Journal of Applied Polymer Science

Preparation and pH-Responsive Performance of Silane-Modified Poly(methylacrylic acid)

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ABSTRACT: The poly(methylacrylic acid) modified by silane [poly(methylacrylic acid-*co*-vinyl triethoxylsilane) (PMAA)] was prepared via free-radical polymerization with different mass ratios of methylacrylic acid to vinyl triethoxylsilane (VTES). The swelling performance of the prepared PMAA in different solutions with various pH values, salt species (NaCl and $CaCl_2$), and concentrations was investigated in detail. The results indicated that the introduction of silane boosted the stability of the obtained PMAA in aqueous solutions in the presence of an increased quantity of VTES additive. Meanwhile, the different swelling ratios of PMAA in various pH solutions showed a high pH responsivity. In addition, we found that when the PMAA underwent a number of swelling–deswelling cycles, it demonstrated the good reversibility properties when the pH value of the swelling medium was changed from 9.0 to 1.4. Moreover, the swelling mechanism of PMAA in different solutions with different pH values was investigated. © 2014 Wiley Periodicals, Inc. J. Appl. Polym. Sci. **2014**, *131*, 40403.

KEYWORDS: functionalization of polymers; properties and characterization; stimuli-sensitive polymers; swelling

Received 4 November 2013; accepted 5 January 2014
DOI: 10.1002/app.40403

INTRODUCTION

pH-responsive polymers, which are a type of so-called stimuli-sensitive or smart polymers, can undergo large volume and morphological changes, depending on the pH values in the surrounding medium and, therefore, have attracted much attention for their enormous potential applications in drug delivery because of their good sensitivity in physiological and biological environments.[1,2] In past decades, much work has been carried out on the environmentally sensitive performance of their controllable volume in response to small variations in the solution conditions, such as in the pH value,[3] ionic strength,[4] and solvent composition.[5] In contrast, poly(methylacrylic acid) (PMA), a typical kind of pH-sensitive polymer,[6,7] can be ionized at certain pH values because of the presence of dissociable acidic groups (—COOH), which usually swell as the pH level increases above the acid dissociation constant (the pK_a of —COOH is about 4.25).[8] Bowersock et al.[9] reported that pH-responsive PMA could be used to orally administer drugs to ruminants. Meanwhile, the ibuprofen loading and release behaviors from pH-sensitive PMA under different pH values were also investigated,[10] and *in vitro* tests showed that the accumulated amount of ibuprofen release was only 26.5% in simulated gastric fluid (pH = 1.2), whereas it was up to 61.9% in simulated intestinal fluid (pH = 7.5). Shen et al.[11] prepared a series of pH-responsive poly(acrylamide-*co*-acrylic acid)s, and the results demonstrate that their effects of the chemical composition on the hydrodynamic diameters, morphology, swelling ratios (SR), pH-responsive behavior, and thermal properties of the obtained polymers were considerable. More recently, Moinuddin et al.[12] synthesized poly(acrylamide-*co*-acrylic acid) loaded with antihypertensive drugs and found that the release behavior at pH 2.0 was much slower than that in a buffer solution at pH 7.4. In addition, Murali Murali et al.[13] and Bajpai[14] discussed the influence of crosslinkers and initiators on the swelling behavior of poly(acrylamide-*co*-maleic acid) and the effects of the pH value, ionic strength, and nature of the counterions on the equilibrium water uptake of the synthesized polymers. However, the poor drug loading of the pH-responsive polymers greatly limited their applications for drug-delivery systems.[15]

Since the discovery of the mesoporous M41s family[16] and the first subsequent report on sustained/controlled delivery systems with MCM-41 as a carrier,[17] the emergence of mesoporous silica could effectively solve the previous problems because of their nontoxic nature, high surface area, large pore volume, tunable pore size, and chemically modifiable surfaces.[18–27] Although on the other hand, the delivery system of the prepared drug-loaded mesoporous matrix did not show pH sensitivity or controlled release performance.

To overcome the problems mentioned previously, many researchers[28–31] have combined pH-sensitive polymers and

mesoporous silicas together to prepare pH-sensitive drug-delivery systems, which not only have a high drug-loading efficiency but can also achieve controlled drug-release capacity in different solutions with various pH values. Song et al.[32] reported that amine-functionalized mesoporous SBA-15 silica loaded with bovine serum albumin was successfully encapsulated with a thin layer coating of poly(acrylic acid), and Cao et al.[33] synthesized MCM-41/poly(acrylic acid) via the *in situ* polymerization of MCM-41 with acrylic acid. Nevertheless, the pH-controlled drug-release properties still showed poor performance because of the weak interaction between the polymer and the mesoporous silicas.

The aim of this study was to obtain a controlled drug-delivery system having both a high drug-loading capacity and a high pH sensitivity. For this purpose, silane-containing double bonds were introduced to modify the pH-responsive PMA. In this case, the silane was not only crosslinked with the methylacrylic acid (MAA) through the free-radical polymerization of double bonds existing in MAA but was also bonded to the surface —OH groups of the mesoporous silicas to form Si—O—Si bonds by means of the hydrolysis of silane. Although a large amount of research on pH-responsive PMA-based polymers has been published in the reported literature, studies regarding the introduction of a silane coupling agent to modify the frameworks of PMA and systematic studies on the monomer ratio, pH values, concentration of the solution, and types of salt solution have been fewer. In this study, poly(methylacrylic acid-*co*-vinyl triethoxylsilane)s (PMAAs) with different monomer mass ratios of MAA and vinyl triethoxylsilane were prepared through the free-radical polymerization of MAA and vinyl triethoxylsilane, whereas the swelling performances of the resulting PMAA, including the chemical composition, pH values, concentration, and species of salt solution were investigated in detail by means of various characterizations, such as Fourier transform infrared (FTIR) spectroscopy and thermogravimetry (TG) measurements.

EXPERIMENTAL

Materials

α-MAA (99%) was purchased from Tianjin Fu Chen Chemical Reagent Factory of China and was distilled under reduced pressure before use. Vinyl triethoxylsilane (VTES, 97%) was obtained from Alfa Aesar. The initiator, 2,2′-azobisisobutyronitrile, was supplied by Sinopharm Chemical Reagent Co., Ltd. (China) and was used after recrystallization. Absolute alcohol, *n*-hexane, hydrochloric acid, ammonia, sodium chloride, and calcium chloride were provided by Beijing Chemical Works (China). Deionized water was used throughout all of the experiments. All of the reagents used were analytical grade.

PMAA Synthesis

The PMAA was synthesized by the free-radical polymerization of MAA and VTES. Typically, certain quantities of MAA and VTES were mixed with 160 mL of absolute ethanol at room temperature. After deoxygenation by bubbling with N_2 for some time, 100 mg of 2,2′-azobisisobutyronitrile was added to the mixed solution during stirring. The solution was then heated to 70°C and kept for 24 h under an N_2 atmosphere to be polymerized. The PMAA solid was precipitated through *n*-hexane extraction. To remove the residual monomer, the dried PMAA solid was redissolved in absolute ethanol. The previous extraction–dissolution process was repeated until the pure PMAA solid was obtained. These samples were denoted as PMAA-*n*, where *n* is the mass percentage of VTES to MAA.

Characterization

The chemical structure of the synthesized polymers was investigated with FTIR spectroscopy, which was recorded over the range of 400–4000 cm^{-1} by the KBr pellet method with an FTIR spectrophotometer (Tensor-27, Bruker). The TG measurements were carried out on a PerkinElmer Pyris1 TG instrument from room temperature to 800°C at a heating rate of 10 K/min under the N_2 atmosphere with a flow rate of 20 mL/min. A sample with a mass of around 3 mg was heated in a standard platinum sample pan. The element analysis of C, H, and N was performed on CHNS/O EA3000 elemental analyzer. The Si content analyses were performed on a PerkinElmer Optima 2000DV Inductively Coupled Plasma (ICP) spectrometer.

Swelling Test

A completely dried disc-shaped PMAA-*n* was weighed and then immersed into an excess of swelling media with different pH values. At various time intervals, the polymers were removed from the solution, wiped superficially with filter paper, weighed, and then placed back into the same bath. The mass measurements were continued until a constant weight (equilibrium swelling) was attained for each sample. The results were calculated according to the following equation:

$$SR = (M_s - M_d)/M_d \quad (1)$$

where M_s is the mass in the swollen state and M_d is the mass in the totally dried state.[34]

To study the pH sensitivity of PMAA-*n*, HCl, deionized water, and ammonia solutions with defined pHs of 1.4, 5.0, and 9.0, respectively, were used. To evaluate the salt effect on the swelling of PMAA-*n*, different salts (NaCl and $CaCl_2$) with various ionic concentrations dissolved in HCl, deionized water, and ammonia solutions were used.

Swelling–Deswelling Test

The solvent replacement method was used for this purpose. The initially dried polymers were placed in an ammonia solution at pH 9.0 and allowed to attain equilibrium swelling during which the volume of PMAA-*n* was increased quickly. Then, the samples were withdrawn and placed in hydrochloric acid at pH 1.4, and a considerable decrease in swelling was observed until a constant weight was achieved. The deswollen sample was again kept in ammonia at pH 9.0 to attain equilibrium swelling and operated repeatedly. This swelling–deswelling process was repeated a number of times. This demonstrated that the volume of the polymer PMAA-*n* was reversible, whereas the pH values were changed constantly. The results were calculated according to the following equation:

$$R = M_t/M_{eq} \quad (2)$$

where R is the deswelling ratio, M_t is the mass in the shrink state, and M_{eq} is mass in the equilibrium swelling state.

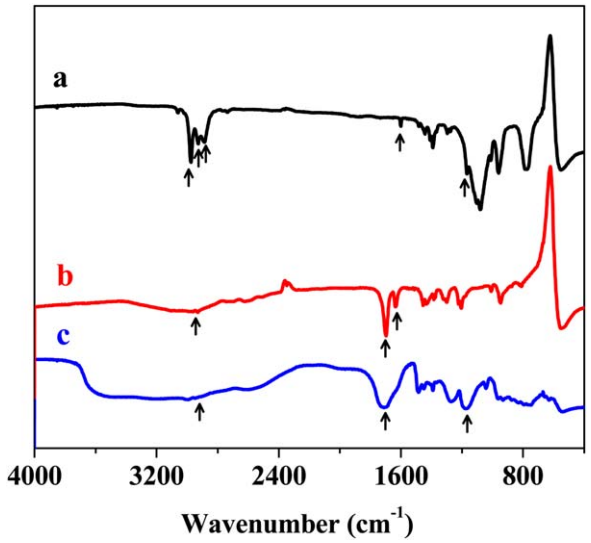

Figure 1. FTIR spectra of (a) VTES, (b) MAA, and (c) PMAA-9. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

RESULTS AND DISCUSSION

Synthesis and Composition of the PMAA

The FTIR spectra of VTES, MAA, and PMAA-9 are presented in Figure 1. As shown, peaks around 3000, 1390, and 770 cm^{-1}, corresponding to the stretching vibrations of C—H,[35] the deformation vibrations of —CH_3, and the rocking vibrations of $(CH_2)_n$,[36] respectively, were observed among the three samples. Additionally, Figure 2(b,c) shows the broad peaks in the MAA and PMAA samples in the ranges 3050–3500 and 1707 cm^{-1}, which were attributed to the stretching vibrations of —OH and C═O in —COOH, respectively. The adsorption peaks at 1166, 1288, and 1450 cm^{-1} in the monomer VTES [Figure 1(a)] and at 1168, 1278, and 1492 cm^{-1} in the polymer PMAA-9 [Figure 1(c)] were attributed to the stretching vibrations of Si—O—C, the symmetric distortion vibrations of Si—C bonds and the asymmetric distortion vibrations of Si—C bonds, respectively.[11]

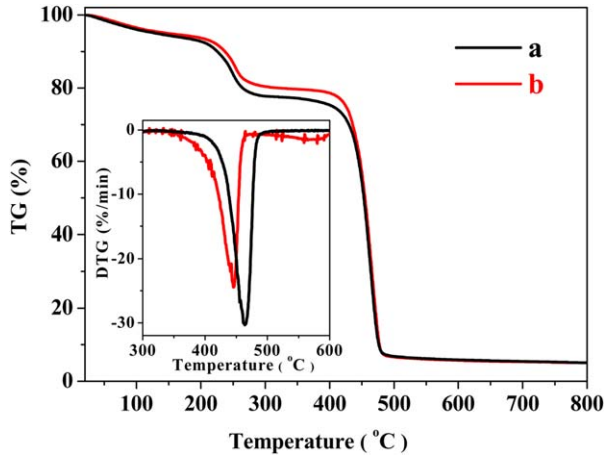

Figure 2. TG curves of (a) PMAA-9 and (b) PMAA-0 and their corresponding DTG profiles (insert). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

Table I. Composition of the Silane-Modified PMA

Sample	C (wt %)[a]	H (wt %)[a]	O (wt %)[c]	Si (wt %)[b]
PMAA-90	52.13	7.356	28.334	12.18
PMAA-18	53.12	7.449	34.401	5.03
PMAA-9	53.16	7.576	37.554	1.71
PMAA-0	53.05	7.558	39.392	0

[a] The results were obtained from element analysis.
[b] The data was from the characterization of ICP-AES.
[c] The content was calculated as 100-C%-H%-Si%.

However, the peaks at 1608 cm^{-1} in the VTES spectrum [Figure 1(a)] and at 1630 cm^{-1} in MAA spectrum [Figure 1(b)] corresponded to the stretching vibration of C═C, which were absent in PMAA-9 spectrum [Figure 1(c)]. These observations clearly indicated that PMAA was synthesized successfully by the copolymerization of MAA (containing C═C, —COOH and —CH_3) and VTES (containing C═C, Si—C and Si—O—C).

Meanwhile, the silane-modified PMAA was quantified from TG analysis, as shown in Figure 2. Apparently, the TG results showed that the weight loss percentages of PMAA-0 and PMAA-9 were almost the same (nearly 95%). In detail, the weight loss of about 10 wt % below 200°C was ascribed to the evaporation of physically absorbed water or residual solvent in both of the polymers. Afterward, two more mass loss procedures in the temperature range 200–500°C occurred. The obvious weight loss around 15 wt % was attributed to the degradation of the oligomer[37] and silicane[38] from 200 to 300°C, and subsequently, a remarkable weight loss of around 70% at a higher temperature of 350–500°C could be assigned to the decomposition of the carboxylic acid[39] existing in the polymer. However, PMAA-9 degraded later than PMAA-0 between 350 and 500°C, as shown in Figure 2. The maximum temperature of the second derivative of the weight loss of PMAA-9 exceeded that of PMAA-0, and this revealed that the silane coupling agent was beneficial for the enhancement of the thermal stability of PMAA and then retarded the pyrolysis of PMAA-9.[40] In addition, as depicted in the differential thermogravimetry (DTG) profiles (insert), the thermal decomposition temperature increased from 480°C for PMAA-0 to 500°C for PMAA-9. This implied that the thermal stability of PMAA-9 was improved by the introduction of the silane coupling agent.

The elemental analysis of C, H, N, and ICP were used to characterize the exact composition of these copolymers. The content of each element is presented in Table I. The content of Si incorporated into the polymers varied in the range 0–12.18 wt % on the basis of the results of ICP. With increasing VTES in the initial mixture, the copolymerization of Si in the final products increased as expected.

Effect of the pH Values on the Swelling Capacity

The swelling performance is one of the fundamental criteria for characterization and evaluation of the polymer. In essence, a pH-sensitive polymer swells or shrinks dynamically depending on the pH value in the surrounding medium. To determine

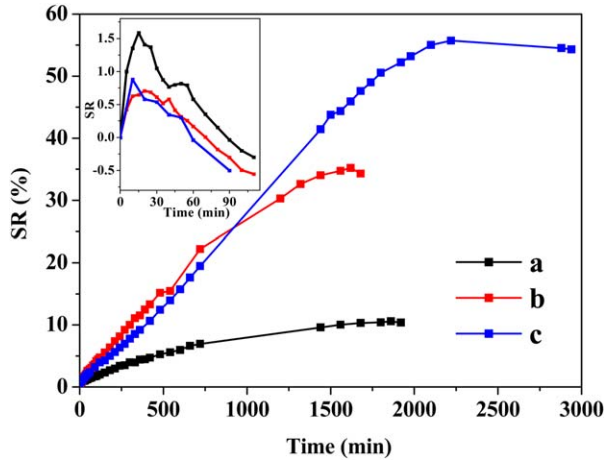

Figure 3. SRs of PMAA-9 and PMAA-0 (insert) in different solutions with different pH values: (a) 1.4, (b) 5.0, and (c) 9.0. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

whether the PMAA-*n* polymers exhibited pH sensitivity, variations in the water-absorption capacity in different solutions with diverse pH values were studied and are presented in Figure 3. As shown, the SR of PMAA-9 modified by silane increased with time until equilibrium was achieved. As a comparison, Figure 3 (insert) shows that the SR of PMAA-0 increased first and then decreased until it disappeared because of its dissolution over a long time (>180 min at pH 1.4, 120 min at pH 5.0, and 90 min at pH 9.0). Therefore, it was evident that the silane was useful for boosting the stability of the synthesized PMAA in aqueous solution. Meanwhile, the SRs of PMAA-0 and PMAA-9 increased simultaneously with increasing pH value of the solution.

Moreover, as shown in Figure 3(a), in case of the pH value of 1.4, both of PMAA-0 and PMAA-9 showed the lowest SRs in comparison with those in water or in the aqueous medium of ammonia. When the pH value of the solution was around 5.0 (>4.7), as shown in Figure 4(b), the SR and equilibrium value of both of PMAA-0 and PMAA-9 increased to 0.70 for PMAA-0 and 35.19 for PMAA-9. When the pH was further increased up to 9.0 [Figure 3(c)], the equilibrium SRs reached maximum values of up to 0.88 for PMAA-0 and 55.71 for PMAA-9, respectively.

In general, the swelling mechanism of polymers containing pH-responsive —COOH groups is governed by the internal electrostatic repulsion and the hydrogen-bonding interaction within the polymer networks.[41–43] When the pH is less than the pK_a, the —COOH groups inside the polymer are in an un-ionized or slightly ionized state; resulting in a relatively weakened internal electrostatic repulsion and minor swelling of the polymer. As the pH value increases and approaches the pK_a, the —COOH groups inside the polymer start to be ionized, and leading to a large SR. With further increases in the pH, the fully charged polymers can easily cause a high water absorbability and can even swell the polymers.

As reported previously,[44] the pK_a of acrylic acid is about 4.7; therefore, at pH values of less than 4, the —COOH groups of these polymers were not ionized, and they presented almost negligible internal electrostatic repulsion but prominent hydrogen-bonding interactions. This resulted in the lowest SR and equilibrium value at pH 1.4. On the contrary, at pH values greater than 4.7, the deprotonation of the —COOH groups in the PMAA structures produced —COO^- ions.[29] This contributed to the increasing charge density on the polymer chains; and led to the weakening or even breaking down of hydrogen-bonding interactions on one side as well as an enhancement of the internal electrostatic repulsion inside the polymer networks on the other side.[45,46] Therefore, along with the increasing pH, the polymer expansion could have been caused by the deprotonation of —COO^- ions. Therefore, the SRs reached to relatively larger values accordingly. Similar results have been proven in some studies, but they have only been about temperature-responsive polymers.[47]

In addition, Figure 4 presents the influences of the used additives of VTES on the swelling behaviors of the synthesized polymer. As illustrated, the equilibrium value of the SRs decreased with increasing amount of the additive VTES from 0.88 for PMAA-0 to 11.30 for PMAA-90, to 25.74 for PMAA-18, and to 55.71 for PMAA-9. This was attributed to the increasing electrical charge on the polymer surface, the strengthening of the electrostatic repulsive forces, and the expansion of the polymers.[48] Therefore, the improvement in the equilibrium swelling capacity with increasing pH value of the external solution arose from the ionization of the —COOH groups.

The swelling mechanism of PMAA in solutions with different pH values are shown in Figure 5. Under very high acidic conditions (pH ≤ 4.0), the —COOH groups in the series of PMAA were converted to a protonated acid. The hydrogen either between the —COOH groups or the polymer chains limited the stretching of the polymers. This resulted in a declining hydrophilicity of the polymer and led to very weak water-absorption performance. When the pH value exceeded 5.0, some —COOH groups were ionized, and that brought about their electrostatic repulsion and caused an increase in the ion osmotic pressure and, therefore, resulted in an enhancement of the swelling capacity.[49] These factors were responsible for the higher ratio of swelling in the medium of pH 5. When the pH reached 9.0, all of the —COOH groups were converted to the salt form, and the

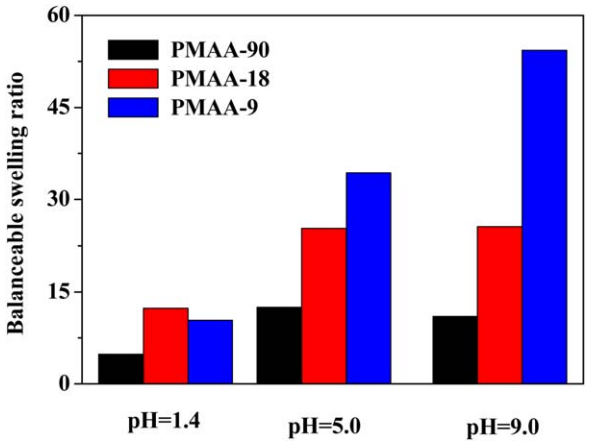

Figure 4. SRs of a series of PMAA-*n* with different pH values. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

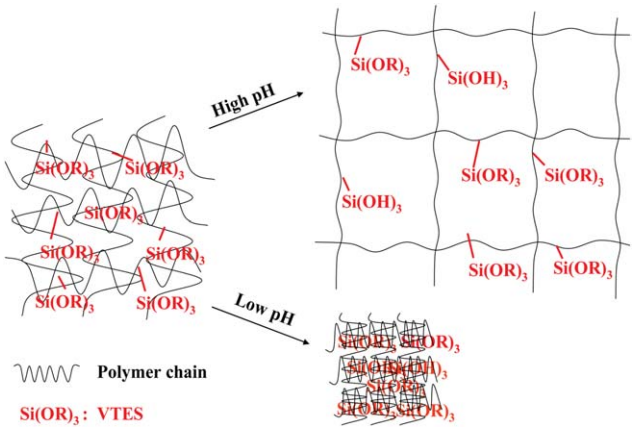

Figure 5. Swelling illustration of silane-modified PMAA in solutions with different pH values. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

maximum swelling capacity was obtained, which accounted for similar swelling behaviors at a pH of 5.0.

Salt Effect on the Swelling Behavior

To further understand the swelling performance of the obtained PMAA, the effects of different concentrations (0, 0.05, 0.10 and 0.20 mol/L) of NaCl aqueous solution and $CaCl_2$ aqueous solution at different pH values on the swelling behavior of PMAA-9 were investigated, and the results are shown in Figure 6. Overall, it was observed that an increase in the concentration of Na^+ and Ca^{2+} ions in the swelling medium yielded a significant decrease in the equilibrium water uptake of PMAA-9. This was mainly due to the decrease in the repulsion force of the $-COO^-$ groups in the presence of cationic media (pH 5.0).[50] It was particularly noteworthy that a balance of the repulsion forces of $-COO^-$ groups existing in the polymer structures mainly originated from the interior of the polymer network and the external immersion medium.[51] Obviously, the repulsion force of the $-COO^-$ groups gradually decreased with increasing cationic concentration in the pH 5.0 medium (>4.7). This led to the occurrence of a shrinkage in the volume of PMAA-9.

On the other hand, according to Figure 6, the decreased SR was also strongly dependent on the type of salt added to the swelling medium. Comparably, it was clear that in the same concentrations of salt solution, the SR decreased with increasing cationic charge from Na^+ to Ca^{2+}. This was consistent with previous studies,[52,53] where the SR of a polymer decreased as the ionic strength increased. Siegel and Firestone[4] reported that an increase in the salt concentration of a swelling solution caused ionic crosslinking and, thereby, decreased the swelling capacity of the polymer. With an increase in charge, the ionic strength of the swelling medium and the ratio of ionic crosslinking increased; this led to difficulty in the penetration of ions into the polymer networks[54] and, therefore, decreased the swelling capacity.[55] Particularly, the enhanced interaction between Ca^{2+} and $-COO^-$ resulted in a comparable increase in the crosslinking density and a decrease in the SR of polymers in $CaCl_2$ solutions.[51,56] Another possible reason was related to their cationic radius or the hydration forces in the aqueous solution. As demonstrated by Mohammad and Hossein,[57] the cationic radius growth was promoted by hydration forces, as a result of which the small cation was surrounded by a large number of water molecules. In other words, in fact, with the lower cationic charge density, the binding ability to the —COOH group was weaker, and this resulted in a large hydration radius of the cationic ions tending to enter the network and then bonding easily to the —COOH groups.

In addition, as shown in Figure 6, the SRs of PMAA-9 in aqueous solution were larger than those in salt solutions at the same pH value (ca. 9.0). This might be due to the unequal distribution of ions in the swelling medium between the concentration of the counterions in the polymer phase and solution phase.[53] Apparently, the repulsion forces between the $-COO^-$ groups in the external solution involving Na^+ or Ca^{2+} were weaker than that in aqueous solutions containing H^+. This caused a decrease in the equilibrium water uptake of the polymers.[51] However, the swelling profile of PMAA-9 in $CaCl_2$ solution, which presented a decreased equilibrium swelling with increasing pH value, was different from that in the NaCl aqueous medium. These results were reasonable because of the microsolubility of $CaCl_2$ in an alkaline solution with fairly high concentrations and led to lower equilibrium swelling in an ammonia solution with a pH of 9.0.

Swelling Reversibility Studies

The swelling and deswelling properties are two aspects of the volume phase transition of pH-sensitive polymers that reflect their intelligent characteristics. Figure 7 illustrates the swelling reversibility of the silane-modified polymers between the solutions with pH values of 1.4 and 9.0.

Obviously, all of the series of PMAA presented favorable reversible swelling performances with quick swelling, shrinking, and reswelling properties in the swelling medium with alternating conditions of the acid (pH = 1.4) and alkali (pH = 9.0). This was accompanied by reductions in the SRs of PMAA-90, PMAA-18, and PMAA-9 to 68, 39, and 28%, respectively. Meanwhile, as shown in Figure 7, the time for polymer swelling in an

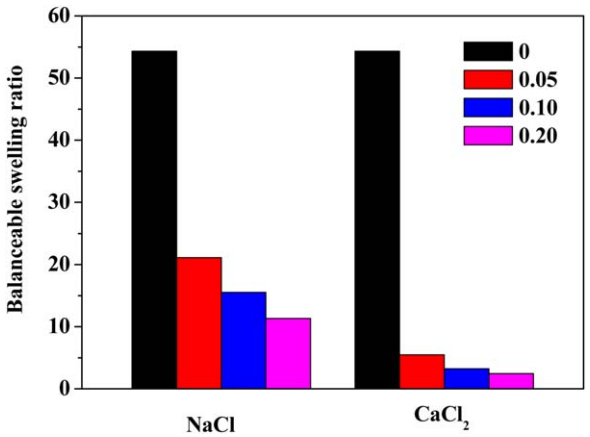

Figure 6. SR of PMAA-9 with different concentrations of salt solution (pH 9.0). [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

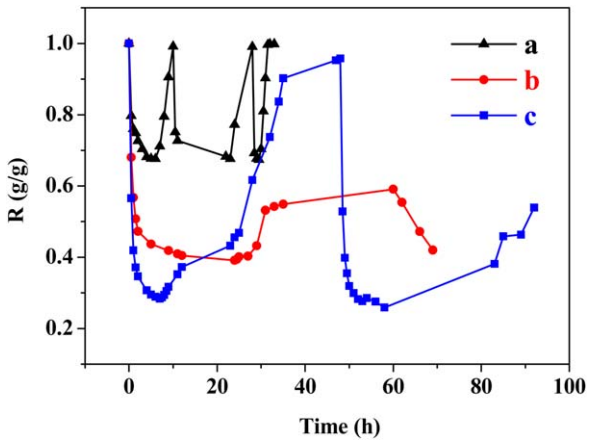

Figure 7. pH sensitivity and reversible SR (pH 9.0) and *R* (pH 1.4) values of (a) PMAA-90, (b) PMAA-18, and (c) PMAA-9. [Color figure can be viewed in the online issue, which is available at wileyonlinelibrary.com.]

alkaline solution was longer than that for deswelling in an acid medium. On the other hand, the swelling rate of the used PMAA was slower with increasing amounts of the additive VTES in the silane-modified polymers in the following order: PMAA-9 < PMAA-18 < PMAA-90. These results could be acceptable because an increasing amount of silane was anchored to the polymer frameworks through the —OH groups with an increasing amount of VTES. This restricted the free chain mobility of the used PMAA.[58] Therefore, the diffusion of the swelling medium into the polymeric matrix was difficult. This finally led to the slow pH-response performances and low SRs after more than three recycling cycles.

CONCLUSIONS

In this study, a silane-modified PMAA was synthesized with the free-radical polymerization procedure. The swelling capacity of the obtained PMAA was elucidated in solutions with different pH values and in aqueous salt (NaCl and $CaCl_2$) solutions ranging in concentrations from 0.05 to 0.20*M*. The results show that the introduction of VTES into the prepared PMAA was beneficial for improving the stability of PMAA in aqueous solutions. However, the swelling ability of the prepared PMAA was significantly affected by the VTES additive, the external pH, the ionic strength, and the salt species. The equilibrium SRs exhibited higher values at pH values of 5.0 and 9.0 compared to those at pH 1.4 and showed a swelling sensitivity because of the ionization of the —COOH groups in the polymer networks. An increase in the ionic strength of the swelling medium from 0.05 to 0.20*M* resulted in a decrease in the SR. Moreover, for the same ionic concentration of alkaline salt solutions, the SRs of the synthesized polymers in the Ca^{2+} solution decreased strongly in comparison with that in the Na^{+} solution. In addition, the resulting PMAA also rapidly reached the equilibrium swelling and deswelling states when the pH changed from 9.0 to 1.4 back and forth. As a result, the swelling properties of the silane-modified PMAA with pH-dependent characteristics may open a potential field of applications for pH-sensitive drug-delivery systems.

ACKNOWLEDGMENTS

This project was supported by the National Natural Science Foundation of China (contract grant numbers 21076003 and 21276005), the National Basic Research Program of China (973 Program 2009CB930200), and the Funding Project for Academic Human Resources Development in Institutions of Higher Learning under the jurisdiction of the Beijing Municipality (contract grant numbers PHR 200907105, PHR 201107104, and 005000543111517).

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