Studies on Preparation and Properties of Porous Biodegradable Poly(NIPAAm) Hydrogels

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ABSTRACT: A series of biodegradable porous hydrogels, based on thermosensitive *N*-isopropylacrylamide (NIPAAm) and biodegradable crosslinker-polycaprolactone diacrylate (PCLdA) that was synthesized from polycaprolactone diol with acryloyl chloride were prepared by photopolymerization at low temperature. The effect of the crosslinker content and gelation method on the swelling behaviors and physical properties for the poly(NIPAAm) hydrogels was investigated. Results showed that the swelling ratio of the gel in deionized water decreased with an increase of the content of polycaprolactone (PCL) segment in the poly(NIPAAm) hydrogels. The properties of the gels crosslinked with PCLdA were compared with those crosslinked with *N*, *N*′-methylenebisacrylamide (NMBA). The results showed that the critical gel transition temperatures (CGTT) of the gels crosslinked with PCLdA were lower than those of the gels crosslinked with NMBA due to the hydrophobicity of the PCL segment. The results also showed that the gels crosslinked with PCLdA had higher mechanical strength and crosslinking density than those gels crosslinked with NMBA. Comparing the porous gels with nonporous gels, the results showed that the swelling ratio and CGTT of the porous gels were higher than those of the nonporous gels, and the transition temperature curve was smoother for the porous gels. The porous gels also exhibited more rapid thermal response and faster degradation rates. © 2008 Wiley Periodicals, Inc. J Appl Polym Sci 109: 1982–1992, 2008

Key words: biodegradable; polycaprolactone diacrylate; *N*-isopropyl acrylamide

INTRODUCTION

Thermosensitive hydrogel, one of the environmental stimuli response hydrogels, is the most extensively investigated intelligent hydrogel at present; especially in the drug delivery system.[1–8] The structure of thermosensitive hydrogel must have the hydrophobic functional group, such as methyl or ethyl group. Poly(*N*-isopropylacrylamide, NIPAAm) hydrogel is a well-known thermosensitive polymeric gel, nearly continuous volume transition and associated phase transition from low temperature, a highly swollen gel network, to high temperature, a collapsed phase near its critical point between 31–35°C.[9] To maintain the three-dimensional structure of hydrogel, crosslinker was usually used. As present, poly(NIPAAm) hydrogels are usually formed by the covalent-crosslinking of poly(NIPAAm) chains with *N*, *N*′-methylenebisacrylamide (NMBA).[10] The clinical applications of poly(NIPAAm) hydrogels are restricted due to their nonbiodegradability. For the application as biomaterials, degradability is especially emphasized on the preparation of the hydrogels. Hence, the bonding of the gel is designed to be instability (labile bond), and it can be degraded by enzyme or chemisorptions in the physiological phenomenon, and the most of the binding is degraded by the way of hydrolysis. Besides being able to be degraded in the organism, the little member degraded must be low toxicity. Zhang et al.[11] modified the hydroxyl groups of dextran to be the crosslinker for preparing the biodegradable poly(NIPAAm)/dextran-allyl isocyanate) hydrogel particles. The dextran is a biodegradable polysaccharide, which is susceptible to enzymatic digestion in human body.[12]

Polyesters having biocompatibility and biodegradability were extensively investigated as biomaterials.[13–15] Polycaprolactone (PCL), a semicrystalline linear resorbable aliphatic polyester, is subjected to biodegradation because of the susceptibility of its aliphatic ester linkage to hydrolysis. The products generated are either metabolized via the tricarboxylic acid (TCA) cycle or eliminated by direct renal secretion. At present, PCL is regarded as a soft and hard-tissue compatible material including resorbable suture, drug delivery system, and recently are used to prepare the bone graft substitutes.[16–19] However, applications of PCL might be limited because degradation and resorption kinetics of PCL are considerably slower than other aliphatic polyester due to its hydrophobic character and high crystallinity. Kweon et al.[20] synthesized PCL macromer by acrylation of

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acryloyl chloride to build the scaffold and drug delivery matrix. Marra et al.[21] reported that PCL is a comparable substrate for supporting cell growth resulting from two-dimensional bone marrow stromal cell culture.

To offer the biodegradability of poly(NIPAAm) hydrogels, the polycaprolactone diacrylate (PCLdA) crosslinker was designed and synthesized at first through the reaction of PCL diol ($\overline{M_w}$ = 2000) with acryloyl chloride. Then, a series of biodegradable hydrogels based on NIPAAm and PCLdA crosslinker were prepared in this study. The effect of the content of crosslinker and the method of gelation (thermal- and photo-polymerization) on the swelling behaviors and physical properties of the poly(NIPAAm) copolymeric hydrogels was investigated. The formation of PCLdA was confirmed with Fourier transform infrared (FT-IR), nuclear magnetic resonance (NMR), and differential scanning calorimetric (DSC). Biodegradation studies were performed in phosphate buffer with enzyme-lipase. The photopolymerization of the gels was performed in DMSO at low temperature (4–6°C) to produce the channel pores in the series gels.

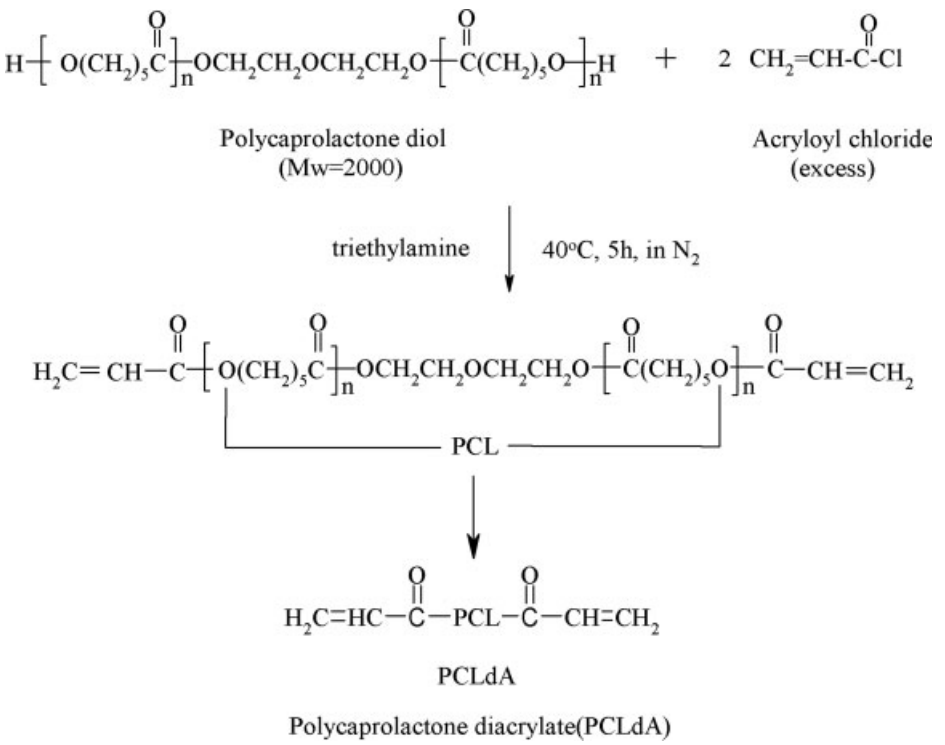
EXPERIMENTAL

Materials

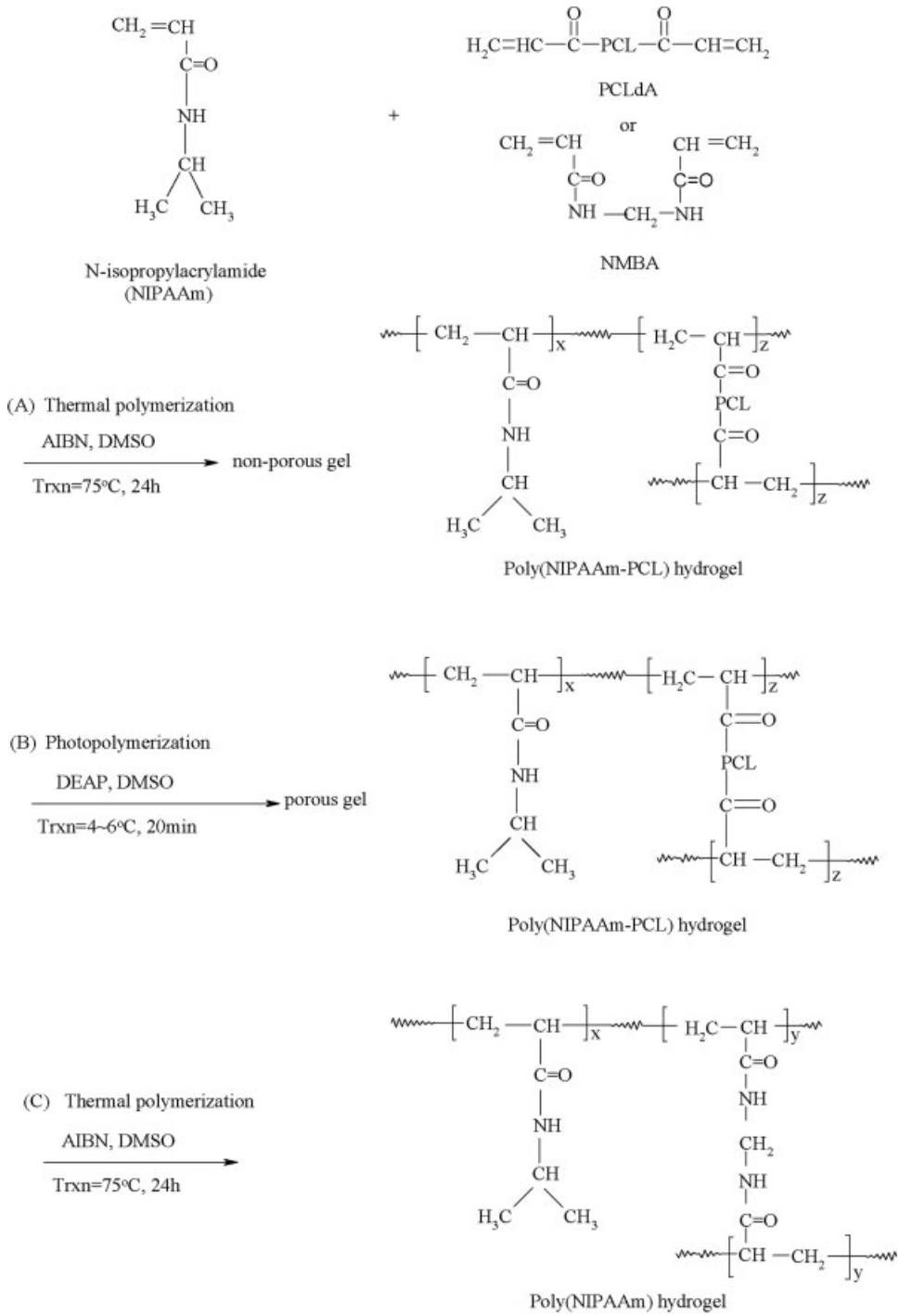
N-isopropylacrylamide (NIPAAm) (Wako Pure Chemical Co. Ltd. Osaka, Japan) as monomer was recrystallized in *n*-hexane before use. Polycaprolactone diol (PCL diol, $\overline{M_w}$ = 2000) (Aldrich Chemical Co. St. Louis MO.) was purified by precipitation from methylene chloride into diethyl ether and then dried at 40°C under vacuum. Triethylamine and acryloyl chloride (Fluka Chemical Co.) as reactant of acrylation were used as received. Dimethyl sulfoxide (DMSO) and benzene dried over calcium hydride as solvents, hexane as precipitant (Tedia Company Inc.), and *N*,*N*′-methylenebisacrylamide (NMBA) (Sigma, St. Louis, MO) as crosslinking agent were used as received. Diethoxyacetophenone (DEAP) and azobisisobutyronitrile (AIBN) (Aldrich Chemical Co.) was further purified by recrystallization as initiators.

Preparation of polycaprolactone diacrylate (PCLdA) as a crosslinker

The synthesis of PCLdA was illustrated in Scheme 1. Polycaprolactone diol, which itself was α- and ω-terminated by hydroxyl groups, were end-capped with acrylated groups to form a crosslinking agent (PCLdA). Briefly, 10 g (0.005 mol) of PCL diol ($\overline{M_w}$ = 2000) was dissolved in 50 mL of benzene in a 250 mL of round-bottom flask and 1.53 mL (0.015 mol) of triethylamine was added, then, 1.22 mL (0.015 mol) of acryloyl chloride, dissolved in a small amount of benzene, was added dropwise over 30 min. The reaction mixture was stirred for 5 h at 40°C. The reaction mixture was filtered to remove



Scheme 1 Synthetic scheme of polycaprolactone diacrylate (PCLdA).



Scheme 2 Synthetic scheme of the poly(NIPAAm) hydrogels.

triethylamine hydrochloride, and then the product was obtained by dropping the filtrate into an excess of *n*-hexane. Finally, the precipitated PCLdA was dried at 40°C under reduced pressure for 24 h.

Preparation of poly(NIPAAm) hydrogels

The preparation of poly(NIPAAm) hydrogels by thermal polymerization in DMSO was illustrated in Scheme 2(A,C). NIPAAm (0.01 mol) and crosslinkers, NMBA (Nx-series) or PCLdA (Px-series), with various molar ratios (based on monomer content) were dissolved in DMSO. To this solution, 1 mol % AIBN as initiator was added, the mixture was immediately injected into the space between two glass plates with a 2-mm silicone rubber as a spacer. Polymerization was carried out at 75°C for 1 day. After the gelation was completed, the gel membrane was cut into disks, 10 mm in diameter, and immersed in an excess of acetone to remove the residual unreacted

TABLE I
Feed Compositions, Yield, and Equilibrium Swelling Ratio of poly(NIPAAm) Copolymeric Hydrogels

Sample code	NIPAAm (M)	NMBA (mol %)	PCLdA (mol %)	Initiator (mol %)	Yield (%)	(SR_{eq}) (g/g)
N2	1	2		1	93.5	43.7
N3		3			98.1	29.8
N4		4			98.5	16.0
N5		5			98.4	12.8
P2	1		2	1	86.1	0.64
P3			3		87.3	0.22
P4			4		89.7	0.15
P5			5		90.8	0.12
P2-s	1		2	1	81.5	4.98
P3-s			3		89.3	3.15
P4-s			4		79.8	2.95
P5-s			5		89.9	1.11

Px-s, gel polymerization was performed with UV-irradiation at low temperature (4–6°C) below the freezing point of DMSO; SR_{eq}, the equilibrium swelling ratio in deionized water at 25°C.

monomer, then immersed in deionized water for 5 days. The gels were lyophilized for 3 days, and then further dried in a 25°C vacuum oven for 1 day. The sample compositions, yields, and equilibrium-swelling ratios of the gels were listed in Table I.

Preparation of porous poly(NIPAAm) hydrogels

The preparation of porous poly(NIPAAm) hydrogels (Px-s series) by UV irradiation in DMSO (mp 18°C) at low temperature (4–6°C) was illustrated in Scheme 2(B). NIPAAm (0.01 mol) and crosslinker, PCLdA, with various molar ratios (based on monomer content) were dissolved in DMSO. To this solution, 1 mol % DEAP as photoinitiator were added, the mixture was immediately injected into the space between two glass plates with a 2 mm silicone rubber as a spacer. Polymerization was carried out by exposing the monomer solution to 600 W UV light (wavelength: 365 nm, Hexman Co. Inc., Taiwan) irradiation at 4–6°C for 40 min. After gelation was completed, the gel membrane was cut into disks, 10 mm in diameter, and immersed in an excess of acetone to remove the residual unreacted monomer, and then immersed in deionized water for 5 days. The gels were lyophilized for 3 days, and then further dried in a 25°C vacuum oven for 1 day. The sample compositions, yields, and equilibrium-swelling ratios of the gels were also listed in Table I.

Instrumental analysis

IR spectra were recorded from pressed KBr pellets containing about 1% of the sample with a Perkin–Elmer Spectrum GX Fourier transform infrared (FT-IR) system to confirm the formation of sample. ^1H NMR spectra were measured with a Bruker AV-500 FT-NMR spectrometer. Differential scanning calorimetry (DSC) measurement was performed on a Perkin-Elmer Pyris 1 DSC at a heating rate of 5°C/min under nitrogen. The melting point (T_m) was determined at the maximum enthalpy (ΔH) of melting endotherm.

Measurement of swelling ratio

The preweighed dried gels (W_d) were immersed in 10 mL of deionized water (or various volume ratios of $EtOH/H_2O$ or phosphate buffer solution) at 25°C until swelling equilibrium was attained. Each gel was then removed from the water bath, tapped with filter paper to remove excess surface water, and weighed as the wet weight (W_w). The swelling ratio (SR_{eq}) was calculated from eq. (1):

$$SR_{eq} = \left(\frac{W_w - W_d}{W_d}\right) \quad (1)$$

Measurement of dynamic swelling

The dried gels were immersed in an excess amount of deionized water (or phosphate buffer solution, pH = 7.4) at 25°C. The swelling ratio was obtained by the weight of the initial and swollen samples at various time intervals. The amount of water absorbed (W_t) was reported as a function of time and the equilibrium absorption at an infinitely long time was designated as W_∞. The eq. (2) was used to calculate the diffusion coefficient (D) for $W_t/W_\infty \leqq 0.8$[22]:

$$\frac{W_t}{W_\infty} = \left(\frac{4}{\pi^{0.5}}\right)\left(\frac{Dt}{L^2}\right)^{0.5} \quad (2)$$

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 data were fitted to the exponential heuristic eq. (3) for $Wt/W_\infty \leqq 0.6$[23,24]:

$$\frac{W_t}{W_\infty} = Kt^n \tag{3}$$

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

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 (SR_{eq}) in distilled water at 25°C in advance. After wiping off water on the surface with filter paper, the weight (SR) of the gel was recorded during the course of deswelling at each regular time interval. The deswelling ratio (DSR) (%) is defined as follows:

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

Fast swelling–deswelling behavior of the copolymeric gels

Preweighed dried gels were at first immersed in 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. Above steps were repeated for 2 h and the weight of the gel was measured to calculate the swelling ratio for each time interval.

Measurement of equilibrium swelling ratio at various temperatures

Two preweighed dried gels were immersed into 10 mL of deionized water for 2 days at different temperatures from 17 to 40°C. After swollen equilibrium was attained, the equilibrium–swelling ratio for the gels at every temperature was calculated as eq. (1).

Measurement of physical properties

The gel strength of these samples was measured by a uniaxial compression experiment with a universal tester (LLOYD LRX, Poole, UK). eq. (5) was used to calculate the shear modulus (G)[25,26]:

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

where τ is the compression stress, F is the compression load, A is the cross-sectional area of swollen gels, and λ is the compression strain ($\Delta L/L_0$) where ΔL is the difference of the thickness of deformed gel and initial swollen gel L_0. At low strains, a plot of τ versus $-(\lambda - \lambda^{-2})$ yielded a straight line, the slope of which was shear modulus (G). The effective crosslink density (ρ_x) was calculated from G and the polymer volume fraction (ν_2) as follows:

$$\rho_x = G/{\nu_2}^{1/3}RT \tag{6}$$

where R is the ideal gas constant (8.48×10^4 g cm/mol K) and T is the absolute temperature.

Morphologies

Samples were equilibrated in deionized water for 3 days and the swollen gels were frozen to –20°C and then fractured and freeze-dried. Scanning electron microscopy (SEM; JEOL JXA8600, Tokyo, Japan) with an acceleration voltage of 15 kV was used to examine the morphologies of the fractured specimens. The specimens were coated with a gold metal layer to provide proper surface conduction.

Biodegradability

The dried polymer discs were equilibrated in phosphate buffer solution (0.2*M*, pH 7.4) containing 0.02 wt % sodium azide to inhibit bacterial growth and 1 mg/mL of lipase, and then incubated at 37°C. Weight loss was gravimetrically monitored at various time intervals.

RESULTS AND DISCUSSION

Characterization of PCL diacrylate (PCLdA)

The FT-IR spectra of PCL diol and PCLdA are shown in Figure 1. PCLdA shows absorption bands at 1641 and 813 cm^{-1} assigned to the C—C due to acrylation of PCL diol. Those peaks are not observed in PCL diol [Fig. 1(a)]. The absorption bands at 1725 and 1110 cm^{-1}, which appeared in both PCL diol and PCLdA, are attributed to ester and ether stretching peaks, respectively.

The ^{1}H NMR spectra of PCL diol and PCLdA are shown in Figure 2. The ^{1}H NMR (500 MHz, chloroform-d, δ, ppm) spectrum of PCL diol is shown in Figure 2(a). The chemical shifts of the corresponding peaks are at 1.39 ppm (quintet, J = 18.05 Hz, 4H, Hc), 1.64 ppm (multi, J = 32.9 Hz, Hb = 4H, Hc = 4H), 2.32 ppm (J = 13.6 Hz, He), 3.76 ppm (J = 18.58 Hz, Hg), 4.07 ppm (J = 6.7 Hz, Hg), and 4.24 ppm (triplet, J = 4.95 Hz, Hf). The formation of PCLdA is also confirmed by ^{1}H NMR spectra [Fig. 2(b)], the similar chemical shifts for the corresponding peaks are also found in the Figure 2(b), except

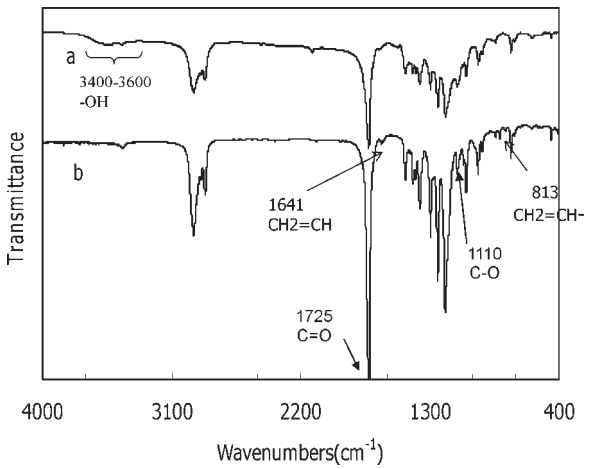


Figure 1 FT-IR spectra of PCL diol (a) and PCL diacrylate (b).

the vinyl groups of the PCLdA appeared at the range of 5.8–6.4 ppm. From the above results, the terminal hydroxyl groups in the PCL diol were converted to acrylate groups by the reaction with acryloyl chloride.

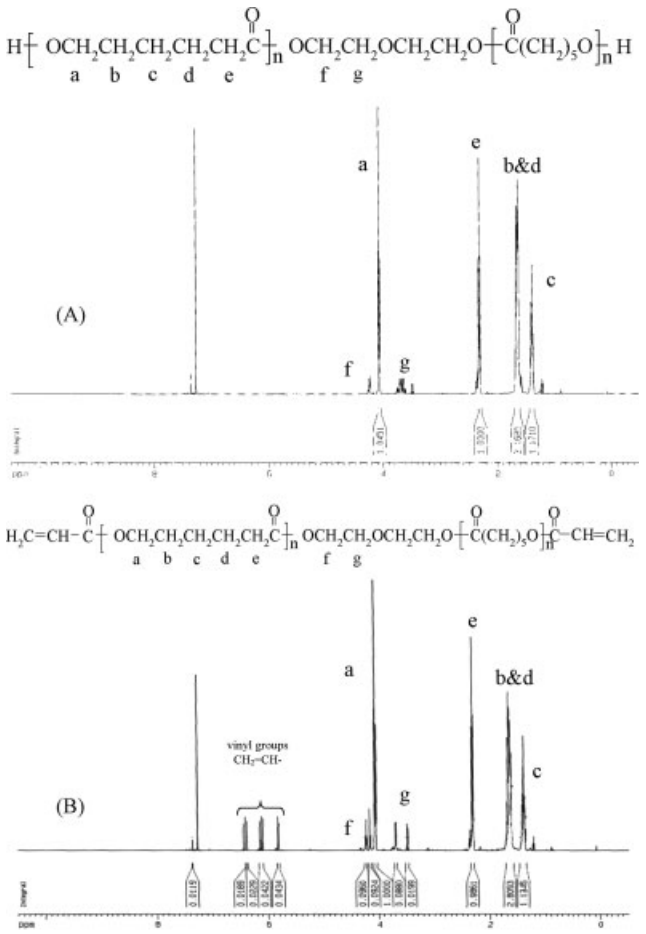


Figure 2 ^{1}H NMR spectra of PCL diol (a) and PCL diacrylate (b).

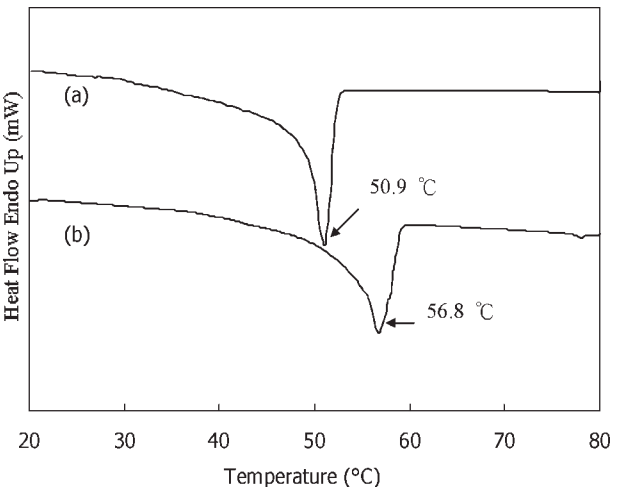


Figure 3 DSC thermograms of PCL diacrylate (a) and PCL diol (b).

Figure 3 shows DSC thermograms of PCL diol ($\overline{M_w}$ = 2000) and PCLdA. The melting temperature (T_m) of PCLdA was lower than that of PCL diol due to the modification of PCLdA with acrylate groups at both ends. The corresponding T_m, enthalpy of fusion (ΔH), and crystallinity (X_c) are summarized in Table II. The X_c of the PCL was calculated from ΔH assuming proportionality to the experimental enthalpy. The reported enthalpy of fusion (135.44 J/g) was used as a reference of 100% X_c of PCL.[27] As shown in Table II, the T_m (50.9°C) and X_c (56.4%) of PCLdA are lower than those of PCL diol (56.8°C and 76.8%, respectively) due to incorporation of acrylate group into PCL diol and decrease of the intermolecular interaction force (hydrogen bonding).

Characterization of the poly(Nipaam) hydrogels

The preparation of three series of poly(NIPAAm) hydrogels was described in experimental section. The average yields shown in Table I for the Nx, Px, and Px-s series gels are 97, 88, and 85%, respectively. This result indicates that the yield for the gels depends on the type of the crosslinker and gelation method. Table I also shows the dependence of equilibrium swelling ratios (SR_{eqs}) at 25°C on the compo-

TABLE II
Melting Point, Enthalpy of Fusion, and Crystallinity of PCL Diol and PCLdA

	Melting point T_m (°C)	Enthalpy of fusion ΔH (J/g)	Crystallinity X_c (%)
PCL diol	56.8	103.99	76.8
PCLdA	50.9	76.44	56.4

X_c (%), Crystallinity obtained by the value of enthalpy of fusion divided by 135.44 J/g.

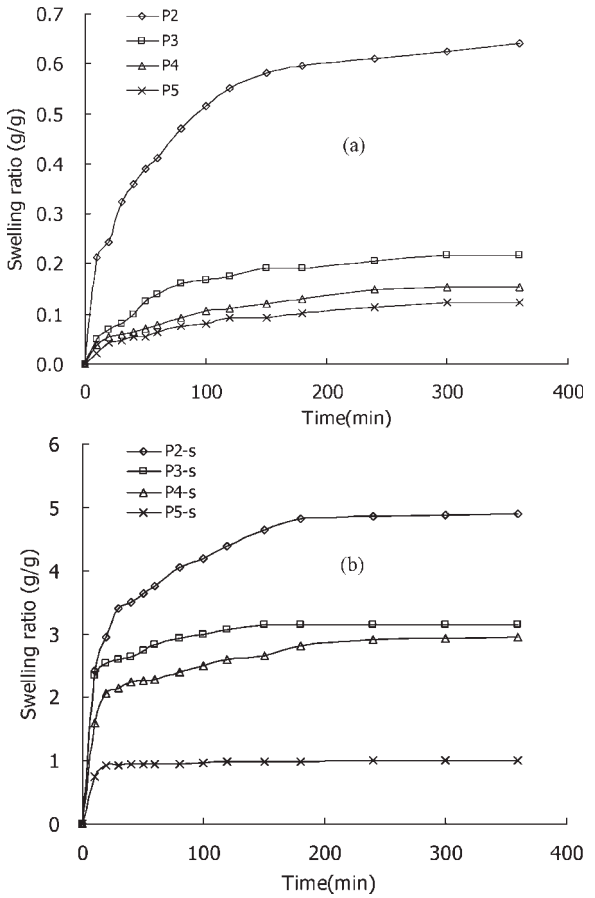


Figure 4 The swelling kinetic profile of the nonporous (a) and porous (b) poly(NIPAAm) hydrogels in deionized water at 25°C.

sition and gelation method of the poly(NIPAAm) hydrogels. The results show that the SR_{eqs} of the poly(NIPAAm) hydrogels decrease with increasing of the content of crosslinker. The SR_{eqs} for Px series gels (from 0.64 to 0.12 g/g) are much lower than those for Nx series gels (from 43.7 to 12.8 g/g). This is because PCL segment has stronger hydrophobicity. To improve low swelling ratio of Px series gels, the low temperature polymerization was chosen to create the porous of the gel. Hence, the DMSO solvent was used in this system, because the freezing point of DMSO is 18°C. The Px-s series gels were prepared by this method. The results in Table I show that the porous Px-s series gels have higher swelling ratio than nonporous Px series gels.

Swelling kinetics for the poly(NIPAAm) hydrogels in deionized water

The swelling kinetic profiles of the Px-s series and Px series copolymeric hydrogels in deionized water at 25°C are shown in Figure 4. The results show that the initial swelling rates from the dried state at 25°C decrease as the content of hydrophobic PCL increases in the copolymeric gels. That is because the penetration of water into the Px series gels is not easy and results a very slow penetration. Oppositely, the water is easily penetrated into the Px-s series gels. According to the classification of diffusion mechanism presented by Alfrey et al.,[28] the transport mechanism of the series of poly(NIPAAm) hydrogels all belongs to Fickian diffusion because n values are lower than 0.5 (not shown). However, D values of these gels could not calculate because the experimental points of M_t/M_∞ value are not enough much to the limitation $M_t/M_\infty \leq 0.8$.

TABLE III
Gel Strength and Crosslinking Density Values of the poly(NIPAAm) Hydrogels

Sample code	$G \times 10^{-2}$ g/cm^2	$\rho \times 10^3$ mol/cm^3
N2	5.89 ± 1.2	0.07 ± 0.02
N3	9.43 ± 2.0	0.09 ± 0.02
N4	16.25 ± 1.6	0.15 ± 0.01
N5	21.81 ± 2.5	0.20 ± 0.04
P2	412.08 ± 35	1.67 ± 0.03
P3	539.29 ± 24	2.24 ± 0.1
P4	1218 ± 186	5.13 ± 0.79
P5	1543 ± 367	6.39 ± 1.41
P2-s	288.62 ± 30	1.18 ± 0.02
P3-s	323.15 ± 44	1.32 ± 0.03
P4-s	583.72 ± 84	2.4 ± 0.13
P5-s	812.33 ± 82	3.33 ± 0.35

Mechanical properties of poly(NIPAAm) hydrogel

The gel strength was accessed by the shear modulus (G) obtained from eq. (5). The results in Table III indicate that the G values and the effective crosslink

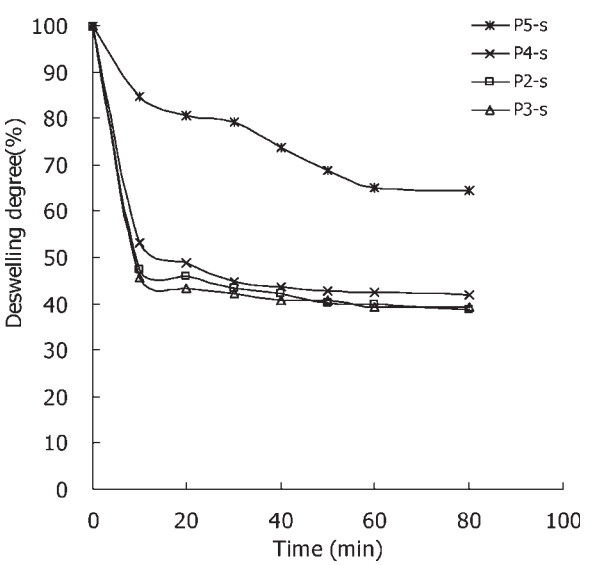


Figure 5 The deswelling kinetic profile of the porous poly (NIPAAm) hydrogels in deionized water at 45°C.

densities (ρ_x) of the gels increase with an increase of the content of PCL segment. In addition, the mechanical strengths for the gels crosslinked with NMBA (Nx series gels) are much weaker than those for the gels crosslinked with PCLdA (Px series gels). At the same time, the mechanical strengths for Px series gels are higher than those for Px-s series gels. In general, a decrease in shear modulus (G) was usually accompanied by a decrease in the effective crosslink density (ρ_x) for hydrogels. The hydrophobicity of PCL segment made the gel structure to be tighter. From above results, the gels crosslinked with PCLdA can enhance their gel strength.

Deswelling behaviors for the porous poly(NIPAAm) hydrogels

The deswelling behaviors of the Px-s series gels are shown in Figure 5. The results indicate that the P2-s, P3-s, and P4-s gels could rapidly drain out over 50% water inside the gels during the first 10 min. However, the P5-s gel only drains out about 35% water due to its higher crosslink densities (see Table III) and its pore size was smallest than other three gels (also see Fig. 10), so this condensed structure hampered the water inside the gels to drain out.

Fast swelling–deswelling behavior for the porous poly(NIPAAm) hydrogels

Because the Px-s series gels showed fast deswelling behavior at higher temperature, their fast swelling–deswelling behavior was carried out and shown in Figure 6. The results indicate that the formed pores provide the gels rapid thermally response. The response time means the time needing to swell to unit swelling ratio for the gels. For Px-s series gels, after 80 min the difference of swelling ratios between at low temperature and at high temperature still maintains 20–55%; but for P2 gel, that only maintains at 2–10%. The reason why the porous gels could swell so fast in the short time interval, that is due to the presence of open pores in the gel formation in which provides capillary channels. Hence, water can be taken up into the gels by capillary action. On the contrary, the swelling–deswelling rates for Px-series gels are very slow; this is also due to the tight structure in the gel.

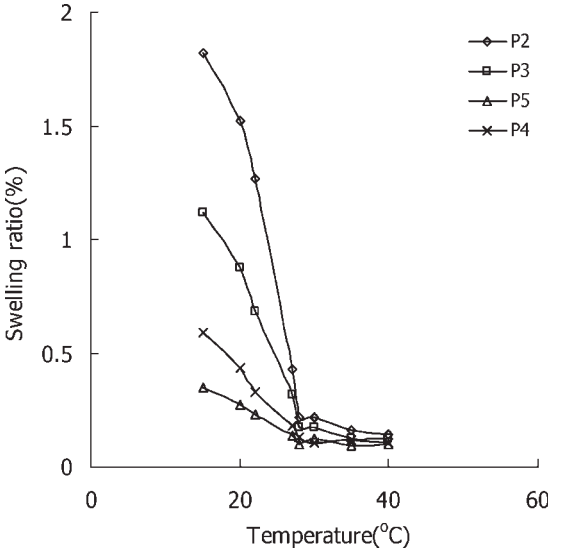


Figure 7 Equilibrium swelling ratio as a function of temperature for the poly(NIPAAm) hydrogels in deionized water.

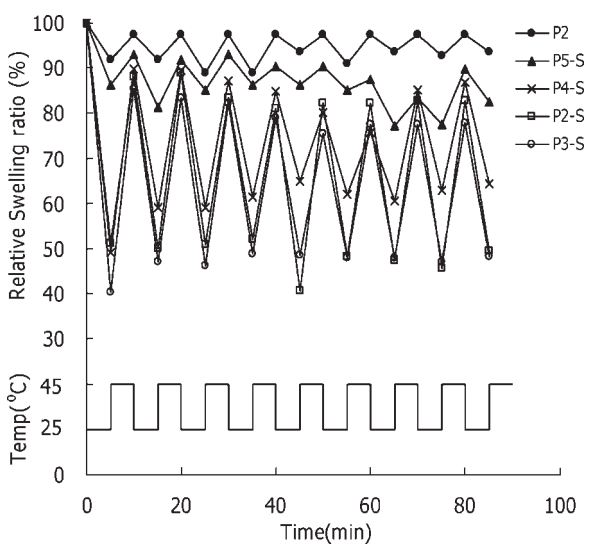


Figure 6 Fast swelling–deswelling behavior of the porous and nonporous poly(NIPAAm) hydrogels in deionized water between 25 and 45°C.

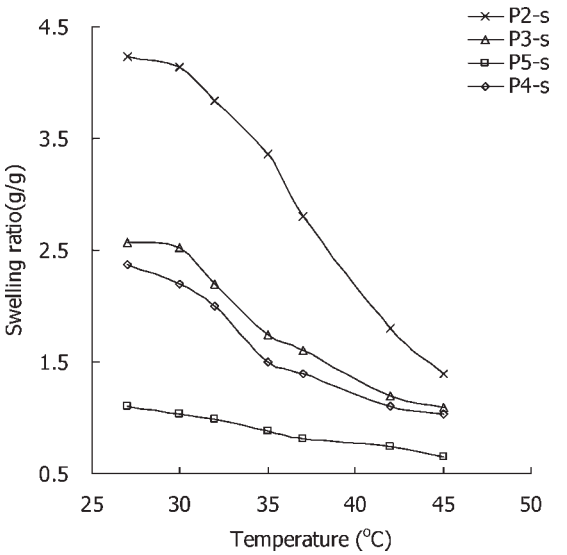


Figure 8 Equilibrium swelling ratio as a function of temperature for the porous poly(NIPAAm) hydrogels in deionized water.

Effect of temperature on swelling ratio

According to the present records, the CGTT is around 32°C for the poly(NIPAAm) hydrogel. For NIPAAm gel, the hydrophilic group (amido-NHCO-) in the polymer structure would form an intermolecular hydrogen bond with surrounding water at low temperature (below gel transition temperature). Hence, water penetrated into the NIPAAm gels is in a bound state at low temperature. The water molecule would gain an enthalpy during the temperature increase, and the hydrophilic groups (amido group) in the NIPAAm gel would be turned into intramolecular hydrogen bonds in this condition. At the same time, the hydrophobic forces of isopropyl group of NIPAAm gel increases. These two results make the water molecules inside the gel change from bound state to free state and release out of the gel network. This phenomenon makes the swelling ratio of the gel rapidly decrease at the gel transition temperature. The effect of temperature on the equilibrium-swelling ratio for Px series and Px-s series gels were shown in Figures 7 and 8, respectively. The results in these Figures indicate that the swelling ratio decreases with an increase of the temperature. The CGTT for the Px series gels was lower than reported temperature (32°C) and the result also showed that equilibrium swelling ratio dramatically decrease for lower PCL content (P2) in the gel. But, the profiles of equilibrium swelling ratio as a function of temperature for Px-s gels are different from those of Px series gels and are smoother. Based on this result, we think that the Px-s gels could not deswell as rapid as Px gels when temperature increases because there are many channel pores in the Px-s gels that act as water channels to drain the water out of the gel.

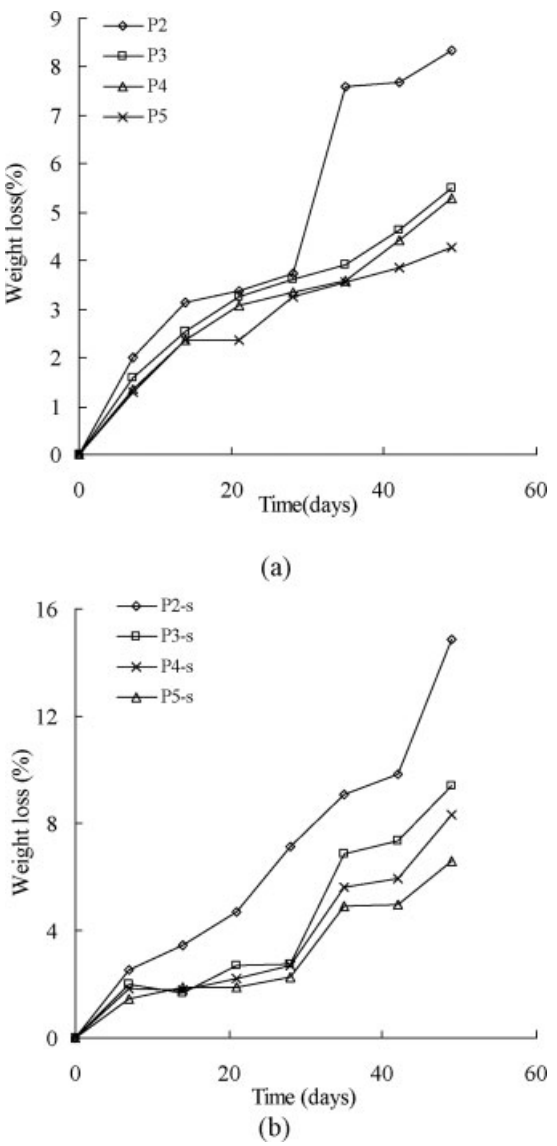


Figure 9 Degradation curves of nonporous and porous poly(NIPAAm) copolymeric hydrogels *in vitro* in PBS buffer solution with lipase (1 mg/mL) (pH 7.4 and 37°C).

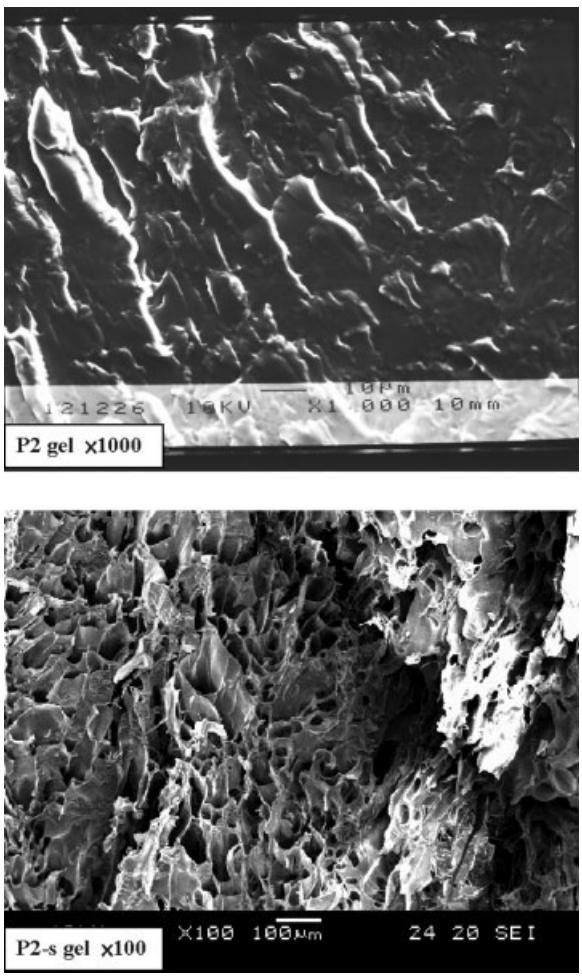


Figure 10 SEM photographs for the cross section of the nonporous (P2) and porous (P2-s) poly(NIPAAm) hydrogels.

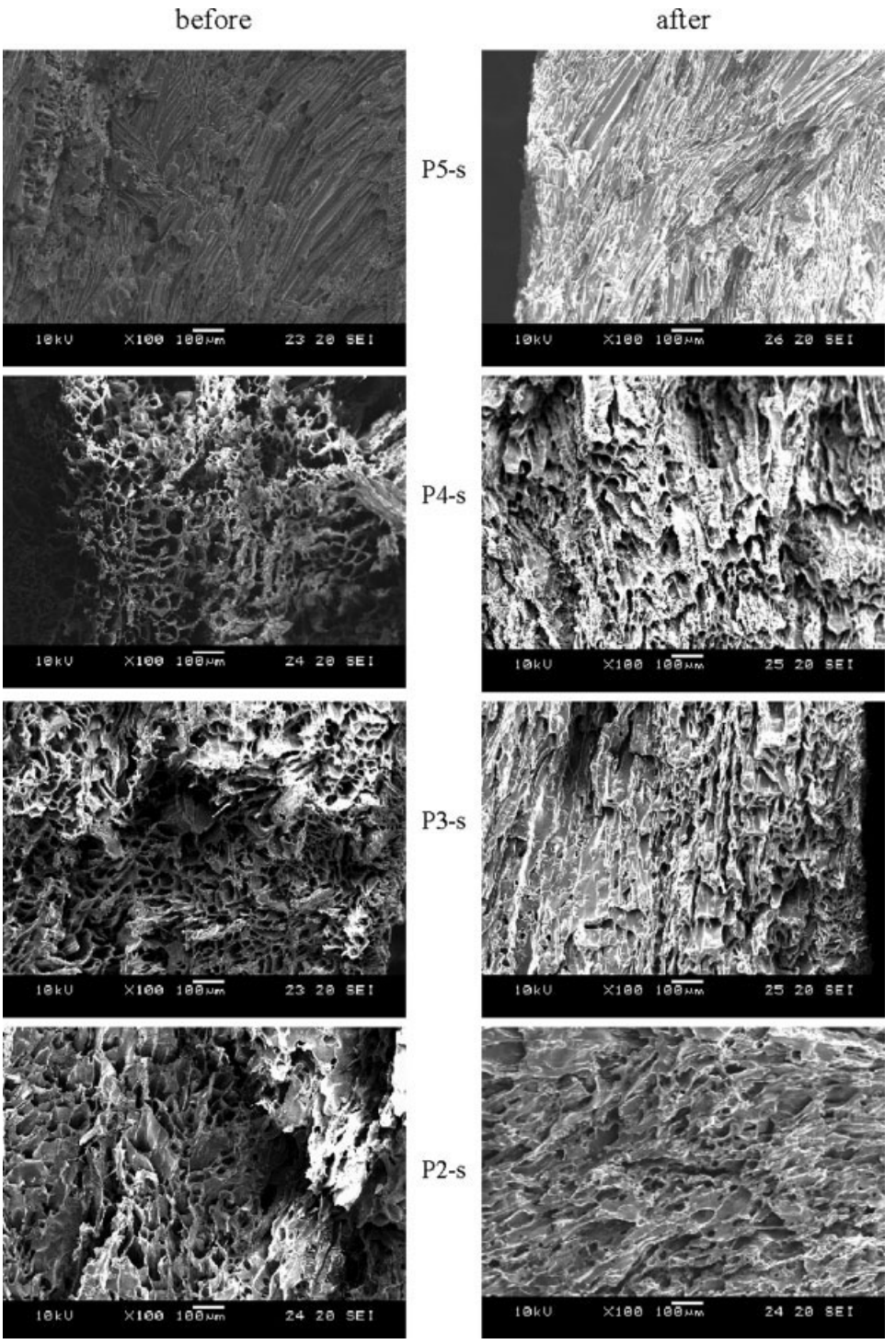


Figure 11 SEM photographs for the cross section of the porous poly(NIPAAm) hydrogels before and after degradation.

Biodegradability

Figure 9 showed the weight loss for Px series and Px-s series gels against incubation time in phosphate buffer solution with lipase (pH = 7.4 at 37°C). The results show that the degradation rates of the poly (NIPAAm) hydrogels have faster degradation kinetics than that of PCL which has been reported. Generally, degradation kinetics of macromolecule was affected by their chemical structure and structural characteristics. Because PCL has higher hydrophobicity, it does not allow water to fast penetrate into the PCL bulk. Although the mechanism of PCL degradation was known as random hydrolytic chain scission of the ester linkage,[19] the degradation rate was relatively lower than other degradable polyesters including poly(lactic acid) and their copolymers

due to the chemical and structural characteristics of PCL. On the other hand, the Px-s series gels showed faster degradation behavior than PCL itself due to the formation of the porous structure in the gel. At the same time, the degradation rates of the Px-s series gels [Fig. 9(b)] are higher than that of the Px series gels [Fig. 9(a)]. And, the degradation rate decreased with increase in the content of PCL in the Px-s series gels.

Morphologies

The SEM interior morphologies for the Px and Px-s gels degraded by lipase are shown in Figures 10 and 11, respectively. Figure 10 shows that the porous morphology of P2-s gel is different from the P2 gel that with tight structure. This is because the porous Px-s gels were formed under lower temperature (4–6°C) than the freezing temperature (18°C) of solvent DMSO. At this lower temperature the DMSO freezed as ice crystal and created the pore during the gel formation. This porous morphology is facilitated to perform biodegradation. The SEM interior morphologies for the Px-s gels degraded by lipase shown in Figure 11 indicate that the more the PCL segment content the smaller the forming channel pores and the pore structure become tighter due to the increase of PCL segment, and the crosslink densities of the gels increase. After degradation by lipase enzyme, the interior morphologies of the gels are more incomplete.

CONCLUSIONS

The poly(NIPAAm) gels crosslinked with biodegradable crosslinker-PCLdA have higher the gel strength and crosslinking density than that crosslinked with NMBA, but lower the swelling ratio. The hydrophobic PCL segment made the gel structure become tighter, and made the water hard to penetrate into the network of the gels. The low temperature photopolymerization method created the more and bigger channel pores in the Px-s gels in which channel pores can act as water channel to improve water penetration into the gel and to diminish the deswelling rate of the gel under higher temperature. This can enhance the biodegradation of the present gel at 37°C. Hence, gels copolymerized with PCLdA under low temperature not only can increase the mechanical strength of normal hydrogels but also can enhance their biodegradation.

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