

Preparation of Polyacrylamide Hydrogels at Various Charge Densities by Postmodification

Eylem Turan, Serkan Demirci, Tuncer Caykara

Department of Chemistry, Faculty of Art and Science, Gazi University, 06500 Besevler, Ankara, Turkey

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ABSTRACT: In this study, first polyacrylamide hydrogels were synthesized by free-radical crosslinking polymerization of acrylamide monomer with *N,N'*-methylenebis(acrylamide) as a crosslinker in an aqueous solution at 22°C. Then, a series of hydrogels at various charge densities were prepared by partial hydrolysis of polyacrylamide precursors in a 0.1M sodium hydroxide solution at 60°C. The hydrolysis time was varied between 20 and 180 min. The chemical structures and internal morphologies of the hydrogels before and after alkaline hydrolysis were characterized with attenuated total reflectance/Fourier transform infrared and scanning electron microscopy measurements. The swelling ratio of the hydrolyzed hydrogels was measured in buffer solutions at various pHs. From differential curves of dQ_v/dpH versus pH

(where Q_v is the equilibrium swelling ratio of the hydrogels), the volume phase transition pH of the hydrogels was found to be 4.33 ± 0.05 , regardless of the charge density of the hydrogels. In water at 22°C, the hydrogels with greater charge density showed a more rapid swelling rate because of their higher porosity and hydrophilicity. Moreover, in buffer solutions with the pH changing from 9.0 to 2.0 at 22°C, the hydrogels with greater charge density also exhibited a more rapid deswelling rate than the hydrogels with less charge density. In conclusion, the postmodification method is a good way of preparing pH-sensitive hydrogels with fast responsiveness. © 2008 Wiley Periodicals, Inc. *J Appl Polym Sci* 111: 108–113, 2009

Key words: hydrogels; modification; networks; swelling

INTRODUCTION

Polyacrylamide [poly(AAm)] hydrogels have broad applications as model drug delivery systems because of their random morphologies with a wide distribution of pore sizes, as electrophoretic media for the separation or purification of biomolecules,^{1,2} and as matrices for enzymes and living cell immobilization because of their controllable pore size, no need for enzyme-reactive groups for attachment to an insoluble support, high residual activity, and so forth.³ Therefore, the investigation of the swelling behavior of poly(AAm)-based hydrogels has received considerable attention in the last 4 decades. These hydrogels are mostly prepared by the free-radical crosslinking copolymerization of acrylamide (AAm) monomer and *N,N'*-methylenebis(acrylamide) (MBAAm) as a crosslinker. To increase the swelling capacity, strong polyelectrolyte types are formed. Several studies have been reported on the swelling properties of poly(AAm) hydrogels as a function of their ionic group content.^{4–7} The results of these studies have indicated that when the ionic group content in the hydrogel is increased, the swelling ratios are also increased. This is mainly due to a simultaneous increase in the number of counterions

inside the hydrogel, which produces additional osmotic pressure that swells the hydrogel.⁸

To prepare strong polyelectrolyte poly(AAm)-based hydrogels, one of the technique for incorporating ionic moieties into poly(AAm) chains is the direct copolymerization of AAm and an ionic monomer.⁹ The other is postmodification of poly(AAm). Poly(AAm) could be very useful as a superabsorbent hydrogel when it is properly hydrolyzed. Kiatkamjornwong and Suwanmala¹⁰ synthesized partially hydrolyzed poly(AAm)-poly(*N*-vinylpyrrolidone) copolymers as superabsorbents via γ irradiation. Feng et al.¹¹ prepared hydrophobically associating poly(AAm)s or hydrophobically associating hydrolyzed poly(AAm)s through partial hydrolysis of hydrophobically associating poly(AAm) precursors with 0.25M sodium hydroxide in a 0.1M sodium chloride solution at 60°C. Their results pointed out that the postmodification method is a more effective way of controlling the composition of hydrophobically associating poly(AAm)s in comparison with a micellar process. However, despite extensive studies on the synthesis and swelling properties of AAm-based hydrogels, systematic investigations of the charge density dependence of the morphological structure and responsive dynamics of hydrolyzed poly(AAm) hydrogels have not been reported before in the literature.

In this study, a series of AAm-based hydrogels at various charge densities were prepared directly

Correspondence to: T. Caykara (caykara@gazi.edu.tr).

through partial hydrolysis of poly(AAm). The chemical structures and internal morphologies of the hydrogels before and after alkaline hydrolysis were characterized with attenuated total reflectance/Fourier transform infrared (ATR–FTIR) and scanning electron microscopy (SEM) measurements. Moreover, the effect of the charge density on the swelling/deswelling behaviors of hydrolyzed poly(AAm) hydrogels was also investigated.

EXPERIMENTAL

Materials

AAm (Aldrich Chemical, Milwaukee, WI), MBAAm (Aldrich Chemical), ammonium persulfate (APS; Aldrich Chemical), and *N,N,N',N'*-tetramethylethylenediamine (TEMED; Aldrich Chemical) were used as received. Glacial acetic acid, phosphoric acid, boric acid, and standardized sodium hydroxide were used to prepare Britton–Robinson buffers. The stock Britton–Robinson buffer solution was prepared with 2.5 mL of glacial acetic acid, 2.7 mL of phosphoric acid, 2.47 g of boric acid, and its dilution with deionized water to 1000 mL. Fifty-milliliter portions of this stock solution were taken, and their pHs were adjusted between 2.0 and 9.0 by the addition of an appropriate amount of a 2.0M sodium hydroxide solution.

Preparation of the hydrolyzed poly(AAm) hydrogels

First, poly(AAm) hydrogels were synthesized by the free-radical crosslinking polymerization of AAm with a small amount of MBAAm as the crosslinker. APS (0.06M) and TEMED (0.064M) were used as the redox initiator system. A solution containing AAm (0.5 g), MBAAm (0.05 g), APS (2.0 mL), and TEMED (2.0 mL) was prepared in 4.0 mL of deionized water. After nitrogen bubbling for 15 min, the solution was placed in poly(vinyl chloride) straws that were 4 mm in diameter and about 20 cm long. The poly(vinyl chloride) straws were sealed and immersed in a thermostated water bath at 22°C, and polymerization was conducted for 24 h. After the reaction was completed, the hydrogels were cut into specimens approximately 10 mm long and immersed in a large excess of deionized water to remove the unreacted species. The water was replaced three to four times every day, and the purified hydrogels were stored in deionized water. After that, to obtain poly(AAm) hydrogels at various charge densities, the purified hydrogels were immersed in a 0.25M sodium hydroxide solution at 60°C. The hydrolysis time was changed from 20 to 180 min. The hydrolyzed hydrogels were washed with deionized water and then freeze-dried in a Virtis freeze drier (Lobconco, Kan-

sas City, MO) for 2 days to completely remove the water. The hydrolysis degree of poly(AAm) to hydrolyzed poly(AAm), determined by the semimicro-Kjeldahl method,¹² gave the nitrogen content in the hydrogels. The difference in the nitrogen content before and after the hydrolysis reaction was calculated as the degree of hydrolysis.

Morphological structure of the hydrogels

SEM (JSM-6360 LV SEM instrument, JEOL, Tokyo, Japan) was used to study the internal or cross-section morphology of the hydrogels. Before the measurements, the swollen hydrogels at 22°C were first freeze-dried and then fractured and sputter-coated with gold.

ATR–FTIR measurements

ATR–FTIR measurements of the freeze-dried hydrogels were made with a Nicolet (Madison, WI) 6700 FTIR spectrometer equipped with a smart orbit assessor in the range of 2000–500 cm⁻¹.

Measurement of the equilibrium swelling ratio

To measure the equilibrium swelling ratio, pre-weighed dry, freeze-dried samples were immersed in the pH buffer solutions. After the excess water was wiped off the sample surface with moistened filter paper, the mass of the swollen samples was measured in the pH range of 2–9. The equilibrium swelling ratio of the hydrogels (Q_v) was determined as follows:

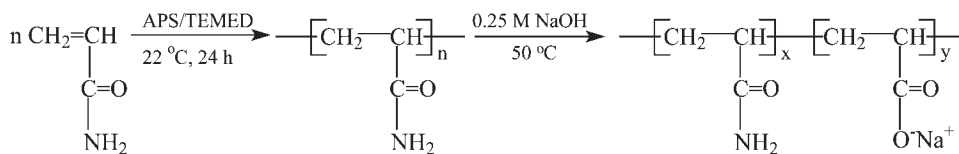
$$Q_v = 1 + \frac{\left(\frac{m_s}{m_d} - 1\right)\rho_2}{\rho_1} \quad (1)$$

where m_s and m_d are the masses of a hydrogel after equilibrium swelling in the pH solution. After drying, ρ_1 and ρ_2 are the densities of polymer network and solvent, respectively. The ρ_1 and ρ_2 values were 1.0 and 1.35 g mL⁻¹, respectively. The density of hydrogel was determined by a pycnometer with acetone as a nonsolvent. The density value of hydrogels did not change so much with the degree of hydrolysis.^{8,16} The volume fraction of the polymer network (v_{2m}) was calculated as follows:

$$v_{2m} = 1/Q_v \quad (2)$$

Measurement of the swelling and deswelling kinetics

For the swelling kinetics measurements, the freeze-dried samples were immersed in deionized water. At a prescribed time interval, the hydrogels were taken out from the water and weighed after the



Scheme 1 Schematic route for preparing the hydrolyzed poly(AAm) hydrogels.

hydrogel surface was wiped off. The swelling ratio of the hydrogels was defined as follows:

$$\text{Swelling ratio} = \frac{m_t - m_d}{m_d} \quad (3)$$

where m_t is the mass of a wet hydrogel at each time.

The deswelling kinetics of the hydrogels were also followed gravimetrically in a pH 2.0 buffer solution. The swollen hydrogels, equilibrated first in a pH 9.0 buffer solution, were transferred to a pH 2.0 buffer solution; then, after a certain time, the hydrogels were surface-dried with filter paper. The mass changes of the hydrogels were recorded during the course of deswelling at these time intervals. The normalized deswelling ratio of the hydrogels was calculated as follows:

$$\text{Normalized deswelling ratio} = \frac{m_t - m_d}{m_e - m_d} \quad (4)$$

where m_e is the mass of the swollen hydrogel at equilibrium. All the reported swelling and deswelling values are averages of at least three separate measurements.

RESULTS AND DISCUSSION

Preparation of the hydrolyzed poly(AAm) hydrogels

Poly(AAm) hydrogels were synthesized by free-radical crosslinking polymerization in an aqueous solution with AAm monomer, MBAAm crosslinker, and redox initiators. The persulfate initiator decomposed under heating to generate sulfate anion radicals. The radicals abstracted hydrogen from TEMED to form the radicals on TEMED. Therefore, this persulfate-TEMED redox system resulted in active centers on the monomers to radically initiate the polymerization of AAm. Because a crosslinking agent (MBAAm) was present in the system, the polymer had a crosslinked structure.

To obtain the hydrogels at various charge densities, the synthesized poly(AAm) hydrogels were hydrolyzed in a 0.25M sodium hydroxide solution at 60°C. As a result of hydrolysis, amide groups of poly(AAm) were converted to carboxylate salt. This reaction is shown in Scheme 1.

Generally, FTIR spectroscopy, ^{13}C -NMR, and elemental analysis methods are used quantitatively to measure the degree of hydrolysis of a hydrogel without the need to accurately measure the mass of the sample. In this work, we used the semimicro-Kjeldahl method, which is an easier technique for determining the nitrogen content resulting from the hydrolysis. The hydrolysis degrees were found to be 19, 33, 45, 52, 63, and 79% for 20-, 40-, 60-, 90-, 120-, and 180-min-hydrolyzed poly(AAm) hydrogels, respectively.

At a low degree of hydrolysis, the expansion of the hydrolyzed poly(AAm) hydrogels in water was less than at higher degrees. However, at a high degree of hydrolysis, the strong electrostatic repulsions among carboxylate anions ($-\text{COO}^-$) could have resulted in an expanded network of the hydrogel, which might have had an extremely high water uptake. Because hydrogel networks have been reported to retain a memory of their formation history and molecular conformation,^{13–15} an expanded network structure with a special conformation would remain even after the hydrogel had been transferred into a basic medium after $-\text{CONH}_2$ had partially converted to $-\text{COO}^-$. The expanded network structure was confirmed by the porous structure observed by SEM after the swollen hydrogel samples were freeze-dried and fractured, as illustrated later.

ATR-FTIR analysis

The ATR-FTIR spectra of the unhydrolyzed and hydrolyzed poly(AAm) hydrogels, which were freeze-dried, are illustrated in Figure 1. For the hydrolyzed poly(AAm) hydrogels, a typical amide I band at 1674 cm^{-1} , which could be observed clearly in the unhydrolyzed poly(AAm) (hydrolysis time = 0), decreased dramatically, and a new band at 1725 cm^{-1} appeared, which could be assigned to carboxylate groups. The ATR-FTIR results showed that after the hydrolysis process of poly(AAm) with sodium hydroxide, the amide groups of poly(AAm) were partly converted to the carboxylate groups. At a high degree of hydrolysis, the number of carboxylate groups was much higher than that of the amide groups. Therefore, the band intensity of carboxylate

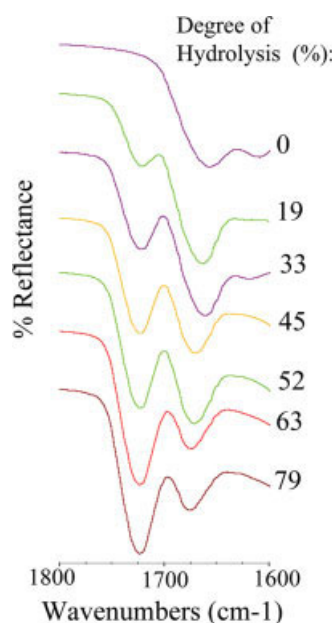


Figure 1 ATR-FTIR spectra of the hydrogels. The degrees of hydrolysis are indicated. [Color figure can be viewed in the online issue, which is available at www.interscience.wiley.com.]

groups at 1725 cm^{-1} was highest for the 79% hydrolyzed poly(AAm) hydrogel.

SEM observation of the internal structure of the hydrogels

Figure 2 shows SEM micrographs of the internal structures of unhydrolyzed [Fig. 2(A)] and hydrolyzed [Figs. 2(B–E)] poly(AAm) hydrogels, from

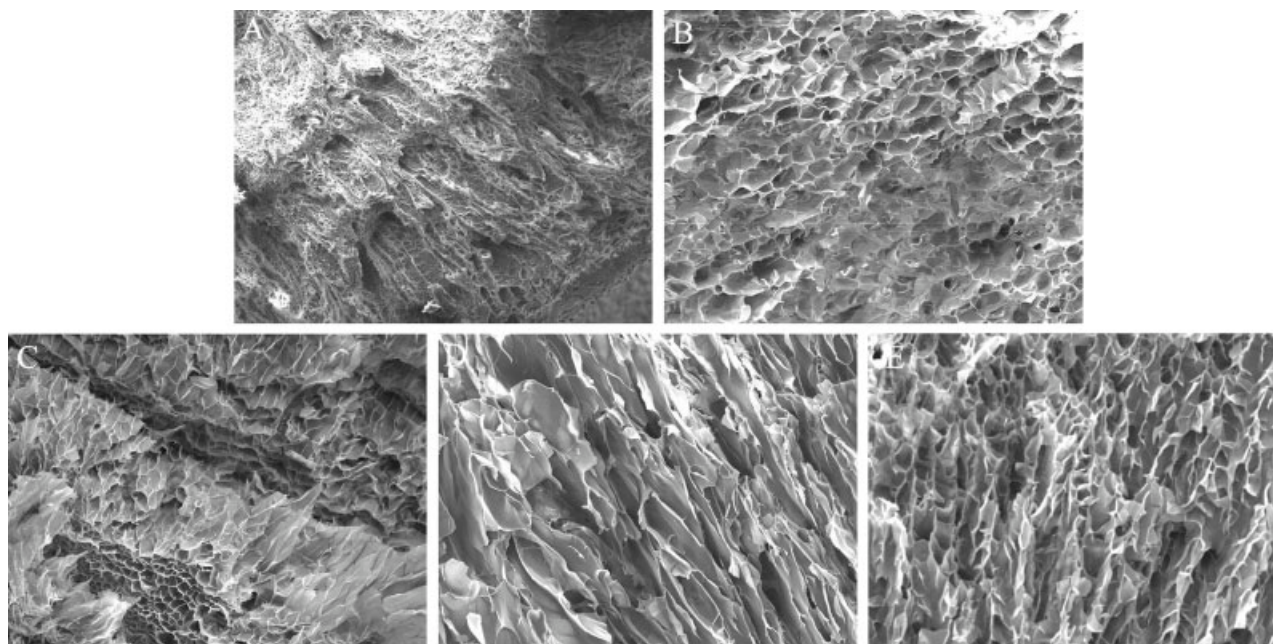


Figure 2 Cross-sectional SEM micrographs (magnification, $300\times$): (A) poly(AAm), (B) 19%, (C) 52%, (D) 63%, and (E) 79%.

which we can see that unhydrolyzed poly(AAm) had a less porous structure, whereas the hydrolyzed poly(AAm) hydrogels showed a more porous network structure. Moreover, their pore sizes increased with an increase in the charge density in the hydrolyzed hydrogels. These results support our previous analysis that a highly expanded network can be generated by electrostatic repulsions among carboxylate anions ($-\text{COO}^-$) during the hydrolysis process. An increase in the hydrolysis time leads to the formation of a more porous structure. When the pH is below the hydrogel's volume phase transition pH (VPT-pH), there is shrinking or deswelling due to hydrogel bond formation between carboxylic acid units of the hydrolyzed hydrogels, and thus the water molecules easily diffuse out as result of numerous small pores in the hydrogel network. Therefore, the response rate could be greatly enhanced by the incorporation of carboxylate ions into the poly(AAm) hydrogel during the deswelling process.

Equilibrium swelling/deswelling behavior of the hydrogels

It is well known that hydrogels made of crosslinked polyelectrolytes display swelling or shrinking in response to changes in the external pH because of the pendant ionizable groups on the molecule. In this work, a series of buffer solutions of different pHs were prepared to determine the pH sensitivity of hydrolyzed hydrogels. As shown in Figure 3, the hydrogels exhibited pH-sensitive swelling behavior. Under an acidic pH (≤ 4), most of the carboxylate

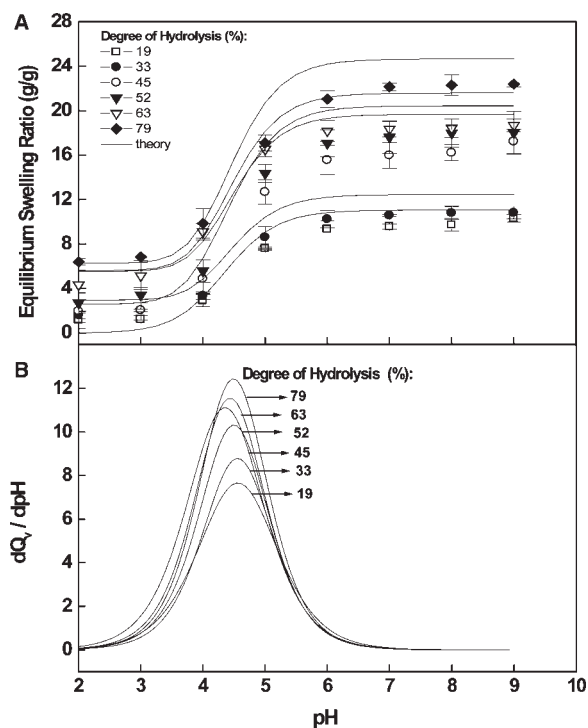


Figure 3 (A) Variation of the equilibrium swelling ratio of hydrolyzed poly(AAm) hydrogels with the pH. The experimental data are shown as symbols. The solid curves were calculated with the swelling theory.¹⁶ (B) Data for the hydrogels in part A are plotted in the differential form of dQ_v/dpH versus pH.

anions were protonated, so the main anion–anion repulsive forces were eliminated. In addition, a screening effect of the counter ions, that is, Cl^- , also shielded the charge of ammonium cations ($-NH_3^+$) and prevented efficient repulsion. In this case, the swelling ratio of the hydrogels decreased. In the pH range of 4.0–6.0, the swelling ratio of the hydrogels drastically increased with increasing pH as a result of electrostatic repulsion. On the other hand, by the presentation of the equilibrium swelling data in a differential form, that is, dQ_v/dpH versus pH, in Figure 3(B), the VPT-pH of the hydrogels can be located more easily. The VPT-pH value for each hydrogel from the maximum of the curves was found to be 4.46 ± 0.05 , regardless of the degree of hydrolysis. This value is also very close to the pK_a value of acrylic acid.¹⁷ (Upon hydrolysis, the $-CONH_2$ groups were converted to the $-COOH$ groups.) Above the VPT-pH value ($pH > 5$), an electrostatic repulsive force operating between the charged carboxyl groups increased the hydration of the hydrogels, causing swelling. On the contrary, the hydration of the hydrogels decreased below the VPT-pH value because the electrostatic repulsive force vanished between the uncharged carboxyl groups. In addition, the pH sensitivity of the hydrogels was proportional to the charge density, that is,

the degree of hydrolysis. An increase in the charge density in the hydrogels produced an equilibrium swelling ratio, which increased dramatically at all pH values, especially for the 19 and 33% hydrolyzed poly(AAm), for which the number of ionic units was relatively high. Also notable is the fact that an increase in the charge density of the hydrolyzed hydrogel by only a minute amount [i.e., 33% hydrolyzed poly(AAm)] radically changed the swelling behavior. This is due to the fact that as the degree of hydrolysis increased, the charges on the polymeric chains also increased. As a result, this led to the expansion of the hydrogels because of the high electrostatic repulsion, so the swelling capacities of the hydrogels increased.

Swelling and deswelling kinetics of the hydrogels

The swelling kinetics of the hydrogels, measured in deionized water at 22°C, are given in Figure 4. The data show that the swelling rate increased with increasing charge density in the hydrogels. The unhydrolyzed hydrogel absorbed about 0.83 water within 40 min or 3.40 within 400 min, whereas the hydrolyzed hydrogel (degree of hydrolysis = 79%) absorbed about 2.03 and 6.80, respectively, within the same frames.

The deswelling kinetics of the hydrolyzed hydrogels from the swollen state in the buffer solution of pH 9.0 to the shrunken state in the buffer solution of pH 2.0 were also measured and are given in Figure 5. The data illustrate that the 19% hydrolyzed hydrogel had the lowest swelling ratio, whereas the 79% hydrolyzed hydrogel had the highest swelling ratio. As a result, the hydrogels with greater charge density showed rapid swelling in deionized water and rapid shrinking in the buffer solution of pH 2.0. In deionized water, the hydrolyzed hydrogels were negatively charged polyelectrolytes because the pH

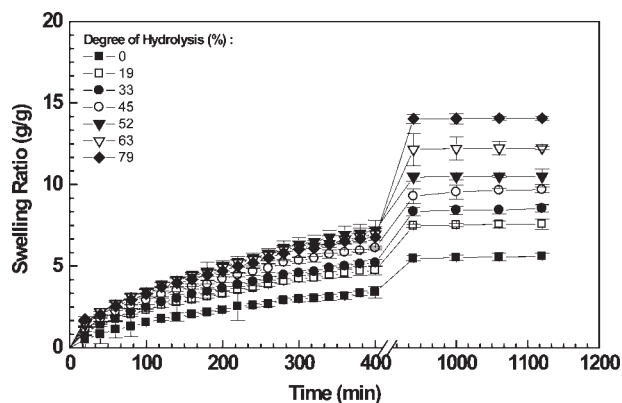


Figure 4 Swelling kinetics of unhydrolyzed and hydrolyzed poly(AAm) hydrogels in water at 22°C. The degrees of hydrolysis are shown as symbols.

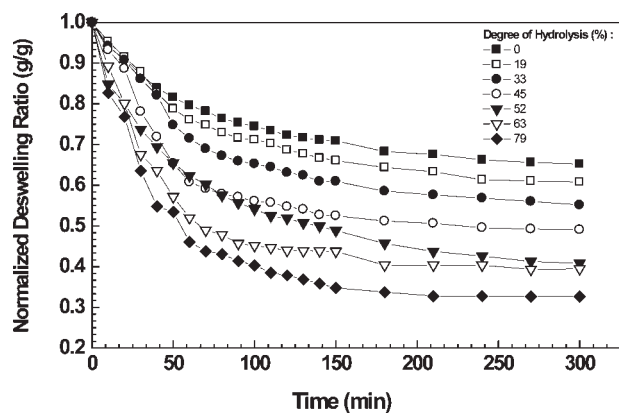


Figure 5 Deswelling kinetics of hydrolyzed poly(AAm) hydrogels in a pH 2 buffer solution at 22°C. The degrees of hydrolysis are shown as symbols.

value was remarkably higher than pK_a of $-\text{COOH}$, and the electrostatic repulsion between $-\text{COO}^-$ groups caused the hydrogels to swell. In the buffer solution of pH 2.0, the hydrolyzed hydrogels shrank and aggregated with one another because of the disappearance of electrostatic repulsion and the generation of hydrophobic interactions due to hydrogen-bond formation between $-\text{COOH}$ and $-\text{CONH}_2$ groups.

CONCLUSIONS

In this study, a series of poly(AAm) hydrogels at various charge densities were prepared by a post-modification method. The effects of the charge density on the properties of poly(AAm) hydrogels, particularly the VPT-pH behavior and response dynamics, were investigated. The swelling data in buffer solutions at various pHs showed that all the poly(AAm) hydrogels had almost the same VPT-pHs within the wide range of charge density levels

studied. The morphological data from SEM revealed that the interior network structure of the hydrogels became more porous with an increase in the level of the charge density. This more porous matrix provided numerous water channels for water diffusion and, therefore, an improved response rate to the external pH changes during the deswelling process. The data obtained in this study are useful for optimizing an ionic poly(AAm) hydrogel for particular biomedical applications via the level of the charge density.

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