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A strategy to introduce the pH sensitivity to temperature sensitive PNIPAAm hydrogels without weakening the thermosensitivity

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Abstract

A series of novel pH and thermosensitive hydrogels, comprised of *N*-isopropylacrylamide (NIPAAm) and *N*-isopropyl-maleamic acid (NIPMMA) units were designed and fabricated. The resultant P(NIPAAm-co-NIPMMA) hydrogels were characterized and it was found, with the increasing content of NIPMMA, that the pH sensitivity of P(NIPAAm-co-NIPMMA) hydrogel improved, whilst the temperature sensitivity remained almost the same. This unique intelligent character was attributed to the existence of a continuous isopropylamide sequence in P(NIPAAm-co-NIPMMA) hydrogels.

Keywords: Hydrogel; Thermosensitive; pH sensitive

1. Introduction

During the last decade, great attention has been focused on environmentally sensitive polymers due to their special properties and potential applications in biomedical fields and in industry (Dong & Hoffman, 1986; Miyata, Asami, & Uragami, 1999; Osada, Okuzaki, & Hori, 1992; Stayton et al., 1995). Poly(*N*-isopropylacrylamide) (PNIPAAm) is one of most extensively studied thermosensitive polymers and shows a low critical solution temperature (LCST) or transition temperature (T_{tr}) at ~33 °C in aqueous solutions (Hirokawa & Tanaka, 1984; Hoffman, 1991). This distinctive property of PNIPAAm is attributed to its unique rapid alternation in hydrophilicity and hydrophobicity around LCST (Feil, Bae, Feijen, & Kim, 1993; Zhang, Yang, Chung, & Ma, 2001). The hydrophilic groups (–CONH–) of PNIPAAm hydrate to form an expanded structure when the temperature is below LCST. However, as the PNIPAAm hydrogel is heated above LCST, the polymer chains collapse abruptly and phase separation occurs. Such a unique phase transition of the PNIPAAm hydrogel upon external temperature changes has been investigated widely (Kayaman, Kazan, Erarslan, Okay, & Baysal, 1998; Liang, Feng, Liu, Rieke, & Fryxell, 1998; Liu, Tao, & Zhuo, 1993; Ramkissoon-Ganorkar, Liu, Baudys, & Kim, 1999; Shiroya, Tamura, Yasui, Fujimoto, & Kawaguchi, 1995).

Besides the thermosensitive hydrogel, another class of typical environmentally sensitive hydrogels is pH sensitive hydrogels, which may change their shapes and volumes with the variation of external pH. The hydrogels bearing weakly acidic pendant groups would exhibit pH sensitivity due to the alteration of COOH/COO^- upon pH changes. pH sensitive hydrogels have also been extensively investigated both for their intrinsic scientific interest and for their potential applications as biomedical materials (Lim, Kim, & Lee, 1997).

From the viewpoint of applications, it would be favorable if hydrogels could respond to two types of stimuli simultaneously, either mutually or independently, with particular emphasis on the pH and temperature stimuli. Such a pioneer idea was proposed by Chen and Hoffman (1995a) who grafted PNIPAAm to poly(acrylic acid) (PAAc) chains to obtain copolymers exhibiting temperature-induced phase

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separation over a wide range of pH values. Recently, to achieve pH and temperature sensitivity, copolymerizing the temperature sensitive NIPAAm with other monomers containing weakly acidic groups such as acrylic acid has attracted extensive research interest (Bulmus, Ding, Long, Stayton, & Hoffman, 2000; Chen & Hoffman, 1995b; Chen & Hsieh, 2004; Kuckling, Adler, Arbdt, Ling, & Habicher, 2000; Shibayama, Fujikawa, & Nomura, 1996). However, the incorporation of pH sensitivity might ruin the thermosensitivity of copolymerized hydrogels and a high acrylic acid content might lead to the complete suppression of thermosensitivity. For example, Kobayashia et al. (Kobayashia, Kikuchib, Sakaia, & Okano, 2002) prepared poly(NIPAAm-co-acrylic acid-co-*N*-tert-butylacrylamide) (P(NIPAAm-co-acrylic acid-co-tBAAm)) hydrogels. When the content of acrylic acid reached 10 mol%, the P(NIPAAm-co-acrylic acid-co-tBAAm) hydrogel did not exhibit the thermosensitive property. Moreover, Yoo, Sung, Cho, and Lee (1997, 2000) reported with the content of acrylic acid as being over 10 mol %, the temperature response of resultant hydrogels in the aqueous solution did not exist. Lee et al. (Lee & Shieh, 1999) further utilized acrylic acid, which had been neutralized to 50 mol% by sodium hydroxide (SA50), to copolymerize with NIPAAm. It was also found when the content of SA50 reached 16.4 mol%, the thermosensitivity of the resultant hydrogel became extremely weak.

The fading or elimination of thermosensitivity of P(NIPAAm-co-acrylic acid) hydrogel was attributed to the introduction of comonomer. It was proposed that the thermosensitivity of PNIPAAm hydrogel resulted from the continuous isopropylamide groups with a specific hydrophilic/hydrophobic balance (Ebara, Aoyagi, Sakai, & Okano, 2000; Zhang, Wu, & Chu, 2003). Due to the impregnation of acrylic acid units, this continuous sequence of isopropylamide pendant groups was disturbed. As a result, the continuous hydrophilic/hydrophobic balance in PNIPAAm chains was interrupted. As a result, the hydrophobic interactions between isopropyl groups would be expected to be much weakened at a temperature above LCST.

In this paper, a novel monomer, *N*-isopropyl-maleamic acid (NIPMMA) was synthesized and a series of P(NIPAAm-co-NIPMMA) hydrogels with different compositions were fabricated with good thermosensitivity as well as pH sensitivity. As illustrated in Fig. 1, NIPMMA contains both isopropylamide group (–$CONHCH(CH_3)_2$) and weakly acidic group (–COOH). Due to the existence of –COOH groups, the resultant P(NIPAAm-co-NIPMMA) hydrogels could exhibit pH sensitivity. Importantly, besides the pH sensitivity, P(NIPAAm-co-NIPMMA) hydrogels also possess good thermosensitivity since the incorporated NIPMMA in P(NIPAAm-co-NIPMMA) chains do not interrupt the continuous sequence of isopropylamide pendant groups within the network structure. This intact and continuous isopropylamide sequence might therefore provide a similar thermosensitive behavior as does PNIPAAm homopolymer, and therefore appropriate new polymers were investigated in the current work.

2. Experimental

2.1. Materials

N-isopropylacrylamide (NIPAAm) (99%, ACROS), maleic anhydride, isopropylamine, and ammonium persulfate (APS) were of analytical grade and used as received. *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED) was distilled prior to use. *N*,*N*′-Methylenebisacrylamide (BIS) was recrystallized from dimethyl formamide before use. All other reagents were of analytical grade and used without further purification.

2.2. Preparation of N-isopropyl-maleamic acid (NIPMMA)

NIPMMA was synthesized based on reported methods (Reddy, Kondo, Toru, & Ueno, 1997; Zentz et al., 2002). Briefly, maleic anhydride (50 mmol) was dissolved in acetone (8 ml) and maintained in an ice-bath. To this was added dropwise isopropylamine, dissolved in acetone (3 ml),

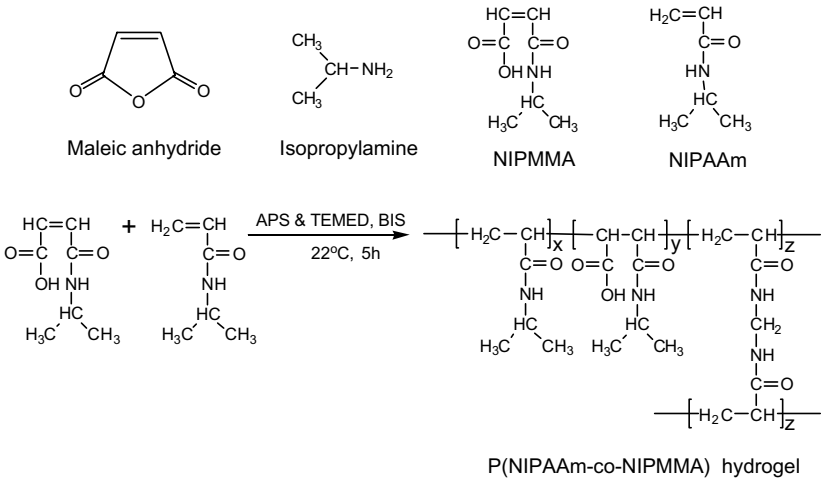

Fig. 1. The chemical structures of maleic anhydride, isopropylamine, NIPMMA, NIPAAm and synthesis route of P(NIPAAm-co-NIPMMA) hydrogel.

then the resultant mixed solution was stirred for 2 h at room temperature (22 °C), the product was filtered off and recrystallized from acetone three times to yield NIPMMA (31 mmol, yield: 62%). The mp of NIPMMA was 102–103 °C (Lit. 103 °C (Zentz et al., 2002)). The ^{1}H NMR spectrum was recorded on a Mercury VX-300 (Varian, USA) spectrometer at 300 MHz by using $CDCl_3$ as a solvent and TMS as an internal standard. ^{1}H NMR (δppm): 1.25–1.27(d, 6H); 4.14–4.15(m, 1H); 6.29–6.33(d, 1H); 6.51–6.59(d, 1H); 7.27(s, 1H); 8.05(s, 1H). FT-IR spectrum (cm^{-1}): 3320(–OH of COOH); 3247(–NH of –CONH–); 3073(CH of –CH=CH–); 2978, 2937(–CH_3 of –CH $(CH_3)_2$); 2878(CH of –CH $(CH_3)_2$), 1707(C=O of –COOH); 1635, 1580(C=O of –CONH–). For the FT-IR measurement, NIPMMA was dissolved in acetone and a film cast on a NaCl slide to obtain a NIPMMA membrane for FT-IR analysis.

2.3. Synthesis of P(NIPAAm-co-NIPMMA) hydrogels

NIPAAm and NIPMMA monomers with different molar ratios and a particular amount of BIS as the cross-linker were fully dissolved in distilled water (2.5 mL) at room temperature. Then the initiators APS and TEMED were added and the mixtures were allowed to copolymerize for 5 h at room temperature. The resultant hydrogels were immersed in distilled water to extract the unreacted chemicals. During purification process, the distilled water was replaced every few hours for two days to obtain the purified and equilibrated hydrogels for following characterizations. The resulting P(NIPAAm-co-NIPMMA) hydrogels were labeled as Gel_x, where x indicates the molar percentage of NIPMMA based on the total monomers (Table 1). The pure PNIPAAm hydrogel without NIPMMA was fabricated under the same condition as a control, designated as CGel.

2.4. FT-IR characterization of P(NIPAAm-co-NIPMMA) hydrogels

The hydrogel samples were dried in vacuum at 55 °C for 24 h (constant weight). The dried hydrogels were analyzed in KBr discs by FT-IR (Perkin Elmer Spectrum One, Wellesley, MA, USA) spectrophotometer in the region of 450–4000 cm^{-1}.

2.5. Interior morphology

The swollen hydrogel samples were first equilibrated in distilled water at room temperature, then quickly frozen in liquid nitrogen and freeze-dried under vacuum at −45 °C for 3 days to completely remove water. After that, the dried hydrogel samples were fractured carefully in liquid nitrogen and the interior morphology of the hydrogel samples was observed by a scanning electron microscope (Hitachi X-650 SEM, Mountain View, CA, Japan) at 25 kV using the hydrogel specimens fixed on aluminum stubs and coated with gold for 7 min.

2.6. Measurement of equilibrium swelling ratio

A classical gravimetric method was used to measure the equilibrium swelling ratio of hydrogel at room temperature. Hydrogel samples were immersed and swollen in distilled water at room temperature for at least 24 h to reach the equilibrium states. Then excess water on the swollen hydrogel surface was removed by wet filter paper and the gel then weighed. Taking the average value of three measurements for each sample, the equilibrium swelling ratio, SR_{eq}, is defined as follows:

$$SR_{eq} = W_s/W_d \quad (1)$$

where, W_s is the weight of water in the equilibrium swollen hydrogel (wet weight − dry weight) and W_d is the initial weight of dry hydrogel.

2.7. Temperature dependence of the swelling ratio

The temperature dependence of equilibrium swelling ratio of P(NIPAAm-co-NIPMMA) hydrogels was studied gravimetrically at 22–55 °C. The samples were immersed in distilled water to swell for at least 24 h at each predetermined temperature, after which the samples were taken out, and the excess water on the surface was blotted by wet filter papers and then the samples were weighed. The hydrogel samples were then re-equilibrated in distilled

Table 1
Feed compositions for synthesis of P(NIPAAm-co-NIPMMA) hydrogels

	Sample ID				
	CGel	$Gel_{7.5}$	$Gel_{15.4}$	$Gel_{23.3}$	$Gel_{41.6}$
NIPAAm (mmol)	3.5	3.2	2.8	2.5	1.8
NIPMMA (mmol)	0	0.26	0.51	0.76	1.28
Molar percentage of NIPMMA (%)	0	7.5	15.4	23.3	41.6
BIS (mmol)	0.1	0.1	0.1	0.1	0.1
TEMED (μl)	150	150	150	150	150
APS (mg)	10	10	10	10	10
Conversion (%)[a]	93.9	79.2	72.1	68.3	51.7

[a] Conversion based on the weight percentage of the synthesized hydrogel from the total monomers.

water at another predetermined temperature and then weighed using the same method as above. The dry weight of each sample was finally measured after drying in vacuum at 55 °C for 24 h to reach a constant weight. The swelling ratio at each temperature was calculated according to Eq. (1).

2.8. Study on the deswelling kinetics

The deswelling kinetics of P(NIPAAm-co-NIPMMA) hydrogels were studied by immersing the swollen hydrogels at room temperature into hot water at 50 °C. At predetermined time intervals, the hydrogel samples were taken out from the hot water and weighed after blotting excess water on the surface by wet filter papers. Water retention is defined as follows:

$$[\text{Water retention}]_t = [(W_t - W_d)/W_s] \times 100 \quad (2)$$

where, W_t the weight of wet hydrogel at time t at the temperature of 50 °C, W_s is the weight of water in the equilibrium swollen hydrogel (wet weight − dry weight) and W_d is the initial weight of dry hydrogel.

2.9. Study on the reswelling kinetics

The dried samples were placed in distilled water at room temperature to swell and then removed from water at regular time intervals. The same method was utilized to record the weights of samples. The water uptake at time t is defined as follows:

$$[\text{Water uptake}]_t = [(W_t - W_d)/W_s] \times 100 \quad (3)$$

Here, W_t is the weight of the wet hydrogel at time t at the temperature of 22 °C, and the other symbols (W_s, W_d) are the same as above.

2.10. Study on the pH sensitivity

The hydrogel samples were immersed in distilled water at room temperature for at least 24 h to reach equilibrium. The swollen samples were transferred to buffer solutions of different pH values (1, 6, 13; $I = 0.1$ M), and the samples were immersed in the buffer solutions at room temperature for at least 24 h. After that, the weights of the samples were measured gravimetrically and the swelling ratio at each pH value was calculated according to Eq. (1).

3. Results and discussion

3.1. Synthesis of P(NIPAAm-co-NIPMMA) hydrogels

The chemical structures of maleic anhydride, isopropylamine, NIPMMA, NIPAAm and the synthesis route of P(NIPAAm-co-NIPMMA) hydrogel are shown in Fig. 1. During the preparation of NIPMMA, it was found that if the reaction temperature was around 0 °C, the conversion became higher. During of formation of hydrogels, the conversion decreased with the increasing content of NIPMMA as indicated in Table 1. The conversion of pure PNIPAAm hydrogel (CGel) is 93.9%, while the conversion of $Gel_{7.5}$ is 79.2%. With the increasing content of NIPMMA, the conversion further decreased, the conversions of $Gel_{15.4}$, $Gel_{23.3}$ and $Gel_{41.6}$ being 72.1%, 68.3% and 51.7%, respectively. Such a tendency is attributed to the conjugated effect of maleic anhydride based monomers. It is well known that maleic anhydride has strong conjugated effect due to the property of electron attraction of carboxyl (Braun, Aziz, Sayed, & Pomakis, 1969; Capraro, Winkler, & Martin, 1983). As a derivative of maleic anhydride, NIPMMA also has a certain conjugated effect even though it has an asymmetric chemical structure. In fact, attempts to prepare P(NIPAAm-co-NIPMMA) hydrogel with the content of NIPMMA above 52 mol.%, resulted in hydrogels too soft for further investigation.

3.2. FT-IR spectra of P(NIPAAm-co-NIPMMA) hydrogels

The FT-IR spectra of P(NIPAAm-co-NIPMMA) hydrogels are shown in Fig. 2. It is difficult to identify each hydrogel from the different relative intensities of the peaks in FT-IR spectrum since both monomeric units, either NIPAAm or NIPMMA have the *N*-isopropylamide group. From the spectra presented in Fig. 2, although all the hydrogels exhibited a typical band in the range of 3100–3700 cm^{-1} (band a in Fig. 2), the band of P(NIPAAm-co-NIPMMA) hydrogels is broader than the corresponding one of CGel, due to the existence of the hydroxyl of carboxylic acid group (–COOH) in NIPMMA. Thus, it was deduced that NIPMMA had been successfully incorporated into the resultant P(NIPAAm-co-NIPMMA) hydrogels. Besides, the typical amide I and II bands in the NIPAAm and NIPMMA are obvious at ~1646 and 1530 cm^{-1} (bands b and c in Fig. 2).

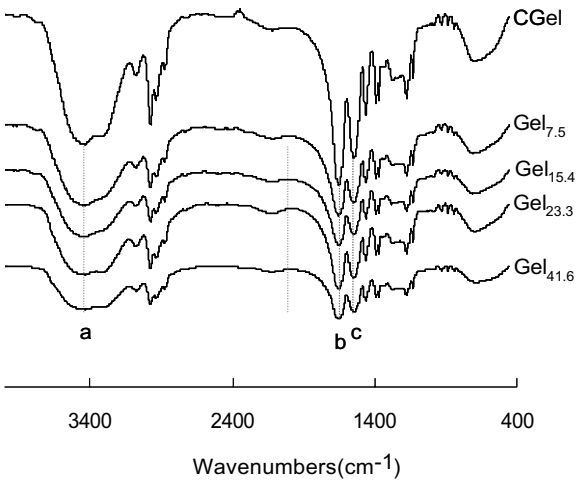

Fig. 2. FT-IR spectra of P(NIPAAm-co-NIPMMA) hydrogels: (a) 3100–3700 cm^{-1} (b) ~1646 cm^{-1} (c) 1530 cm^{-1}.

3.3. Interior morphology

The interior morphology of P(NIPAAm-co-NIPMMA) hydrogels (Fig. 3) illustrates the dependence of the hydrogel morphology on the hydrogel composition. It was found that the P(NIPAAm-co-NIPMMA) hydrogel network has a different interior structure, such as the porous structure. The average pore size becomes smaller as the content of NIPMMA increases, i.e. CGel has the largest pore size while $Gel_{41.6}$ has the smallest one. As shown in Fig. 1, NIPMMA contains extra hydrophilic carboxylic acid group, so the hydrophilicity of NIPMMA is stronger. As a result, when the content of NIPMMA increases, more hydrogen bonds are formed between NIPAAm and NIPMMA, which prevent the polymeric chain expanding further. Thus, with the content of NIPMMA increasing, the pore size of the resultant hydrogel becomes gradually smaller.

3.4. Equilibrium swelling ratio at room temperature

Fig. 4 exhibits the equilibrium swelling ratio in distilled water of P(NIPAAm-co-NIPMMA) hydrogels at room temperature. From the data in Fig. 4, it was found that the equilibrium swelling ratio of P(NIPAAm-co-NIPMMA) hydrogels increased with increasing NIPMMA content in the corresponding hydrogel.

As mentioned, the hydrophilicity of NIPMMA is stronger than NIPAAm. Consequently, the hydrophilicity of resultant P(NIPAAm-co-NIPMMA) hydrogels should become stronger compared with the pure PNIPAAm hydrogel. That is, from CGel to $Gel_{41.6}$, the hydrophilicity becomes stronger gradually, resulting in increased equilibrium swelling ratios of corresponding hydrogels.

3.5. Temperature dependence of the swelling ratio

The temperature dependence of the swelling ratio of P(NIPAAm-co-NIPMMA) hydrogel over a temperature range from 22 to 55 °C (Fig. 5) shows that P(NIPAAm-co-NIPMMA) hydrogels had favorable temperature responses, which was attributed to the existence of the temperature sensitive group, isopropylamide, in the NIPAAm and NIPMMA units. With increasing temperature, the swelling ratios of all the hydrogels decreased because the hydrophobic interactions between the hydrophobic groups in hydrogels became dominant, thus the hydrogels matrices started to shrink and the phase separation took place. From Fig. 5, it can be seen that the swelling ratio of CGel decreased for 12.5 when the temperature increases from 22 to 50 °C, while the corresponding changes in swelling ratio for $Gel_{7.5}$, $Gel_{15.4}$, $Gel_{23.3}$ and $Gel_{41.6}$ were around 12.8, 13.1, 13.3 and 15.8.

The lower critical solution temperature (LCST) of a PNIPAAm hydrogel is regarded as the temperature at which the phase-separation degree (changes in the swelling ratio vs. temperature changes ($\Delta SR/\Delta T$)) is the largest or the swelling ratio of the hydrogel decreases most dramatically. In general, the main mechanism for the phase separation of PNIPAAm hydrogels is based on the changes in their hydration and dehydration behavior, and the phase separation temperature is conventionally regarded as the

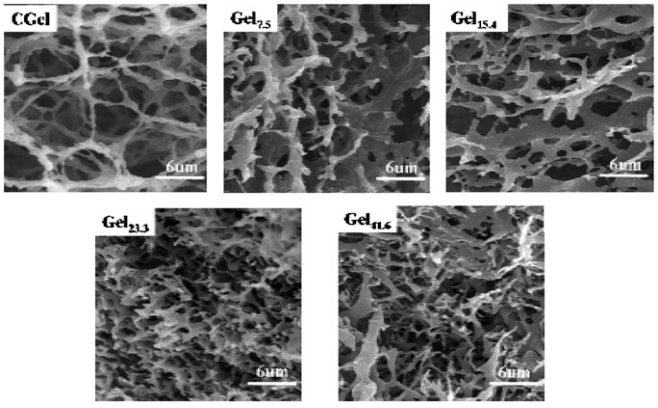

Fig. 3. SEM micrographs of P(NIPAAm-co-NIPMMA) hydrogels.

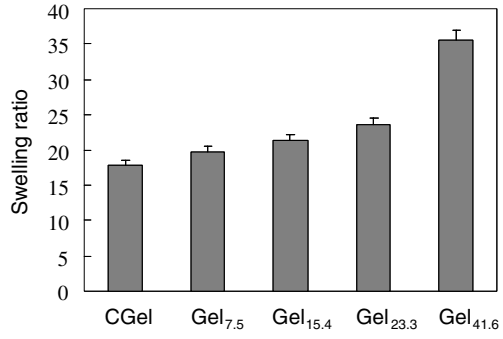

Fig. 4. The equilibrium swelling ratios of P(NIPAAm-co-NIPMMA) hydrogels in distilled water at room temperature.

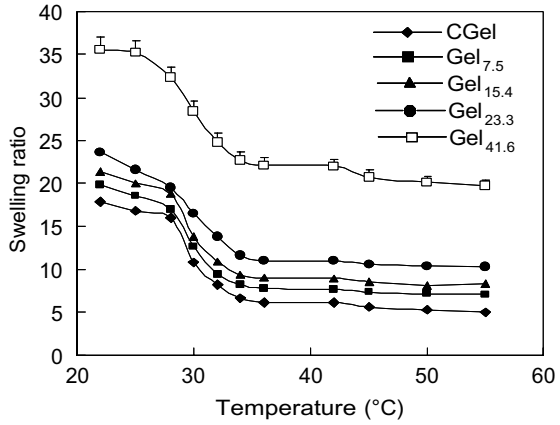

Fig. 5. Temperature dependence of the swelling ratio of P(NIPAAm-co-NIPMMA) hydrogels in distilled water over the temperature ranging from 22 to 55 °C.

hydrophilic/hydrophobic balance of the network. Thus, when incorporating the hydrophilic moiety into the PNIPAAm chains, the phase separation temperature will become higher (Shibayama et al., 1996; Vernon, Kim, & Bae, 2000). Since the hydrophilicity of NIPMMA is stronger than NIPAAm, when copolymerizing NIPMMA with NIPAAm, the phase separation temperature of the resultant hydrogel should become higher. However, from this standpoint, it is evident from the data in Fig. 5 that all the hydrogels exhibit similar phase transition temperatures at around 32 °C, regardless of the NIPMMA content, which is contrary to prediction. Such an unusual phenomenon was attributed to the existence of the isopropylamide group in NIPMMA; the continuous sequence of isopropylamide pendant groups of pure PNIPAAm structure is not disturbed apparently when incorporating NIPMMA into PNIPAAm chains. Since the phase separation temperature mainly depends on the polymeric backbone, the phase separation behaviors of $Gel_{7.5}$, $Gel_{15.4}$, $Gel_{23.3}$ and $Gel_{41.6}$ are almost identical to that of CGel. Thus, the thermosensitivity of all these hydrogels should be similar although the detailed swelling ratios are different due to the incorporation of hydrophilic NIPMMA. In fact, a similar phenomenon was also previously reported (Ebara et al., 2000).

3.6. Deswelling kinetics at 50 °C

To understand further the temperature sensitivity upon heating, the deswelling rate of P(NIPAAm-co-NIPMMA) hydrogel at 50 °C was investigated (Fig. 6). It is well known, due to a dehydration effect as the external temperature is increased above LCST, that polymer chains aggregate abruptly, leading to shrinkage of the hydrogel and extrusion of freed water. As mentioned above, due to the similar continuous sequence of isopropylamide pendant groups, both PNIPAAm hydrogel and P(NIPAAm-co-NIPMMA) hydrogels would have a similar deswelling rate upon heating. As indicated in Fig. 6, when transferred into hot water of 50 °C, the decrease in swelling ratio (ΔSR) of CGel hydrogel is 9.8 within 75 min, while that of $Gel_{7.5}$, $Gel_{15.4}$, $Gel_{23.3}$ and $Gel_{41.6}$ are 10.1, 10, 10.6 and 15.6, respectively within the same time frame.

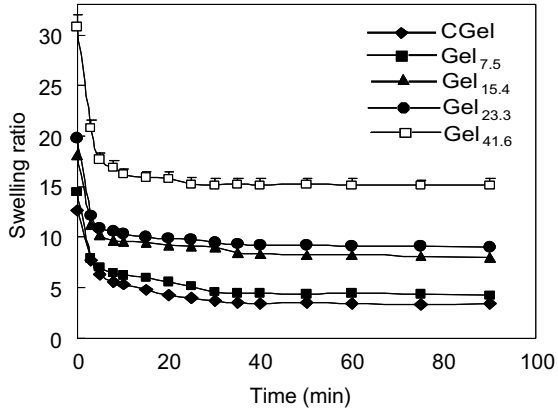

Fig. 6. Deswelling kinetics of P(NIPAAm-co-NIPMMA) hydrogels in distilled water at 50 °C.

3.7. Reswelling kinetics at room temperature

From data on the reswelling behaviors of dried P(NIPAAm-co-NIPMMA) hydrogels at room temperature (Fig. 7) it was found that the reswelling rates of hydrogels became improved with the increasing content of NIPMMA. Among the P(NIPAAm-co-NIPMMA) hydrogel series, $Gel_{41.6}$ has the fastest reswelling rate. In detail, within the initial 29 min, the swelling ratio of CGel reached 16.6, while that of $Gel_{7.5}$ reached 18.2. With further increases of NIPMMA content, the swelling ratio of $Gel_{15.4}$, $Gel_{23.3}$ and $Gel_{41.6}$ reached 18.3, 19.9 and 31.5, respectively within 29 min. This tendency is easily understood if we take into account of the hydrophilic nature of the incorporated NIPMMA.

3.8. pH sensitivity at room temperature

Displays of the pH sensitivity of P(NIPAAm-co-NIPMMA) hydrogel in buffer solutions ($I = 0.1$ M) with different pH values at room temperature (Fig. 8) show that the

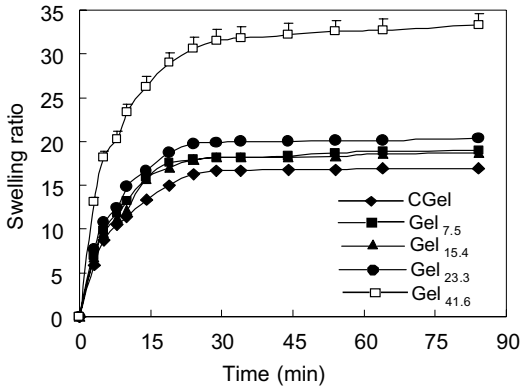

Fig. 7. Reswelling kinetics of P(NIPAAm-co-NIPMMA) hydrogels in distilled water at room temperature.

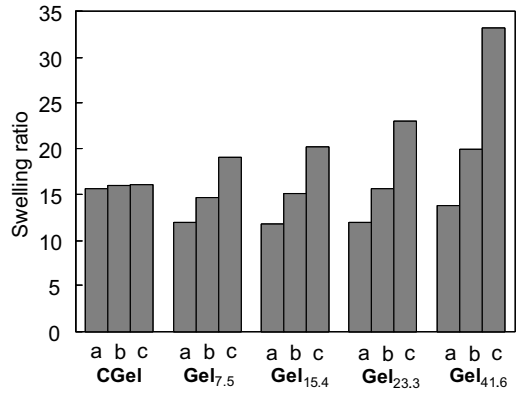

Fig. 8. pH sensitivity of P(NIPAAm-co-NIPMMA) hydrogels at room temperature. (a) pH 1; (b) pH 6; (c) pH 13.

hydrogels exhibited lower swelling ratios in an acidic medium. Due to the existence of carboxylic acid groups in NIPMMA, there existed a lot of hydrogen bonds in an acid medium. The hydrogen bond complex would restrict the movement or relaxation of network chains. A compact hydrogel network would be formed and thus, a lower swelling ratio was observed. But in neutral and alkaline media, these free carboxylic acid groups would be ionized, which would break hydrogen bonds and generated electrostatic repulsion among polymer chains. This repulsive force would push the network chain segments apart and attract more water into the hydrogel, so a higher swelling ratio would be observed (Kim, Won, & Chu, 1999; Zhang, Wu, & Chu, 2004).

In addition, Fig. 8 also demonstrates that the pH sensitivity of the hydrogel increases from CGel to $Gel_{41.6}$. As for CGel, while the pH of the medium varies, the swelling ratio keeps almost the same. With respect to $Gel_{7.5}$, $Gel_{15.4}$, $Gel_{23.3}$ and $Gel_{41.6}$, the pH response increases. The reason is that with the increasing content of NIPMMA, the content of carboxylic acid groups increases, consequently, the pH response capability of the resultant hydrogel gets strengthened accordingly.

4. Conclusions

In summary, a novel monomer, *N*-isopropyl-maleamic acid (NIPMMA) and a series of pH and thermosensitive P(NIPAAm-co-NIPMMA) hydrogels have been designed and synthesized. Due to the existence of carboxyl groups in the resultant P(NIPAAm-co-NIPMMA) hydrogels, these hydrogels possess significant pH sensitivity. Also quite importantly, besides the pH sensitivity, P(NIPAAm-co-NIPMMA) hydrogels also exhibit good thermosensitivity, even the content of NIPMMA reaches 41.6 mol.%. The good thermosensitivity of P(NIPAAm-co-NIPMMA) hydrogels is attributed to the remaining continuous sequence of isopropylamide pendant groups in P(NIPAAm-co-NIPMMA) chains. The pH and thermosensitive P(NIPAAm-co-NIPMMA) hydrogel exhibited an interesting insight to the construction of novel intelligent devices, which would find potential and promising applications in many fields, such as intelligent drug delivery systems.

Acknowledgments

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