

# Synthesis of Poly(*N,N*-diethylacrylamide-*co*-acrylic acid) Hydrogels with Fast Response Rate in NaCl Medium

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Received 23 November 2007; accepted 19 March 2008

DOI 10.1002/app.28439

Published online 20 May 2008 in Wiley InterScience (www.interscience.wiley.com).

**ABSTRACT:** A series of thermo- and pH-sensitive poly(*N,N*-diethylacrylamide-*co*-acrylic acid) (P(DEA-*co*-AA)) hydrogels were prepared in NaCl aqueous solutions with different concentrations. Swelling and deswelling studies showed that in comparison with conventional P(DEA-*co*-AA) hydrogels (prepared in distilled water), the P(DEA-*co*-AA) hydrogels thus prepared had almost the same volume phase transition temperature (VPTT), but exhibited much faster response rates as the temperature was raised above

their VPTT. Besides, the hydrogels prepared by this method had faster response rates in low pH buffer solutions, and the response rates increased with the increased concentration of the NaCl solutions used during the polymerization. © 2008 Wiley Periodicals, Inc. *J Appl Polym Sci* 109: 3037–3043, 2008

**Key words:** poly(*N,N*-diethylacrylamide-*co*-acrylic acid); hydrogel; salt; pH sensitive; temperature sensitive

## INTRODUCTION

In the past two decades, a considerable amount of research has been focused on smart hydrogels that can undergo volume transition in response to external physical or chemical stimuli such as pH,<sup>1,2</sup> electric field,<sup>3</sup> ionic strength,<sup>4,5</sup> and temperature.<sup>6–9</sup> Among stimuli-sensitive hydrogels, poly(*N,N*-diethylacrylamide) (PDEA) gel has attracted much attention, from both the academic and technological viewpoints.<sup>10</sup> PDEA gel undergoes an abrupt volume change at the phase transition temperature (~ 32°C),<sup>11</sup> which can be utilized in several promising applications such as drug delivery systems and actuators.

For better performance of these applications, several strategies<sup>12–14</sup> have been reported to exploit the rapid volume change of temperature-sensitive hydrogels. Phase separation is one of the widely used methods to prepare a heterogeneous structure of the resulting hydrogels. Hirasa et al.<sup>15</sup> have synthesized macroporous poly(vinyl methyl ether) (PVME) hydrogels by radiation crosslinking PVME during a temperature rise from 32.5 to 42.5°C. The lower critical solution temperature (LCST) of PVME is approximately 38°C. Their hydrogels exhibit very

fast volume change between 20 and 40°C. Kabra and Gehrke<sup>16</sup> synthesized fast responsive poly(*N*-isopropylacrylamide) (PNIPA) hydrogels using a phase separation technique by polymerizing monomer at 22°C for 9 min and then continuing the polymerization at 37.9°C [over the volume phase transition temperature (VPTT) of the PNIPA hydrogel] over the next 24 h. Wu and Hoffman<sup>17</sup> developed a method which is based on the phase separation technique. They prepared macroporous PNIPA hydrogels by polymerizing the monomer at 50°C and evacuating the reactor near the end of the reaction. Recently, Zhuo and coworkers<sup>18</sup> developed a new method to prepare macroporous thermosensitive PNIPA hydrogels by polymerizing NIPA in inorganic salt aqueous solution. The hydrogels thus prepared had larger equilibrium swelling ratios below the VPTT and much faster response rates when compared with the conventional hydrogels.

However, as far as we know, there is no report on creating thermo- and pH-sensitive hydrogels with fast response rates by salt effect during the polymerization in NaCl aqueous solution. In this study, a series of fast responsive thermo- and pH-sensitive hydrogels have been synthesized by using NaCl aqueous solutions as the reaction medium.

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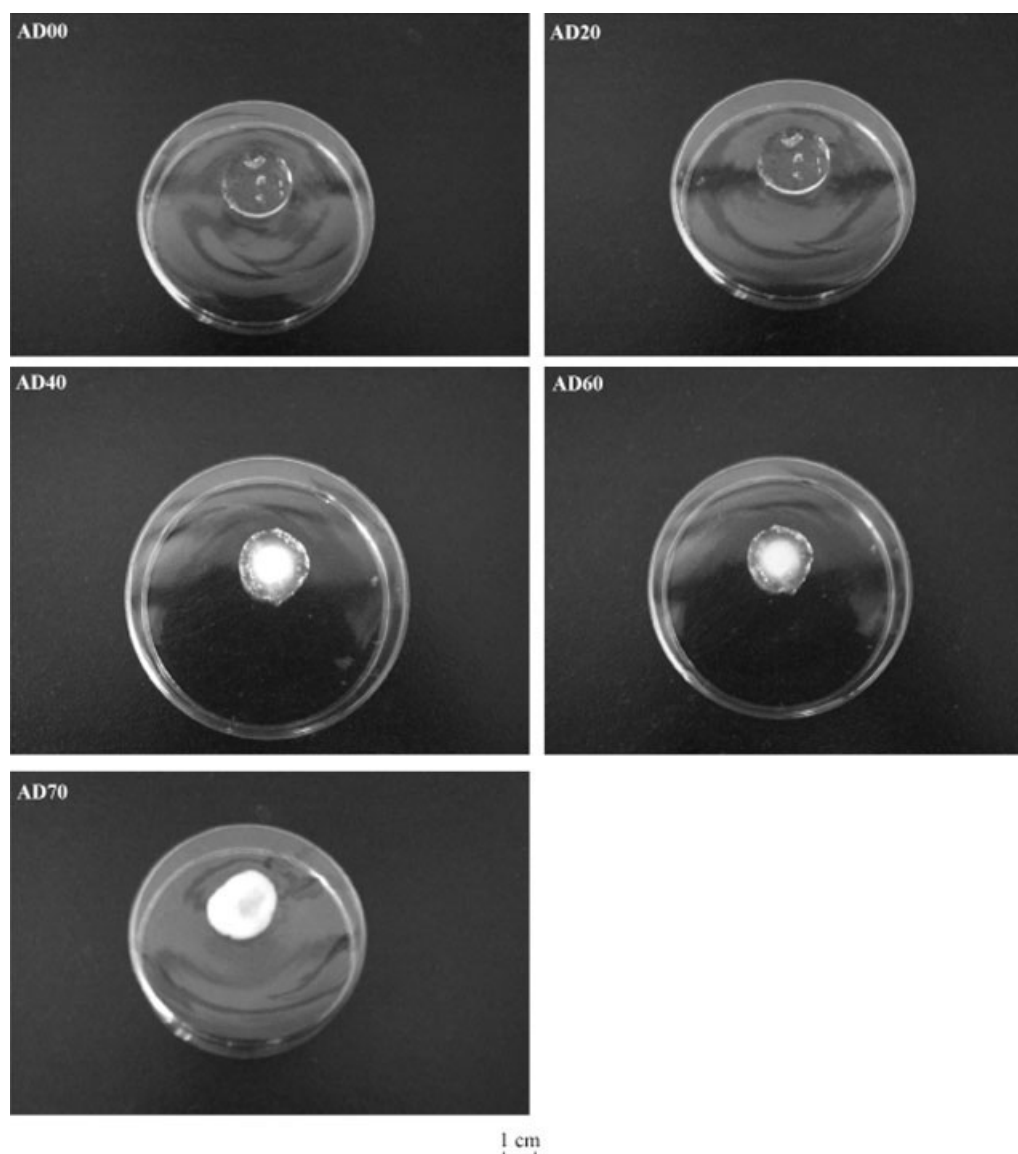
Contract grant sponsor: Special Doctoral Program Funds of the Ministry of Education of China; contract grant number: 20030730013.

## EXPERIMENTAL

### Materials

Acrylic acid (AA) (A.P. grade) (Tianjin Chemical Company, Tianjin, China) was distilled under reduced





**Figure 1** Optical photos of the P(DEA-co-AA) hydrogels prepared in pure water (AD00) and NaCl aqueous solution with different concentrations of 2.0 wt % (AD20), 4.0 wt % (AD40), 6.0 wt % (AD60), and 7.0 wt % (AD70).

### Characterization of hydrogels

#### Surface morphology observation

Scanning electron microscopy (JSM-5600LV SEM, Japan) was used to observe the surface morphology of the P(DEA-co-AA) hydrogels. To prepare samples for SEM, the hydrogels swollen at room temperature (18°C) were freeze-dried for 15 h with freeze-dry system (LABCONCO 2.5 L, USA) to avoid the collapse of porous structure and then sputter-coated with gold.

#### Swelling properties measurement

Swelling studies were performed in distilled water with different temperatures (from 18 to 50°C) and in different pH buffer solutions (from 1.50 to 9.32) at

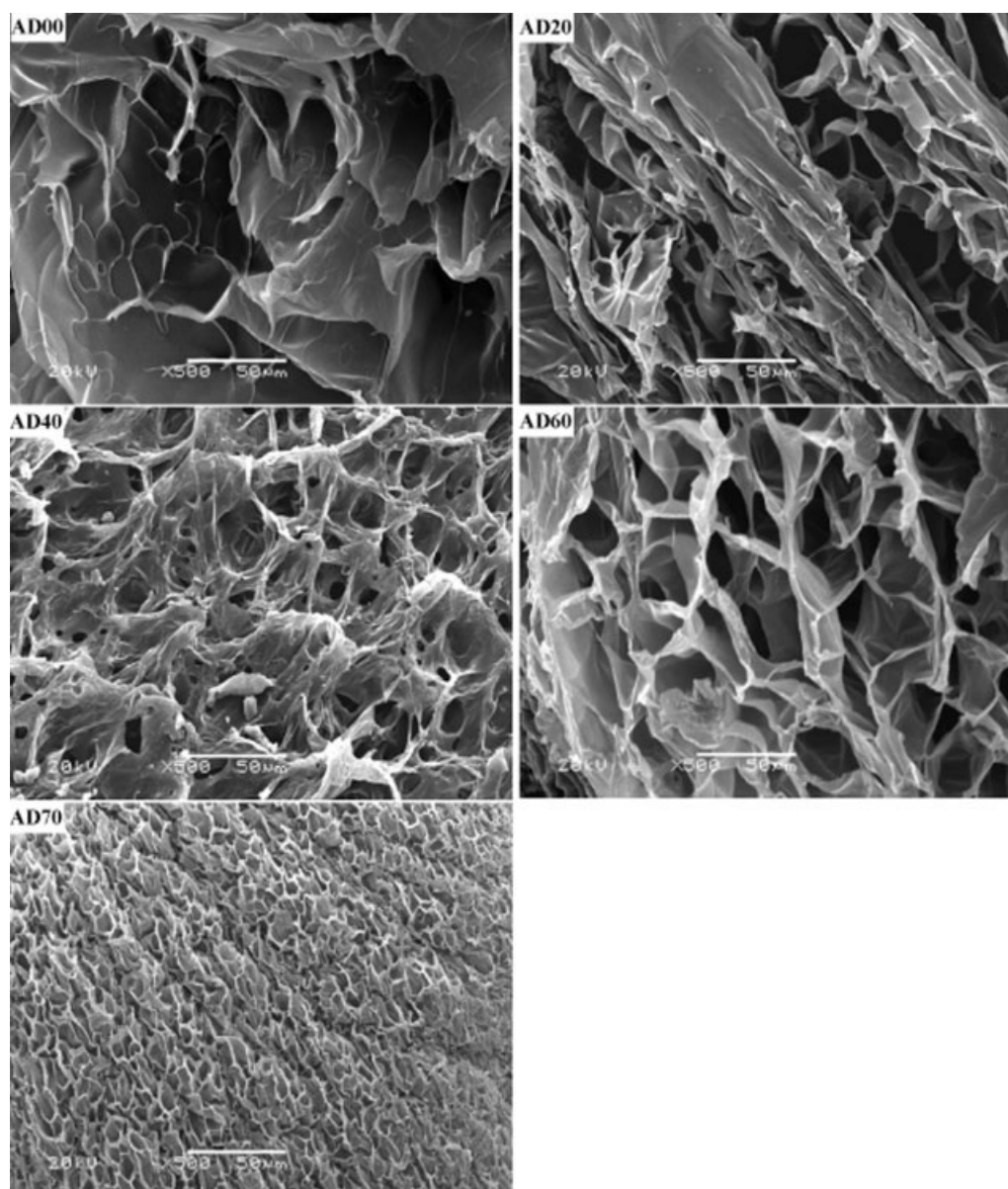
fixed ionic strength ( $I = 0.1M$ ). The equilibrium swelling ratio (ESR) is defined as follows:

$$ESR = (W_s - W_d)/W_d$$

where  $W_s$  and  $W_d$  are the weight of the equilibrium swollen and dried hydrogels, respectively. ESR of hydrogels was measured gravimetrically after wiping off the excess surface water with moistened filter paper.

#### Deswelling kinetic measurement

To study the deswelling kinetics, equilibrium-swollen hydrogels in distilled water at 18°C were transferred into distilled water at 60°C and pH = 3.02 buffer solutions at 18°C, respectively. The weight changes of hydrogels were recorded during the course of



**Figure 2** SEM images of the P(DEA-co-AA) hydrogels prepared in pure water (AD00) and NaCl aqueous solution with different concentrations of 2.0 wt % (AD20), 4.0 wt % (AD40), 6.0 wt % (AD60), and 7.0 wt % (AD70).

deswelling after blotting the excess water on the surface with moistened filter paper at regular time intervals. Water retention (WR) is defined as follows:

$$WR = 100 \times (W_t - W_d) / (W_e - W_d)$$

where  $W_e$  is the weight of equilibrium-swollen hydrogel at 18°C,  $W_t$  is the weight of hydrogel at regular time intervals, and  $W_d$  is the weight of the dried gel.

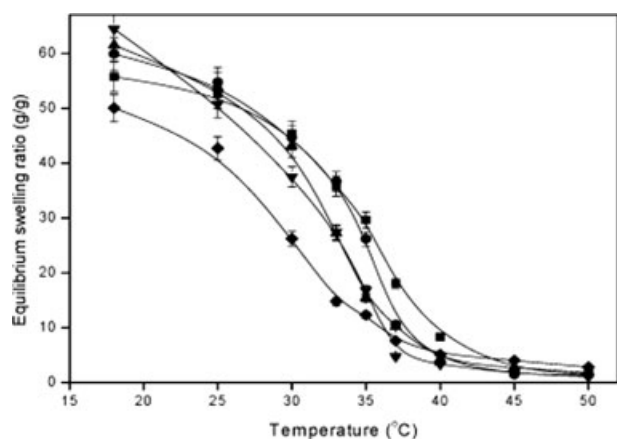
## RESULTS AND DISCUSSION

### Fabrication of hydrogels

From the polymerization it was found that the presence of NaCl in the polymerization medium signifi-

cantly influenced the formation of P(DEA-co-AA) hydrogels. As shown in Figure 1, AD00 and AD20 were transparent, whereas AD40 and AD60 appeared to be translucent with obviously fine opaque domains in the matrix, indicating that their network structure may be heterogeneous. Especially, for AD70, the gel became completely opaque indicating that more pores might be formed within the gel.

It is well-known that a phase separation during the formation of the gel network is mainly responsible for the formation of porous structures.<sup>20</sup> In our study, NaCl aqueous solutions with different concentrations were used as the reaction medium. During polymerization, the formed polymer chains could not dissolve extendedly in the reaction me-



**Figure 3** Temperature dependence of equilibrium swelling ratio of the macroporous hydrogels and conventional hydrogel in distilled water (■: AD00; ●: AD20; ▲: AD40; ▼: AD60; ◆: AD70).

dium. As a result, the polymer chains curled, intertwined to each other, and finally became a nucleus, whereas the reaction solution still remained as the continuous phase. As the concentration of NaCl solution increased, the formation of nuclei became easier, and more nuclei appeared. This agglomeration resulted in the formation of a heterogeneous macroporous structure.<sup>17,18,20</sup> However, in our system, because of the presence of PAA polymer chains, the dissolubility of the whole gel network might be improved, which made the phase separation harder. Therefore, only when the NaCl concentration reached a certain level (4.0 wt %), phase separation could be observed, which was different from the results obtained by Zhuo and coworkers.<sup>18</sup> This was also the reason that AD20 was transparent, whereas AD40 appeared to be translucent.

### SEM micrographs of hydrogels

Figure 2 shows the SEM photos of the surface structure of the freeze-dried gel samples. It can be noticed that most areas of the conventional hydrogel prepared in distilled water and AD20 have relatively dense structure because of their higher homogenous structures. While for gels AD40, AD60, and AD70, obvious porous network structures appear. Especially, gel AD70 has much more pores and a higher porosity. These images clearly indicate that the presence of inorganic salt, NaCl, in the polymerization/crosslinking plays an important role because it leads to a phase separation during the gel formation.

### Stimuli-responsive swelling behaviors

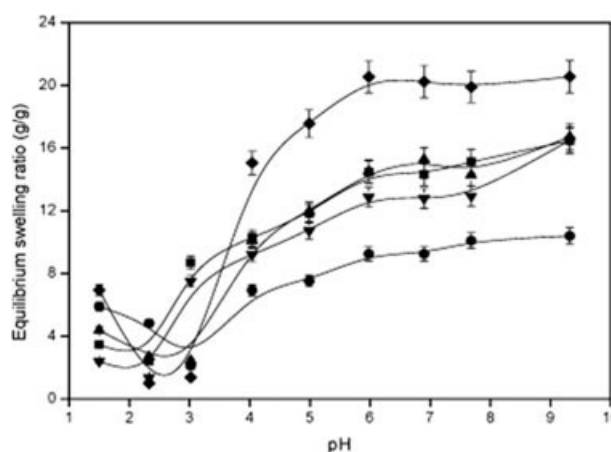
Figure 3 indicates the equilibrium swelling ratios of hydrogels in the temperature range from 18 to 50°C. From Figure 3 we can see that all the hydrogels

have almost the same VPTT, and the VPTTs are close to 37°C, which is close to the physiological temperature.

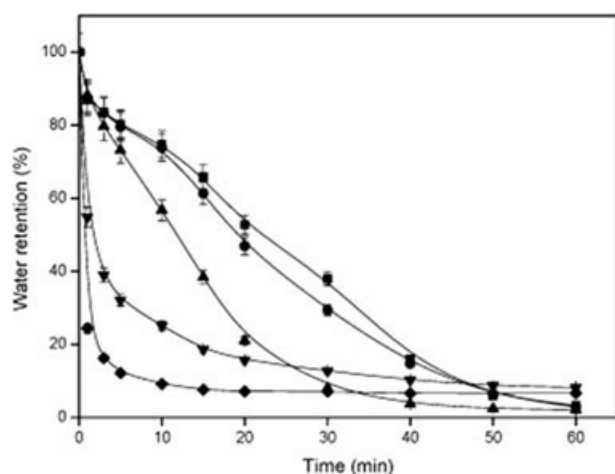
It is well-known that there are hydrophilic groups ( $-\text{CONR}_2$ ) and hydrophobic groups ( $-\text{CH}_2\text{CH}_3$ ) in DEA corresponding to the hydrophilic and hydrophobic regions, respectively, in the PDEA hydrogel. At low temperatures, the hydrogen-bonding interactions among polymer chains and water are dominant, leading to high swelling ratio. When the temperature is raised above the VPTT, hydrophobic interactions among the polymer chains become dominant and break the delicate balance between hydrogen-bonding and hydrophobic interactions, causing the hydrogel to collapse and decreasing the equilibrium swelling ratio dramatically. When the mole ratio of DEA/AA is constant, the hydrophilic/hydrophobic balance existing in P(DEA-co-AA) hydrogels is invariable, and so the VPTTs of the hydrogels are stable. Therefore, we can draw a conclusion that the presence of NaCl can just influence the network structure of the hydrogels, but cannot change the VPTT of the hydrogels.

pH-sensitive characteristics of the hydrogels are studied by swelling test under pH range from 1.50 to 9.32 ( $I = 0.1M$ ) at 18°C. As shown in Figure 4, the equilibrium swelling ratios of the hydrogels level off when  $\text{pH} > 5.0$ , then decrease dramatically in the range of pH from 5.0 to 2.5, and increase again with further decrease of the pH value.

This phenomenon can be understood as follows: At high pH values ( $\text{pH} > 5.0$ ), the carboxylic acid groups become ionized ( $-\text{COO}^-$ ) completely, which destructs the hydrogen bonds formed among carboxylic acid groups of PAA and amide groups of PDEA. Meanwhile, the charge repulsive force among  $-\text{COO}^-$  makes the polymer network expanded. In



**Figure 4** pH dependence of equilibrium swelling ratio of macroporous hydrogels and conventional hydrogel at 18°C (■: AD00; ●: AD20; ▲: AD40; ▼: AD60; ◆: AD70).



**Figure 5** Deswelling kinetics of the macroporous hydrogels and conventional hydrogel as temperature jumping from 18 to 60°C (■: AD00; ●: AD20; ▲: AD40; ▼: AD60; ◆: AD70).

this situation, more solvent molecules are accessible to the gel network and the gel is in a swollen state. In the range of pH from 2.5 to 5.0, the fraction of the carboxylic acid groups ( $-\text{COOH}$ ) is much more than that of the carboxylic anion groups ( $-\text{COO}^-$ ), and the lower the solution pH is, the more is the content of the nonionized carboxylic acid groups. Therefore, with the decreased pH, more and more hydrogen bonds are formed among carboxylic acid groups of PAA and amide groups of PDEA, which leads to high crosslinked density and makes the gel collapsed. When pH is below 2.5,  $-\text{CON}^+\text{HR}_2$  groups are formed in PDEA chains and the electrostatic repulsion again causes the gel to swell.

### Deswelling kinetics of hydrogels

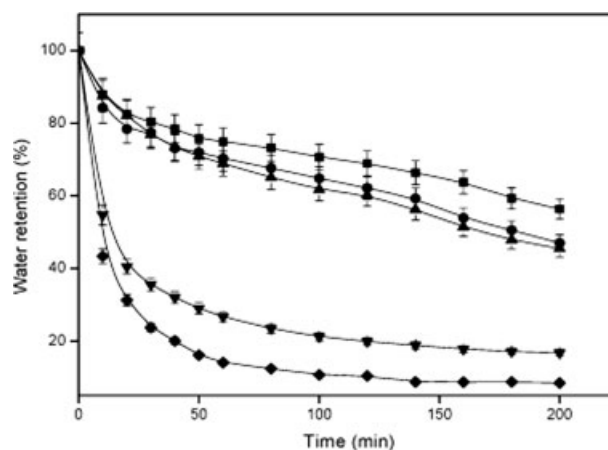
The deswelling kinetics of P(DEA-co-AA) hydrogels at a temperature (60°C) above the VPTT is shown in Figure 5. It is obvious that the shrinking rates of the resulting hydrogels become faster with increased concentration of the NaCl solution in which the polymerization is carried out. Gel AD70 loses 90% water only in 5 min, whereas AD40 and AD00 need 30 and 50 min, respectively. It is regarded that, when the P(DEA-co-AA) hydrogel is transferred into the hot water, the surface layer of the hydrogel is the first region to be affected, and a dense skin layer is formed due to the hydrophobic interactions among the ethyl groups of PDEA chains. Such a dense skin layer would greatly restrict the outward permeation of water from the hydrogel interior.<sup>21</sup> In this work, the porous network structure prepared in NaCl solution retards the formation of such a dense skin layer during the deswelling process and the freed water might diffuse out easily. As a result,

gel AD70 exhibits the fastest response rate upon heating.

We further studied the deswelling kinetics of the hydrogels after a pH jumping from pH = 6.90 to pH = 3.02. Figure 6 demonstrates the deswelling behavior of the porous and conventional hydrogels. It can be seen that the higher the NaCl concentration of the reaction medium, the faster is the shrinking rate of the corresponding hydrogel prepared in this medium. Gel AD70 loses 60% water in 12 min, whereas AD00 only loses 40% of water in 200 min. This can be explained as follows: as pH decreases, a higher concentration of protons is available in buffer solutions for protonating the ionized carboxylic acid within the gel network. Therefore, more hydrogen bonds will be formed among the polymer chains, and then the hydrogel will shrink. For gels AD00 and AD20, their surfaces seem smoother and less porous. Consequently, during the deswelling process, a rigid and glassy layer forms around the gel disc, which will make the diffusion of the freed water harder. However, no rigid and glassy layer is generated in AD60 and AD70 due to their porous network structure and the freed water might diffuse out quickly. From these, it would be easy to understand why AD60 and AD70 shrink faster than the other three ones.

### CONCLUSIONS

A series of porous P(DEA-co-AA) hydrogels with thermo- and pH-response are successfully prepared by using NaCl aqueous solutions as the reaction medium. In comparison with the conventional P(DEA-co-AA) hydrogels, the P(DEA-co-AA) hydrogels prepared in NaCl solutions have similar temperature and pH sensitivity, but exhibit much faster deswel-



**Figure 6** Deswelling kinetics of the macroporous hydrogels and conventional hydrogel as pH jumping from 6.90 to 3.02 at 18°C (■: AD00; ●: AD20; ▲: AD40; ▼: AD60; ◆: AD70).

ling response rates when they are transferred into distilled water from 18 to 60°C, and from pH = 6.90 buffer solution to pH = 3.02 buffer solution. These improved properties are attributed to the porous network structure formed by using NaCl solution as the polymerization/crosslinking medium, a finding that is further confirmed by SEM micrographs. It is expected that this fast responsive thermo- and pH-sensitive P(DEA-co-AA) hydrogels might have potential applications in biomedical fields for stimuli-responsive drug delivery systems.

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