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Freezing Effects of PEG-Modified Poly(*N*-isopropylacrylamide) Gel on Deswelling Acceleration

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Fast response hydrogel was synthesized with applying a freezing method to poly(ethylene glycol) (PEG) modified poly(*N*-isopropylacrylamide) (PNIPA) gels. Previously, an effective and simple method of preparing fast-responsive gel was developed; a freeze-drying and subsequent rehydration of thermosensitive gels changes their microstructural properties of three-dimensional polymer network due to ice crystal formation inside gels during freezing. SEM images and the dynamic mechanical measurements indicated that different type of heterogeneous microstructure was formed on the PEG modified PNIPA gels during freezing. Deswelling kinetics of PNIPA gel sheets copolymerized with PEG macromonomer as PEG monomethacrylate (PEGMA) (PEGMA/NIPA = 0/100, 20/80, 40/60 mol/mol) with or without the freezing treatment was elucidated by mass change when the temperature was jumped from 22 to 60°C in water. Both the freezing treatment and PEG incorporation were effective to accelerate the gel deswelling. An effective diffusion coefficient of deswelling could be increased to 5.5×10^{-4} cm^2/s by the freezing method, while that for the conventional PNIPA gel was 2.3×10^{-7} cm^2/s.
Key words: thermosensitive gel, freeze-drying, fast response, *N*-isopropylacrylamide, porous gel

1. INTRODUCTION

Control of the gel microstructure is responsible for controlling a variety of gel functions such as stimuli-responsive rates, solute permeability, and equilibrium swelling degree [1]. For most application of gels, to maximize or control the response rate is the key factor for technical and commercial success. Expansion or collapse rates of gels are generally determined by the cooperative diffusion of the polymer in the solvent. Since the diffusion coefficient of polymers is on the order of 10^{-7} cm^2/s, swelling and deswelling of gels are quite slow [1-3]. To overcome diffusion-limited kinetics in macroscopic gel samples, many efforts were made for preparing porous structure of gels [4-8]. Time needed for network motion depends on the characteristic diffusion path length; network diffusion of porous gels occurs over the scale of the microstructre rather than in macroscopic dimensions.

In our previous papers, we proposed a simple method of preparing fast response gels. The freeze-drying (FD) and subsequent rehydration was effective to make gels microporous [1,8]. The effects of the method were demonstrated with some hydrogels including crosslinked vinyl polymers [8,9] and crosslinked polysaccharide [10]. After the FD-treatment, honeycomb-like pores were observed for thermosensitive poly(*N*-isopropyl-acrylamide) gel, PNIPA gel, of which pore size could be controlled by adjusting water content prior to freezing. Since the size of generated pores depended upon water contents of gels, polymer chains are excluded and aggregated while ice crystals grow inside gels during the freezing process. The heterogeneous three-dimensional network remains apparently with physical cross-linking via hydrophobic interaction and polymer entanglement even after cycles between shrinking and swelling in aqueous milieu. In this report, the FD method was applied to PNIPA gel containing poly(ethylene glycol) (PEG) chains. Since PEG is more hydrophilic than PNIPA, incorporation of PEG chains is expected to change hydrophobic/hydrophilic character of PNIPA gels and the microstructure generated by freezing.

The purpose of this paper is to evaluate the effects of the FD-treatment on weight change kinetics and microstructure of PNIPA gels co-polymerized with PEG macromonomer.

2. EXPERIMENTAL

2.1 Materials

NIPA was purchased from Wako Pure Chemical. Poly(ethylene glycol) methacrylate, PEG-MA, (Average molecular weight 360) was purchased from Aldrich. All other chemicals were of reagent grade.

2.2 Gel synthesis

The gel synthesis procedure followed the basic scheme described in our previous paper [8]. Gels with a PEG–MA mole fraction X at the gel preparation are denoted by NIPA-PEG (X), where X is calculated as PEG-MA/(NIPA + PEG–MA). NIPA and PEG-MA were dissolved in water (X = 0, 0.2, or 0.4), while total concentration of NIPA and PEG-MA monomers keeps to set as 1.0 mol dm^{-3}. The gels were cross-linked with 2 mol% *N*, *N'*-methylenebisacrylamide. The cross-linking reaction was allowed to proceed for 24 h at 22°C between two glass plates separated by silicone rubber gasket (1.5 mm thick). Similarly, NIPA-PEG polymers (X = 0, 0.2 or 0.4) were synthesized without the crosslinker, following dialysis to distilled water for purification and then lyophilizing. Average molecular weights of polymers for NIPA-PEG (0), (0.2), and (0.4) were approximately 53,000, 62,000, and 73,000, respectively.

2.3 Freeze-drying

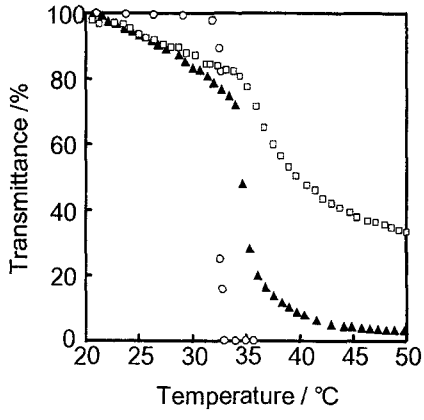

Fig. 1 Effect of PEG monomethacrylate copolymerization on the optical transmittance of PNIPA aqueous solution. The optical transmittance of PNIPA (○), PNIPA-PEG (0.2) (▲), PNIPA-PEG (0.4) (□) were measured at 500 nm with heating, respectively.

After equilibration of NIPA-PEG (0 – 0.4) gel sheets at 22°C in water, the surface of the gel sheet was blotted with lint-free tissue papers and put into a glass flask. Then the flask was immersed in a cooling bath (Tokyo Rikakikai, NCB-2400) at –20°C. The gel sheet was cooled to –20°C within 3 min [9]. After 1 h incubation, the gel sheets were freeze-dried by lyophilizer (Tokyo Rikakikai, FD-1). The gel surface was observed by scanning electron microscope (SEM) operated by 17-18 kV.

2.4 Equilibrium swelling degree

Wet mass of the equilibrated gel sheet was determined with a step change of temperatures. After the measurement of wet mass at 65°C, the dry mass was determined. The equilibrium swelling degree (Q) of the gel sheet was defined as the ratio of wet mass to the dry mass.

2.5 Mass change kinetics

The gel sheet equilibrated at 22°C was transferred to a water bath at 60°C. After a given time t, the gel sheet was separated from water, blotted and weighed. The gel sheet was allowed to equilibrate in the original water bath at 22°C, and then the temperature of the gel sheet was jumped to 60°C again. This procedure was repeated until the gel sheet was fully shrunken.

Deswelling kinetics of the conventional gel without the FD-treatment was determined by another way because of the slow weight change. The gel sheet was immersed in the water bath at 60°C for a desired time, and then separated, blotted and weighed. The gel sheet was placed back to the water bath at 60°C again. This procedure was repeated until the gel weight became independent of time. Total time required for weight readings was always less than 5% of the time required to reach the equilibrium [11]. Swelling kinetics of all gels were determined by the same manner.

2.6 Measurement of the cloud point

Aqueous solution of 1 wt% polymer was used to measure the optical transmittance by UV-VIS spectrophotometer (JASCO, V-55) at 500 nm. Temperature of the polymer solution was detected by a thermocouple inserted into the polymer solution in the cell with stirring. The heating rate was controlled as 0.2°C / min using a peltier thermo-electric controller. A cloud point was determined by curves of the optical transmittance against temperatures.

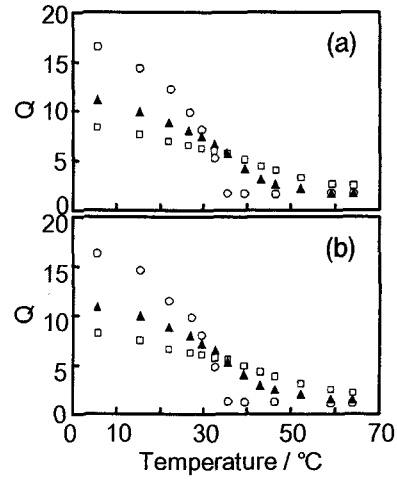

Fig. 2 Temperature dependence of the equilibrium swelling degree of gels before (a) and after (b) the treatments of freezing. Mole-fraction of PEG-MA were 0 (○), 0.2 (▲), and 0.4 (□), respectively.

2.7 Dynamic mechanical measurements

A synthesized wave strain (0.1 Hz) was loaded on the gel sheet by thermomechanical analyzer (Seiko Instruments, TMA/SS6100), while the strain was kept within 1% of the gel thickness. The compressive modulus E' and E'' were determined as the storage and loss modulus, respectively. The loss angle tanδ (=E''/E') was also determined.

3. RESULTS AND DISCUSSION

3.1 Thermosensitive properties of NIPA-PEG polymer

Temperature dependence of the optical transmittance for NIPA-PEG aqueous solutions was investigated (Fig. 1). Since NIPA-PEG polymer solution became cloudy with increasing temperature, Fig. 1 clearly shows that each polymer possessed the thermosensitivity. Incorporation of PEG chains made PNIPA networks hydrophilic because the transmittance of the solution at 50°C increased with increasing PEG contents. Also, the cloud points increased with increment of PEG contents; those for X = 0, 0.2, and 0.4 respectively were 31.9, 34.0, and 34.4°C. The cloud points are defined as the temperatures, at which the transmittance curves bend greatly during the heating process.

Since each polymer has the cloud point, Q of its crosslinked gel also depended upon temperatures (Fig. 2). Weight change of gels was determined between 5 and 65°C before or after the FD-treatment. According to Fig. 2b, temperature dependency of Q was not affected by the FD-treatment irrespective of PEG contents.

3.2 Microstructure of NIPA-PEG gels

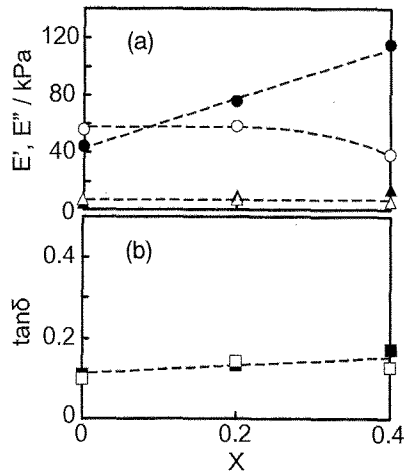

Fig. 3 (a) Relationship between E' or E" for the swollen gel and PEG-MA mole fraction. (b) Relationship between tan δ and the PEG- MA mole fraction. Storage modulus E' (○) and loss modulus E" (△) were determined under 0.1 Hz of synthesized wave strain at 22°C. Open and closed symbols were the gels before and after the treatments of freezing, respectively.

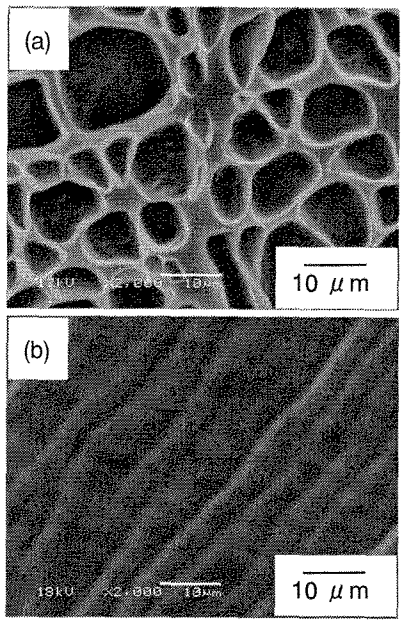

Fig. 4 SEM images of NIPA-PEG gels for X = 0 (a), and X = 0.4 (b). The gels equilibrated at 22 °C were frozen at -20°C and then freeze-dried.

Figure 3 shows the results of dynamic mechanical measurements. The E' of the conventional gel was almost independent of PEG contents X, while that of the FD-treated gel increases with increasing X. This result clearly showed that the FD-treatment was responsible for differently formed microstructures. Figure 4 showed the SEM images of FD-treated gel surfaces. Pore formation was observed for NIPA-PEG (0) without PEG chains, while the trench pattern was just observed for NIPA-PEG (0.4). In our previous papers, we hypothesized that polymer chains were excluded and aggregated while ice crystals grew inside gels during

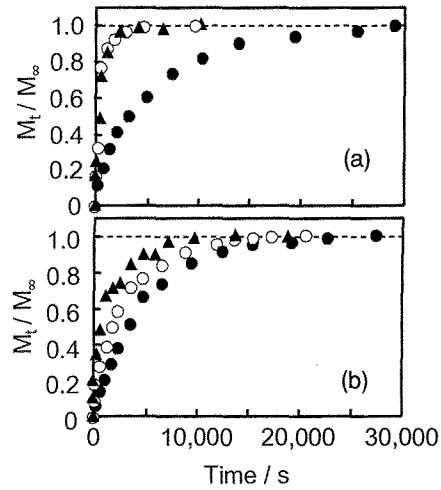

Fig. 5 Weight change kinetics of the NIPA-PEG gel sheets without the freezing treatments. Shrinking (a) and swelling (b) kinetics of gel sheets, of which PEG-MA contents were X = 0 (●), 0.2 (○), and 0.4 (▲), were elucidated due to the temperature jump between 22 and 60°C.

freezing [1, 9, 10]. It is plausible that PEG modified gel becomes hydrophilic and the freezing point of hydrated water in the hydrophilic gel becomes lower. For the FD-treated gels, E' increased due to the heterogeneous network apparently formed with physical forces such as hydrophobic interactions and polymer entanglements. Note that most pores as shown in Fig. 4a were closed cells. Although pore size or trench width should not directly control the water release rates from gels, SEM images and viscoelastic properties of gels reveals that the incorporation of PEG graft chains leads different microstructures during freezing.

3.3 Weight change kinetics

Weight change kinetics for deswelling/swelling were determined by the gravimetric technique. Fractional mass change (M_t/M_∞) was plotted against time t , where M_t and M_∞ are the mass of the water absorbed or desorbed at time t and equilibrium, respectively. Deswelling acceleration of conventional NIPA-PEG gels was caused by PEG incorporation as shown in Fig. 5a. However, some cracks appeared on surfaces of NIPA-PEG (X = 0.2 and 0.4) within 5 min after a step change of temperatures from 22 to 60°C. It's easy for cracked gels to expel water through generated channels that water can flow. Fast deswelling probably depended upon cracks irregularly generated, while swelling rates clearly increased with increasing X. Incorporation of hydrophilic PEG chains should be responsible for the heterogeneous structure of gels containing hydrated PEG domains and aggregated PNIPA domains during deswelling; such a heterogeneous polymer network probably caused to locally crack due to high deswelling pressure. On the contrary, swelling rates of NIPA-PEG gel increased because hydrophilic polymer is easy to hydrate during swelling.

Similarly, deswelling/swelling kinetics were investigated for the FD-treated gel sheets. Figure 6 clearly showed that deswelling time for any gels drastically reduced by the FD-treatment, while the

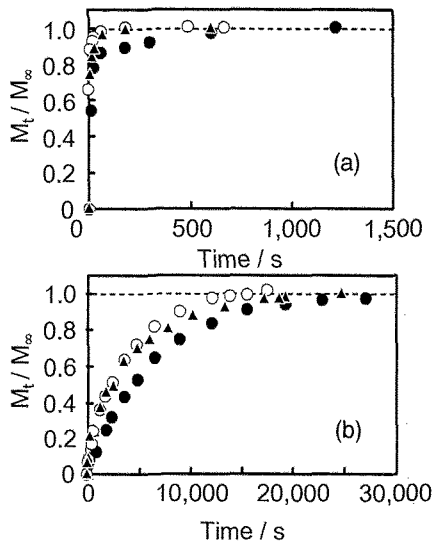

Fig. 6 Weight change kinetics of the NIPA- PEG gel sheets after the freezing treatments. Shrinking (a) and swelling (b) kinetics of gel sheets, of which PEG-MA contents respectively were X = 0 (●), 0.2 (○), and 0.4 (▲), were elucidated due to the temperature jump between 22 and 60°C.

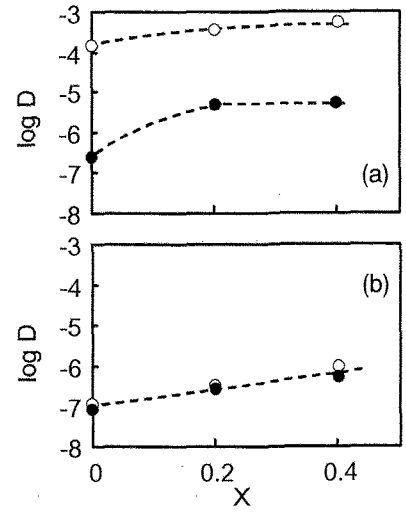

Fig. 7 Dependence of the PEG content on the effective diffusion coefficient of weight change. Deswelling (a) and swelling (b) kinetics were determined between 22 and 60°C using the conventional (○) and the FD-treated (●) gel sheets.

treatment was not so effective to alter the swelling rates. As for swelling process, similar results of thermosensitive hydroxypropyl cellulose gels were reported in our previous paper [10].

An effective diffusion coefficient, D (cm^2/s), was determined by fitting Fick's law of diffusion to the curves (Figs. 5 and 6). The equation of Fick's law for flat sheets could be applied to any data because the aspect ratio of the gel sheet was more than 10 [1, 12]. The magnitude of the deswelling coefficients indicates that the deswelling of the FD-treated gels is probably limited by the convective flow, as unsteady flow through interconnected channels follows the same differential equation as Fick's law. The convective process leads much greater coefficients, as obtained here. As shown in Fig. 7, PEG incorporation is effective to increase D for the FD-treated gels. No crack appeared on any FD-treated gel surfaces during deswelling and swelling. This result suggests that FD-treatment can form microscopic heterogeneous structure that leads interconnected channels irrespective of X. Since these fast deswelling can repeatedly observed due to an abrupt temperature jump (data not shown), the heterogeneous polymer network is stable in aqueous milieu. These results mean that application of the freezing method to PEG-incorporated PNIPA gels successfully accelerate gel deswelling.

4. CONCLUSION

Deswelling kinetics of thermosensitive PEG incorporated PNIPA gels with or without the FD-treatment were elucidated. Conventional NIPA-PEG gel surfaces cracked during deswelling in response to abrupt temperature change and then the deswelling rates increased, while no crack appeared for any FD-treated gels. Heterogeneous polymer network generated by freezing made easy to expel water due to convective flow through the interconnected channels. The effective diffusion coefficient for deswelling increased in magnitude of 10^3 by cooperative effects between PEG incorporation and the freezing method.

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