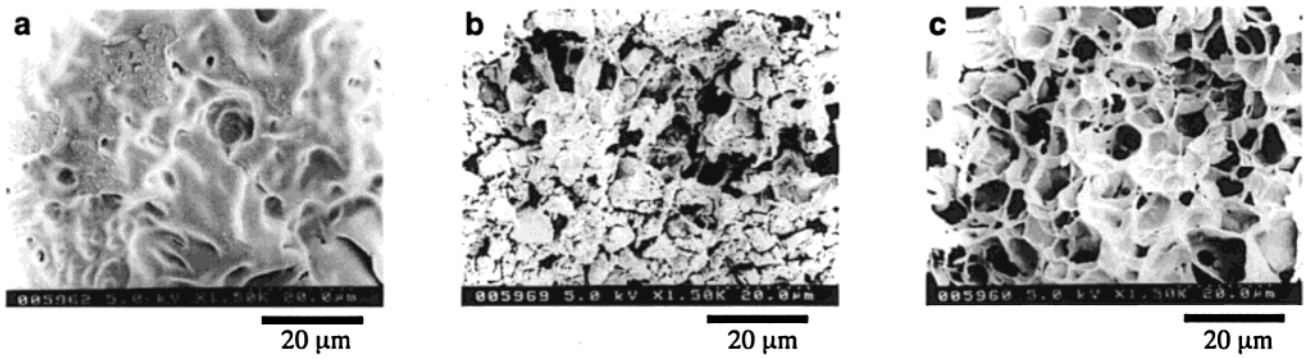

Figure 1. SEM observations of (a) nonporous hydrogel (run 1 in Table 1), (b) 22% v/v silica containing hydrogel, and (c) the resulting porous hydrogel following silica removal (run 4).

Table 1. Preparation of Poly(*N*-isopropylacrylamide) Hydrogel[a]

run	NIPAAm (mmol)	BIS (mol % to NIPAAm)	silica content to solvent (v/v %)	silica content to solvent (w/v %)	yield (%)	swelling ratio (W_s/W_d) 20 °C	swelling ratio (W_s/W_d) 40 °C
1	3.5	5	0	0	82	11	2
2	3.5	5	2	5	81	11	2
3	3.5	5	11	30	79	12	2
4	3.5	5	22	60	80	13	2

[a] Hydrogels were prepared in the presence of APS (1 mol % to NIPAAm), TEMED (5 mol % to NIPAAm) and 5 mL of ultrapure water (solvent).

aqueous HF solution did not damage the amide linkages of NIPPAm. In addition, the porous hydrogels had self-supporting properties even after the silica had been extracted. Figure 1 shows typical SEM observations of hydrogels. The PNIPAAm as a hydrogel component and silica particles were observed in the hybrid, as shown in Figure 1b. After HF treatment, the silica particles had disappeared and pores could be clearly observed in the hydrogel, as shown in Figure 1c. On the other hand, pores were not observed in hydrogels prepared without the silica particles, as shown in Figure 1a. These observations indicate that porous PNIPAAm hydrogels were successfully prepared by the present technique.

Before the analysis of deswelling and swelling rates, the equilibrium−swelling ratio at each temperature was analyzed by two methods. The weight ratios of swollen to dried hydrogels (W_s/W_d) at 20 and 40 °C were almost the same, even for porous hydrogels prepared with different silica contents, as shown in Table 1. The diameter ratios of the hydrogels (D/D_0) were also the same at each temperature. The ratio decreased at approximately 30 °C, however, indicating that the hydrogels showed a volume−phase transition at this temperature. This temperature is consistent with the LCST of PNIPAAm. To analyze the deswelling and swelling rates in situ, the diameter ratios were applied to the process. Figure 2 shows the time dependence of the deswelling of porous hydrogels prepared with various amounts of silica when the temperature of the aqueous media was quickly changed from 20 to 40 °C. The deswelling rate drastically increased with increased silica content. We also found that the deswelling rate could be easily controlled by manipulation of silica content. The deswelling and swelling cycle was repeatable and reproducible at least three times, even for the porous hydrogels. To analyze the results quantitatively, the time dependence was applied to this first-order process, as shown in Figure 3. The plots were linearly fitted with a coefficient of variation of more than 0.999,

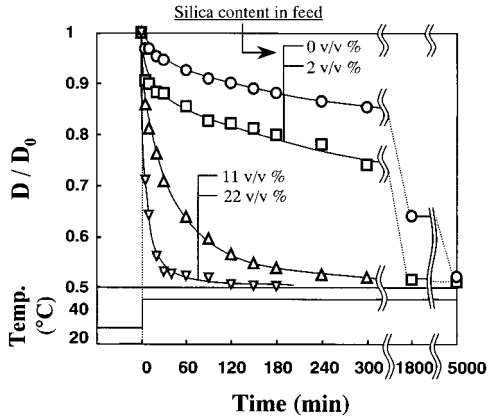

Figure 2. Time dependence of the swelling ratio (D/D_0) when temperature was increased from 20 to 40 °C.

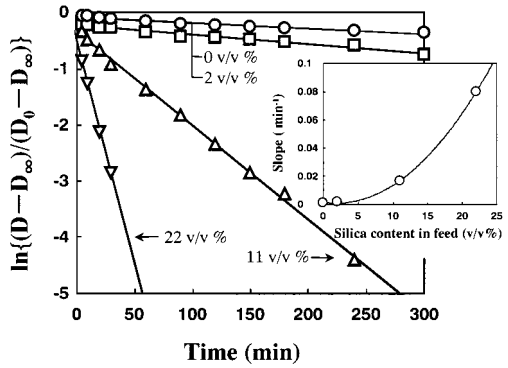

Figure 3. Rate analysis of the deswelling properties of porous hydrogels.

indicating the deswelling process can be apparently governed by the first-ordered manner. The slope for the hydrogel prepared from the 22% v/v silica was 80 times greater than that for the conventional hydrogel prepared without silica. Note that the first 5 min of deswelling was ignored in the fitting since the initial deswelling was faster than the subsequent shrinkage. Further study of this initial step is necessary. The inset of Figure 3 shows the dependence of the slope on silica content. The plot could be fitted to the following equation with a coefficient of variation of 1.0

$$Y = 2.0 \times 10^{-4}X^2 - 7.7 \times 10^{-4}X + 1.6 \times 10^{-3}$$

where Y and X indicate the y and x axes in the inset of Figure 3, respectively. Accordingly, it is possible to design any hydrogel with desired deswelling behavior by controlling the silica content. On the other hand, the

swelling process of the porous hydrogels was independent of the silica content when the temperature of the aqueous media was quickly changed from 40 to 20 °C. The swelling of all hydrogels were reached to be equilibrium after 60 min. As the swelling was rapid, the porous structure of the hydrogels did not apparently affect the kinetics of the process, as demonstrated in a previous study.[15] The rate-limiting step in the swelling seemed to be independent of the porosity of the hydrogels.

Porous PNIPAAm hydrogels were prepared by free radical copolymerization of its monomer and a cross-linker in the presence of silica particles and the subsequent acid treatment for the silica extraction. The porous hydrogels demonstrated a deswelling rate at least 80 times greater than that of conventional hydrogels, when the temperature was increased above the LCST of PNIPAAm. The deswelling rate could be easily regulated by manipulation of silica content. Swelling of the hydrogels was not affected by the porous structure, since this process was rapid. The present methodology is very easy and applicable to other stimuli-responsive hydrogels. Further research regarding other factors affecting the thermoresponsiveness, mechanical properties, and controlled release of substances from porous hydrogels are now in progress.

Acknowledgment. This work was financially supported in part by a Grant-in-Aid for Scientific Research in the Priority Area of "Molecular Synchronization for Design of New Materials System" (No. 404/11167270, 13022258) and by a Grant-in-Aid for Scientific Research (No. 476/12750802 and No. 10555326) from the Ministry of Education, Culture, Sports, Science, and Technology, Japan.

Supporting Information Available: Figure showing FT-IR spectra of (a) conventional PNIPAAm hydrogels, (b) silica particles, (c) silica-incorporated PNIPAAm hydrogels prepared in the present study, and (d) porous hydrogels prepared by the subsequent acid treatment. This material is available free of charge via the Internet at http://pubs.acs.org.

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MA011362+