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Studies on preparation and properties of NIPAAm/hydrophobic monomer copolymeric hydrogels

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Abstract

A series of thermoreversible copolymeric hydrogels with various molar ratios of *N*-isopropylacrylamide (NIPAAm) and hydrophobic monomers such as 2,2,3,3,4,4,5,5-octafluoropentyl methacrylate (OFPMA) and *n*-butyl methacrylate (BMA) were prepared by emulsion polymerization. The effect of hydrophobic monomer on the swelling behavior and mechanical properties of the present copolymeric hydrogels was investigated. Results showed that the equilibrium swelling ratio and critical gel transition temperature (CGTT) decreased with an increase of the content of hydrophobic monomer, but the gel strength of the gel increased with an increase of the content of hydrophobic monomer. Due to stronger hydrophobicity of OFPMA, the NIPAAm/OFPMA copolymeric hydrogels had lower swelling ratios and higher gel strengths than NIPAAm/BMA copolymeric gels.

Keywords: *N*-Isopropylacrylamide; Perfluoroalkyl methacrylate; Hydrogel

1. Introduction

Hydrogel is a hydrophilic three-dimensional network polymer, so it cannot dissolve when it hold a large amount of water and biochemical fluid. The swelling ratio and gel volume of those gels would be affected by the change of surrounding conditions such as temperature [1,2], pH [3,4], ionic strength [5] and electric field [6], so it was extensively used for the separation of solute and control of drug delivery [7–12]. Recently, those hydrogels were applied in drug release and biomedical materials.

The volume variation of the temperature-sensitive gel was caused by different hydrophilic and hydrophobic group in polymeric chain at different temperatures. It is well known that *N*-isopropylacrylamide, NIPAAm, is a temperature-sensitive monomer because it has a lower critical solution temperature (LCST) at about 32 °C. Hence, it was often used for main moiety of temperature-sensitive gels. In recent years, many researches for these hydrogels were focused on drug release and drug delivery.

Fluorine-containing materials had good performance for water resistance. In comparison with poly(*N*-isopropylacrylamide) (PNIPAAm) gel, the incorporation of the hydrophobic component into the NIPAAm gel would provide much more advantages, such as (1) controlling the release rate of hydrophilic drug and (2) increasing the mechanical properties [13]. We expected

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the incorporation of hydrophobic monomer such as perfluoroalkyl methacrylate or *n*-butyl methacrylate (BMA) into PNIPAAm gel would have a fast swelling–deswelling behaviors and better mechanical properties. Hence, two series of copolymeric hydrogels were prepared from NIPAAm and perfluoroalkyl methacrylate or NIPAAm and BMA. The physical properties and swelling and deswelling behavior for these two series copolymeric gels were investigated.

2. Experimental

2.1. Materials

N-Isopropylacrylamide (NIPAAm) (Wako Pure Chemical Industries, Ltd. Osaka, Japan) was recrystallized in *n*-hexane before use. 2,2,3,3,4,4,5,5-Octafluoropentyl methacrylate (OFPMA) (Aldrich Chemical Co. St. Louis, MO), butyl methacrylate (BMA) (Fluka Chemical Co. Buchs, Switzerland), *N*,*N*′-methylenebisacrylamide (NMBA) (Sigma Chemical Co. St. Louis, MO) as a cross-linking agent, and ammonium persulfate (APS) (Wako Pure Chemical Industries, Ltd.) as an initiator were used as received. Sodium lauryl sulfate (SLS) (Nippon Shiyaku Industries Ltd. Osaka, Japan) as an emulsifier and *N*,*N*,*N*′,*N*′-tetramethylethylene diamine (TEMED) (Fluka Chemical Co.) as an accelerator were also used as received. All solvents and other chemicals were of analytical grade.

2.2. Preparation of copolymeric hydrogels

NIPAAm and hydrophobic monomer (OFPMA or BMA) with various molar ratios were dissolved in 10 mL of deionized water. To these solutions, 3 mol% NMBA, 0.2 mol% APS, and 2 mol% SLS were added and well mixed. Finally, 0.2 mol% TEMED was added and the monomer solution was immediately injected into the space between two glass plates. Polymerization was carried out at 25 °C for 1 day. After gelation was completed, the gel membrane was cut into disks, 8 mm in diameter. Then the gels were immersed into an excess amount of deionized water for 3 days. Swollen gels were dried at 40 °C for 2 days and these samples were further dried in a vacuum oven (room temperature) for 1 day. The feed compositions and yields of the copolymeric hydrogels were shown in Table 1.

Table 1
Feed compositions, yields, and equilibrium swelling ratios of the present copolymeric hydrogels

Sample codes	NIPAAm (mol%)	OFPMA (mol%)	BMA (mol%)	Yield (%)	Swelling ratio (g/g)
N	100	0	–	97.8	7.27
OF1	99	1	–	97.2	6.95
OF3	97	3	–	96.3	6.54
OF5	95	5	–	96.8	6.23
OF7	93	7	–	97.5	6.06
B1	99	–	1	95.5	7.08
B3	97	–	3	95.0	6.94
B5	95	–	5	96.4	6.70
B7	93	–	7	94.9	6.21

2.3. Measurement of swelling kinetics

The swelling kinetics of the gels were measured at 25 °C. After wiping off water on the surface with filter paper, the swelling ratio (SR) of the gel was recorded during the course of swelling at each regular time interval.

$$\mathrm{SR} = (W_\mathrm{w} - W_\mathrm{d})/W_\mathrm{d} \tag{1}$$

where W_w is the weight of the wet gel at different times and W_d is the weight of the dry gel.

The dried gels were immersed in an excess amount of deionized water. The swelling ratio was obtained by weighing the initial and swollen samples at various time intervals. The amount of water sorbed, W_t, was reported as a function of time and the equilibrium sorption at an infinitely long time was designated as W_∞. The following equation was used to calculate the diffusion coefficient (D) for $W_t/W_\infty \leqq 0.8$ [14]

$$\frac{W_t}{W_\infty} = \frac{4}{\sqrt{\pi}} \times \left(\frac{D \times t}{L^2}\right)^{1/2} \tag{2}$$

where t is the time and L is the initial thickness of the dried gel. To investigate the diffusion model of the gel, the initial swelling rates were fitted to the exponent heuristic equation for $W_t/W_\infty \leqq 0.6$ [15,16].

$$W_t/W_\infty = kt^n \tag{3}$$

where k is a characteristic constant of the gel and n is a characteristic exponent of the transport mode of the penetrate.

2.4. Measurement of deswelling kinetics

The kinetic of deswelling behavior of the hydrogels was measured at 45 °C. Before the measurement of deswelling kinetics, the hydrogel was reached swollen equilibrium in distilled water at 25 °C in advance. After wiping off water on the surface with filter paper, the weight of the gel was recorded during the course of deswelling at each regular time interval.

The deswelling ratio (DSR)(%) is defined as follows:

$$\mathrm{DSR}(\%) = (\mathrm{SR}/\mathrm{SR}_\mathrm{eq}) \times 100\% \tag{4}$$

where SR_eq is the swelling ratio of the gel at equilibrium.

2.5. Equilibrium swelling ratio at different temperatures

The equilibrium swelling ratios of the gels were measured at different temperatures from 25 to 45 °C. Gel samples were immersed into an excess amount of deionized water for 24 h at each temperature. The equilibrium swelling ratios at different temperatures were calculated as Eq. (1).

2.6. Mechanical properties of the copolymeric gels

The dried gels were immersed into 10 mL of deionized water at 25 °C for 2 days to reach equilibrium. The diameter and thickness of the gels were recorded. The gel strengths of the copolymeric gels were measured by uniaxial compression experiment with universal tester (LLOYD LRX; J. J. Lloyd, Poole, UK). The shear modulus (G) was calculated by the following equation [17,18]:

$$\tau = F/A = G(\lambda - \lambda^{-2}) \tag{5}$$

where τ is compression stress, F is compression load, A is cross-sectional area of the swollen gels, and λ is compression strain ($\Delta L/L_0$). ΔL is difference between the thickness of the dried gel and swollen gels. L_0 is the thickness of the dried gels. At low strain, a plot of shear stress versus $-(\lambda - \lambda^{-2})$ would yield a straight line whose slope is shear modulus (G). The effective crosslinking density (ρ_x) can then be calculated from shear modulus and polymer volume fraction (υ_2) as follows [17,18]:

$$\rho_x = G\upsilon_2^{-1/3}/(RT) \tag{6}$$

where R is gas constant and T is absolute temperature.

2.7. Fast swelling–deswelling behavior of the copolymeric hydrogels

Pre-weighed dried gels were, at first, immersed into deionized water at 25 °C to reach equilibrium. The gels were then transferred into 10 mL of deionized water at 45 °C at each fixed time interval (5 min), then immediately transferred the gels into deionized water at 25 °C. The above measurement for the gels was repeatedly performed for 2 h.

2.8. Morphologies

Samples were equilibrated in deionized water for 1 day, then, the swollen gels were freeze-dried for 2 days. The gels were immersed into liquid nitrogen and fractured. The fractured specimens were examined for morphological details by using scanning electron microscopy (SEM) (JEOL JXA6700, Tokyo, Japan) with an acceleration voltage of 15 kV. The specimens were coated with a gold metal layer to provide proper surface conduction.

3. Results and discussion

3.1. Effect of content of hydrophobic monomer on swelling behaviors

The influence of the hydrophobic monomer content on the swelling ratio for the copolymeric hydrogels is shown in Table 1. The results in Table 1 indicated that

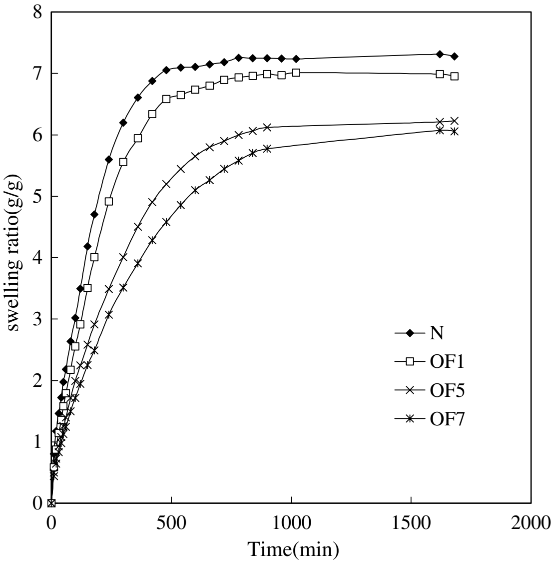

Fig. 1. Swelling ratios as a function of time for the NIPAAm/OFPMA copolymeric gels at 25 °C.

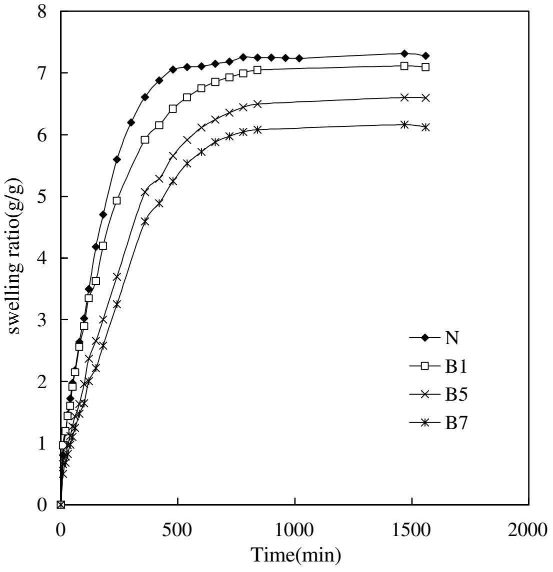

Fig. 2. Swelling ratios as a function of time for the NIPAAm/BMA copolymeric gels at 25 °C.

Table 2
Initial diffusion coefficient of water D, kinetic exponent n and characteristic constant k of water penetrated through copolymeric gels

Sample codes	n	$K \times 10^2$	$D \times 10^8$ (cm^2/s)
N	0.38	1.61	6.57
OF1	0.35	2.00	6.29
OF3	0.33	2.23	4.49
OF5	0.33	2.33	3.67
OF7	0.31	2.54	2.76
B1	0.35	2.25	6.30
B3	0.33	2.37	5.07
B5	0.32	2.46	4.81
B7	0.31	2.68	4.39

the swelling ratios for the copolymeric gels decreased with an increase of the hydrophobic monomer content. This result explicitly indicated that the higher the content of hydrophobic monomer in the gels, the more the hydrophobicity of the gels, and the less the swelling ratio of the gels. Similar results were observed from a previous study [19]. In addition, the results also showed that the swelling ratios of OF-series gels were slightly lower than those of B-series gels. This result also indicated that OFPMA is more hydrophobic than BMA in the copolymeric gel.

3.2. Investigation of water diffusion in xerogels

The swelling ratios as a function of time for OF-series and B-series gels are shown in Figs. 1 and 2, respectively. From these Figures, the swelling parameters such as n, k, and D can be calculated according to Eqs. (2) and (3). The swelling exponents, n, for the copolymeric gels obtained from Eq. (3), shown in Table 2, indicated that the swelling exponents for the copolymeric gels decreased with an increase of hydrophobic monomer content in the copolymeric gels. The values of n for the all gels ranged from 0.38 to 0.31. This evidence indicated that the swelling transport mechanism for the copolymeric gels all belongs to Fickian diffusion ($n < 0.5$) according to the classification of the relative rates of

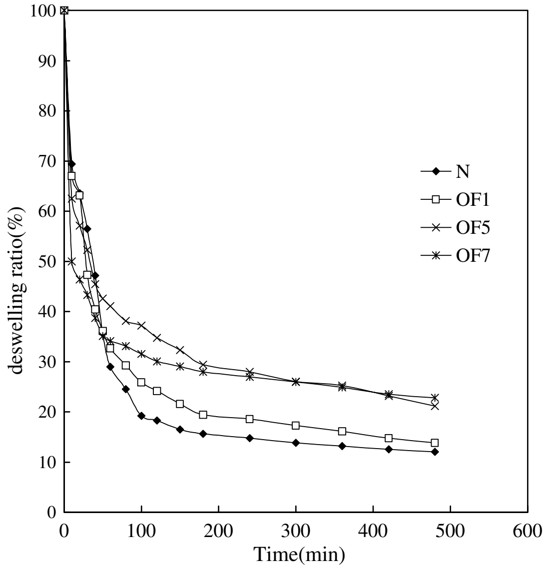

Fig. 3. Deswelling ratios as a function of time for the NIPAAm/OFPMA copolymeric hydrogels at 45 °C.

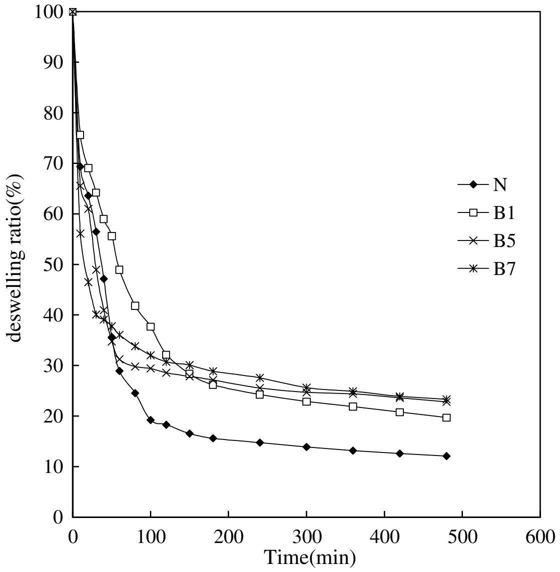

Fig. 4. Deswelling ratios as a function of time for the NIPAAm/BMA copolymeric hydrogels at 45 °C.

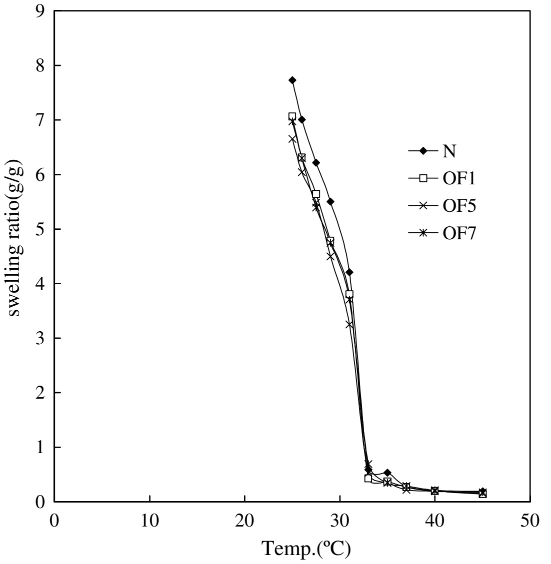

Fig. 5. Effect of temperature on equilibrium swelling ratio for the NIPAAm/OFPMA copolymeric hydrogels.

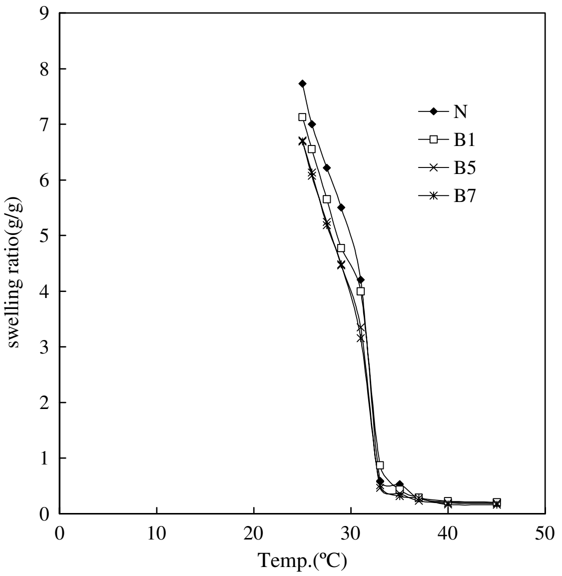

Fig. 6. Effect of temperature on equilibrium swelling ratio for the NIPAAm/BMA copolymeric hydrogels.

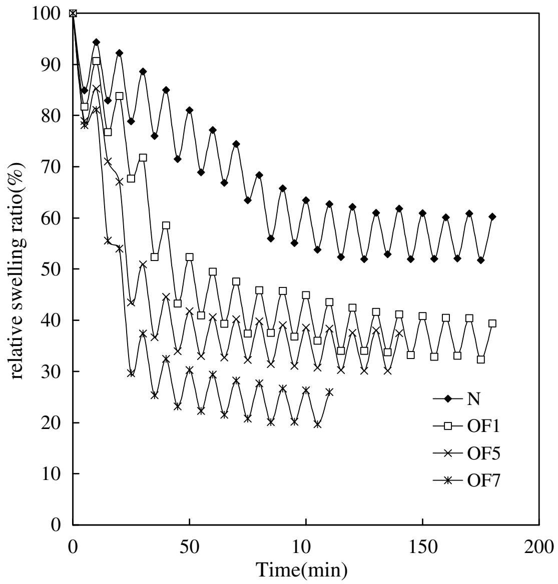

Fig. 7. Fast swelling–deswelling behaviors of NIPAAm/OFPMA copolymeric hydrogels.

Table 3
Gel strength and effective cross-link density of NIPAAm/OFPMA and NIPAAm/BMA copolymeric hydrogels

Sample codes	G (g/cm^2)	$\rho_x \times 10^5$ (mol/cm^3)
N	338	2.59
OF1	424	3.21
OF3	853	6.47
OF5	1006	7.44
OF7	1175	8.47
B1	499	3.79
B3	541	4.02
B5	659	4.85
B7	956	6.92

diffusion and polymer relaxation proposed by Alfrey et al. [20]. In addition, D values obtained from Eq. (2) for the gels decreased with an increase of the hydrophobic monomer content in the copolymeric gel and the D values are lower for OF-series gels than B-series gels. This is a fact that the hydrophobic monomer moiety incorporating into NIPAAm gel would diminish water to penetrate into the gel and the penetration of water into the gel is more difficult for OF-series gels than B-series gels.

3.3. Effect of hydrophobic monomer content on deswelling behaviors

The effect of the hydrophobic monomer content on the deswelling ratio for the copolymeric gels at 45 °C was shown in Figs. 3 and 4 for OF-series and B-series gels, respectively. The results showed that the deswelling ratio for the gels rapidly decreased before 1 h, but the deswelling rate for the gels diminished after 1 h and the deswelling ratio increased with increase in the hydrophobic monomer content in the gels. These results may be attributed to that all gels shrank uniformly with increasing hydrophobicity before 1 h, but after 1 h the surface of the gels formed denser skin layers with increasing hydrophobicity. Hence, the more the content of the hydrophobic monomer the thicker the skin layer

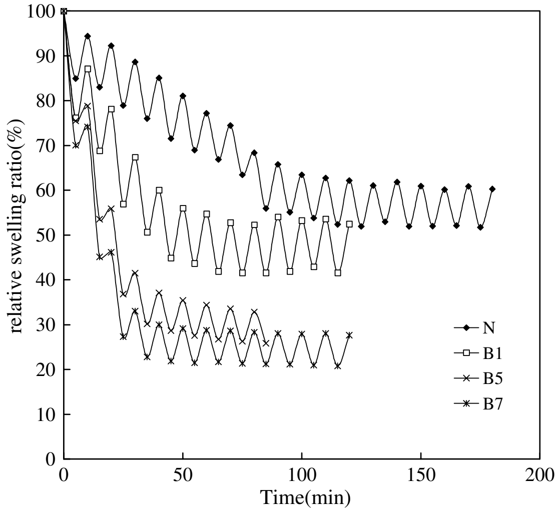

Fig. 8. Fast swelling–deswelling behaviors of NIPAAm/BMA copolymeric hydrogels.

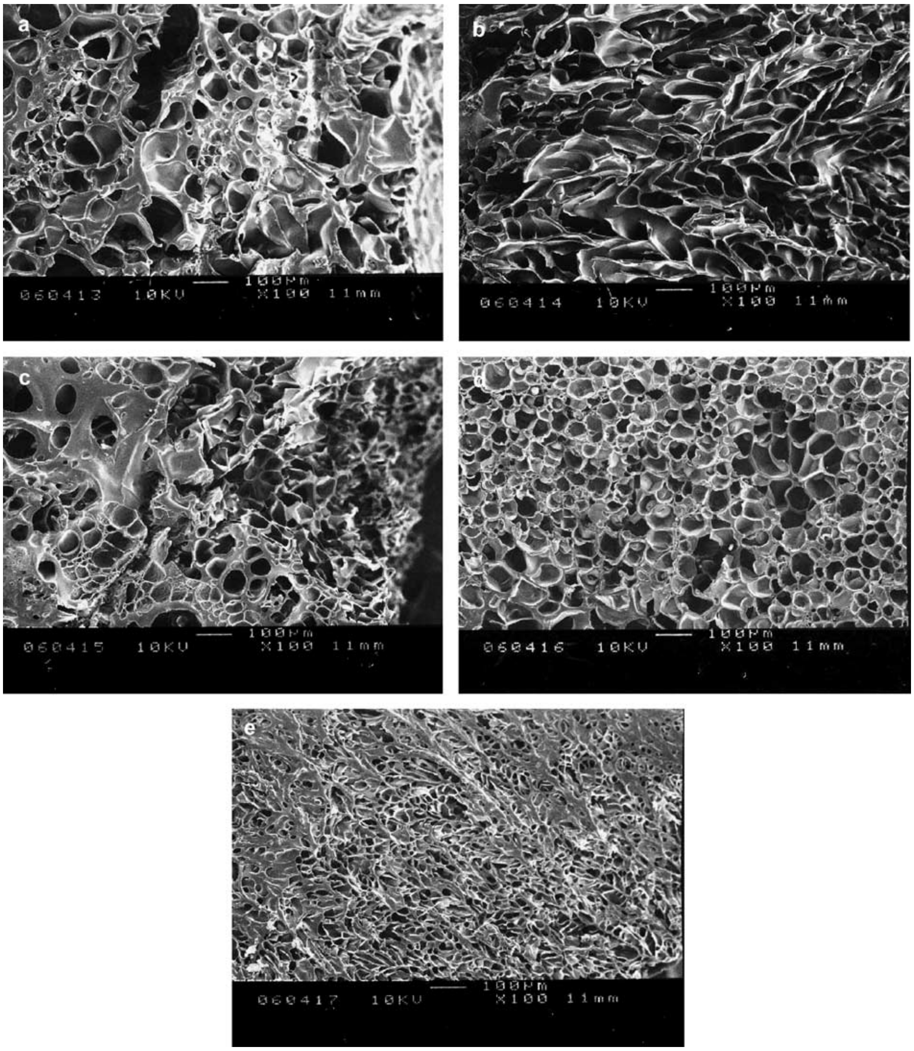

Fig. 9. SEM microphotographs for the copolymeric hydrogels: (a) N; (b) OF1; (c) OF3; (d) OF5; (e) OF7.

of the gels. That would make the water inside the gel to be more difficult to release from the gels. Hence, deswelling ratio of the gels increased with an increase of the hydrophobic monomer content at higher temperature.

3.4. Effect of temperature on equilibrium swelling ratio

The effect of temperature on swelling ratio for the copolymeric hydrogels, shown in Figs. 5 and 6, indicated that the swelling ratio decreased with an increase of the temperature. The critical gel transition temperatures (CGTT) for these two series gels were not obviously changed after adding hydrophobic monomers into the gels and appeared at 30 °C. This result is contrary to our previous study [19] for *N*-ethoxypropyl acrylamide and butyl acrylate copolymeric gels which were prepared from aqueous solution polymerization. This difference maybe resulted from the preparation method.

3.5. Effect of hydrophobic monomers on mechanical properties

The gel strength can be assessed by the shear modulus (G) calculated from Eq. (5). The results in Table 3 indicated that the G values increased with an increase of the hydrophobic monomer content in the copolymeric gels. Comparing these two hydrophobic monomers, OFPMA and BMA, we found that the gel strengths were higher for OF-series gels than those for B-series gels. This is because the atomic size of fluorine is larger than that of hydrogen; the molecular chain packing of OF-series gels is denser than that of B-series gels. According

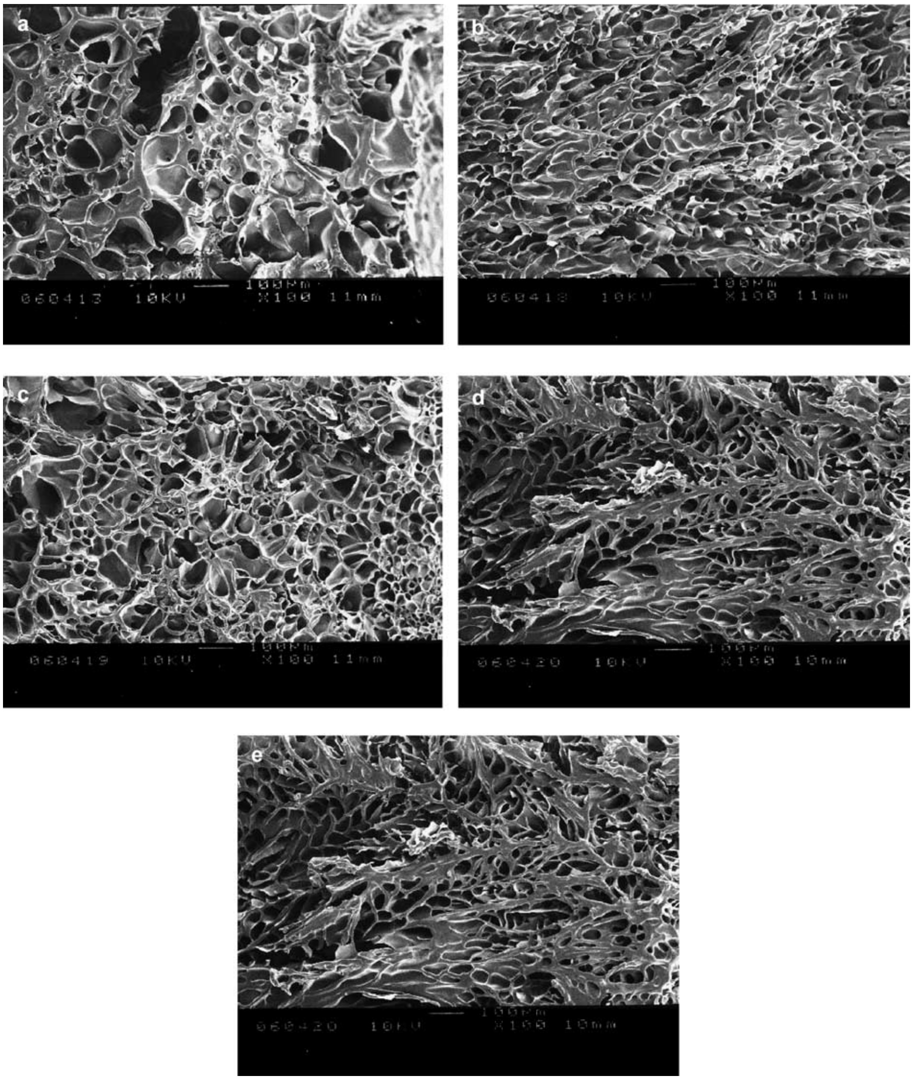

Fig. 10. SEM microphotographs for the copolymeric hydrogels: (a) N; (b) B1; (c) B3; (d) B5; (e) B7.

to Eq. (6), the effective cross-linking density (ρ_x) depends on the swelling ratio and shear modulus at constant temperature. Because the swelling ratio decreased with an increase of the hydrophobic monomer content of the gels, the ρ_x values increased with increase in the content of hydrophobic monomers.

3.6. Effect of hydrophobic monomers on fast swelling–deswelling behavior

The influence of hydrophobic monomers on fast swelling–deswelling behavior was respectively shown in Figs. 7 and 8 for these two series gels. The results indicated that the higher the hydrophobic monomer content in copolymeric hydrogel, the less the water content in the gel after 2 h. After some time periods, the gels reached swelling–deswelling equilibrium. The gels reached swelling–deswelling equilibrium more quickly when the content of hydrophobic monomer of gels increased. This result also showed that the higher content of hydrophobic monomers in the gels would enhance deswelling rate of the gels at initial deswelling stage.

3.7. Morphologies

The SEM microphotographs for OF-series and B-series gels were shown in Figs. 9 and 10, respectively. The results shown in Fig. 9 indicated that the pore size became smaller when the content of OFPMA monomer increased, but a contrary result was observed from

B-series gels shown in Fig. 10. This is attributed the higher hydrophobic chain of OFPMA to be more shrank when the hydrogels immersed into the water. So the hydrogels copolymerized with OFPMA could not have larger swelling ratios.

4. Conclusions

NIPAAm/hydrophobic monomer copolymeric hydrogels had better gel strengths than PNIPAAm gel. Hydrophobic groups also improved deswelling rate of the gels. However, strong hydrophobicity made gels form thicker and denser skin layer at surface under high temperature, so the hydrogels could not reswell to maximum swelling ratio at a short time period. So, their response times could not be shortened effectively. At the same time, swelling ratio could not be decreased effectively. To overcome this problem, the fast swelling deswelling hydrogels will be further investigated in the next study.

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