Synthesis and Swelling Properties of 2-Hydroxyethyl Methacrylate-*co*-1-vinyl-3-(3-sulfopropyl)imidazolium Betaine Hydrogels

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Received 17 August 2000; accepted 5 November 2000

ABSTRACT: A series of 2-hydroxyethyl methacrylate/1-vinyl-3-(3-sulfopropyl)imidazolium betaine (HEMA/VSIB) copolymeric gels were prepared from various molar ratios of HEMA and the zwitterionic monomer VSIB. The influence of the amount of VSIB in copolymeric gels on their swelling behavior in water and various saline solutions at different temperatures and the drug-release behavior, compression strength, and crosslinking density were investigated. Experimental results indicated that the PHEMA hydrogel and the lower VSIB content (3%) in the HEMA/VSIB gel exhibited an overshooting phenomenon in their dynamic swelling behavior, and the overshooting ratio decreased with increase of the temperature. In the equilibrium water content, the value increased with increase of the VSIB content in HEMA/VSIB hydrogels. In the saline solution, the water content for these gels was not affected by the ion concentration when the salt concentration was lower than the minimum salt concentration (MSC) of poly(VSIB). When the salt concentration was higher than the MSC of poly(VSIB), the deswelling behavior of the copolymeric gel was more effectively suppressed as more VSIB was added to the copolymeric gels. However, the swelling behavior of gels in KI, KBr, $NaClO_4$, and $NaNO_3$ solutions at a higher concentration would cause an antipolyelectrolyte phenomenon. Besides, the anion effects were larger than were the cation effects in the presence of a common anion (Cl^-) with different cations and a common cation (K^+) with different anions for the hydrogel. In drug-release behavior, the addition of VSIB increased the drug-release ratio and the release rate. Finally, the addition of VSIB in the hydrogel improved the gel strength and crosslinking density of the gel.
 J Appl Polym Sci 81: 2888–2900, 2001

Key words: hydrogels; 2-hydroxyethyl methacrylate; 1-vinyl-3-(3-sulfopropyl)imidazolium betaine; swelling behavior

INTRODUCTION

Hydrogels are crosslinked, three-dimensional hydrophilic polymer networks, which swell but do not dissolve when brought into contact with water. There are some hydrogels which sometimes undergo a volume change in response to a change in the surrounding conditions such as temperature,[1–3] pH,[4–7] ion strength,[8] electric field,[9–11] light (ultraviolet[12] or visible[13]), and chemicals.[14–16] Therefore, they are extensively applied in biochemistry. The biocompatibility of hydrogels is attributed to their ability to simulate material tissues due to their high water content and their special surface properties. They have been

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Contract grant sponsor: Tatung University.

Journal of Applied Polymer Science, Vol. 81, 2888–2900 (2001)

investigated for applications ranging from solute separation[17,18] to controlled delivery of solutes.[19–22] The general name "sulfobetaine-based polymers" refers to a type of macromolecule in which a zwitterion or "inner salt" has been incorporated into the side chain. The solution behavior of some polyzwitterions[23–25] has the following general features for these materials in aqueous systems: (1) They are mostly insoluble in water[26] or display unusual phase behavior as a function of the concentration[27] and (2) the presence of salts enhances chain expansion (antipolyelectrolyte effect).

The dynamic swelling behavior of poly(2-hydroxyethyl methacrylate) (PHEMA) was reported by Peppas et al.[28–30] For example, Shieh and Peppas[28] reported on copolymers prepared from the copolymerization of HEMA with tetraethylene glycol dimethacrylate (TeEGDMA). The swelling dynamics of the P(HEMA-*co*-TeEGDMA) with 55 mol % HEMA exhibited a slight water uptake over the equilibrium value, a result similar to the one obtained by Franson and Peppas.[29,30] They described copolymers prepared from the copolymerization of HEMA with methyl methacrylate (MMA) or *N*-vinyl-2-pyrrolidone (NVP). The swelling dynamics of the poly(HEMA-*co*-NVP) gel exhibited a slight water uptake over the equilibrium value. This can be attributed to molecular relaxation. The water diffuses into the network before the chains of the network have enough time to relax (diffusion is faster than is relaxation), and the fractional uptake curve reaches a maximum, the overshoot value. When the chains do finally relax, water is forced out of the network and the water uptake eventually reaches its equilibrium value.

Hydrogels containing the zwitterionic monomer or the sulfobetaine monomer have been infrequently reported on in the literature.[31–34] Huglin and Rego[31–33] reported on copolymeric gels prepared from the copolymerization of HEMA and a zwitterionic monomer, *N,N*-dimethyl-*N*-methacryloyloxyethyl-*N*-(3-sulfopropyl)ammonium betaine (SPE), and described their swelling behavior in the presence of the salt potassium thiocyanate (KSCN). In addition, Baker et al.[34] reported on ampholytic hydrogels prepared from the copolymerization of acrylamide with zwitterionic monomers, *N*-(3-sulfopropyl)-*N*-methacrylamidopropyl-*N,N*-dimethylammonium betaine (SB1; AAm/SB1) or *N*-(3-sulfopropyl)-*N*-methacroyloxyethyl-*N,N*-dimethylammonium betaine (SB2; AAm/SB2), and a cationic monomer, [(methacrylamido)propyl]trimethylammonium chloride (MAPTAC), and an anionic monomer, sodium styrenesulfonate (SSS; AAm/MAPTAC/SSS). They investigated the swelling behavior of these three xerogels in water and in various concentrations (from 10^{-5} to 5*M*) of a sodium chloride aqueous solution. Their results showed that antipolyelectrolyte behavior was observed for the ampholytic hydrogels. The ampholytic hydrogel reswelled as the sodium chloride concentration increased to over 0.1*M*.

The synthesis and aqueous solution properties of a series of polysulfobetaines were studied previously in our laboratory.[35–45] We found that the solution properties of polysulfobetaines in aqueous salt solutions were related to the kind of salts used. Salamone et al.[46] reported on the aqueous salt solution behavior of poly[1-vinyl-3-(3-sulfopropyl)imidazolium betaine] [poly(VSIB)]. In our previous report,[47] we investigated the swelling behavior of NIPAAm-*co*-VSIB copolymeric hydrogels. Hence, a series of the HEMA/VSIB copolymeric gels were prepared with various molar ratios of HEMA to the zwitterionic monomer, VSIB. The effect of this sulfobetaine component on the swelling ratios of HEMA hydrogels, as well as the influence of the amount of VSIB in the copolymeric gels on the swelling behavior in water, various saline solutions, and temperature are reported in this article. In addition, the drug-release behavior and the compression strength of the gels were also investigated.

EXPERIMENTAL

Materials

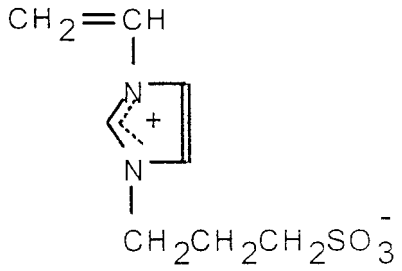
HEMA (TCI Co., Tokyo, Japan) was further purified by vacuum-distillation at 68°/5 mmHg. 1-Vinylimidazole (Fluka Chemical Co., Buchs, Switzerland), 1,3-propanesultone (TCI Co.), *N,N′*-methylene bisacrylamide (NMBA; SIGMA Chemical Co., St. Louis, MO) as a crosslinker, and *N,N,N′,N′*-tetramethylethylenediamine (TEMED; Fluka Chemical Co.) as an accelerator were used as received. Ammonium persulfate (APS; Wako Pure Chemical Co. Ltd., Osaka, Japan) as an initiator was further purified by recrystallization.

Synthesis of VSIB Monomer

The monomer VSIB was prepared according to the procedure of Salamone et al.[46] Yield: 94.3%; mp: 190°C. The structure is given below:

Table I Characterization of HEMA/VSIB Copolymeric Gels

Sample No.	Feed Composition (mol %)		Appearance of Gel Membrane	Equilibrium Water Content at 25°C (%)
	HEMA	VSIB		
V0	100.0	0.0	Transparent	37.43
V3	97.0	3.0	Transparent	38.65
V6	94.0	6.0	Transparent	39.80
V9	91.0	9.0	Transparent	41.20
V12	88.0	12.0	Transparent	42.66



Preparation of Hydrogels

Various ratios of HEMA, VSIB, and 3 mol % NMBA based on the total monomers were dissolved in 5 mL of deionized water and 5 mL of alcohol. To this solution, 1 wt % APS and 1 wt % TEMED as redox initiators were added, and the mixture was immediately injected into the space between two glass plates. The thickness of the gel membrane was adjusted with a silicone spacer between the two glass plates. Polymerization was carried out at room temperature (28°C) for 1 day. After the gelation was completed, the gel membrane was cut into disks and immersed in an excess amount of deionized water for 7 days to remove the residual unreacted monomers. Swollen polymer gels were dried at room temperature for 2 days, and these samples were further dried in a vacuum oven for 1 day at 60°C. The thickness of the dried gel was about 1–1.5 mm and the diameter was about 4–5 mm.

Measurement of Water Content

The dried gels were immersed in a 10 mL of deionized water or various saline solutions with different concentrations at 25°C until swelling equilibrium was attained. The weight of the wet sample (W_w) was determined after removing the surface water by blotting with filter paper. The weight of the dry sample (W_d) was determined after drying the gel in a vacuum oven for 1 day. The water content and swelling ratio (Q) was then calculated using the following equations:

$$\text{Water content} = (W_w - W_d)/W_w \quad (1)$$

$$\text{Swelling ratio}(Q) = (W_w - W_d)/W_d \quad (2)$$

Dynamic Swelling

The dried gels were immersed in 10 mL of deionized water at different temperatures. Q was obtained by weighing the initial and swollen samples at various time intervals. The amount of water sorbed, Mt, was reported as a function of time, and the equilibrium sorption at infinitely long time was designated M_∞. The following equation can be used to calculate the characteristic constant, k, and exponent, n, for $Mt/M_\infty \leq 0.6$ (ref. 48):

$$\frac{Mt}{M_\infty} = kt^n \quad (3)$$

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

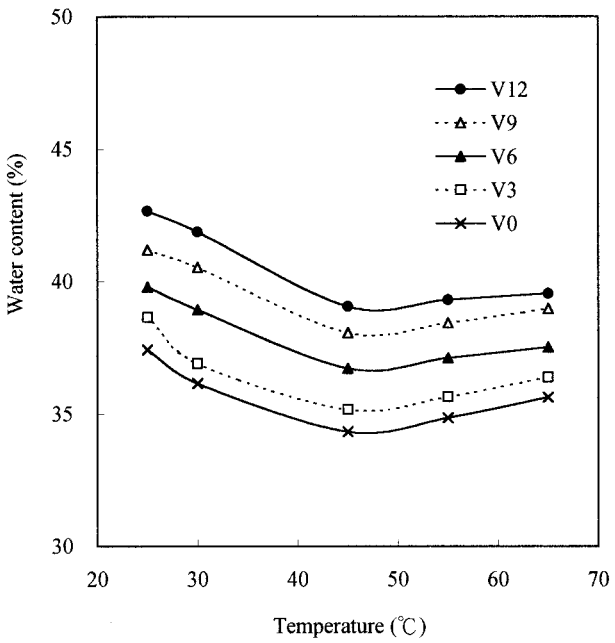


Figure 1 Equilibrium water contents as a function of temperature for HEMA/VSIB copolymeric gels.

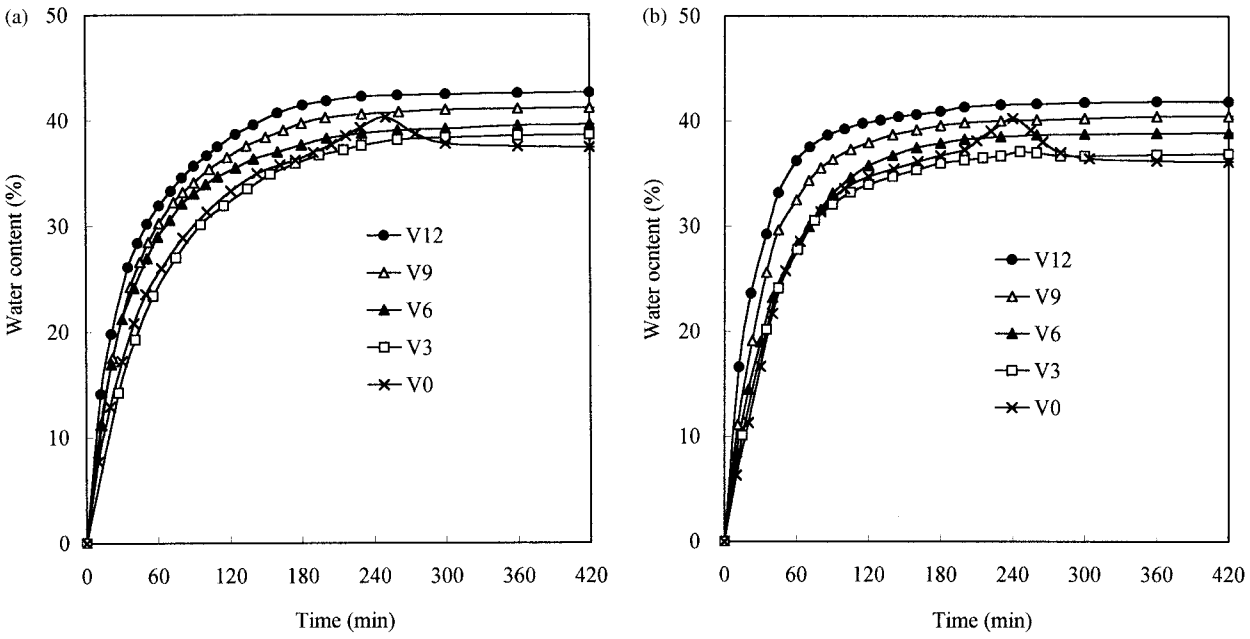


Figure 2 Water contents as a function of time for HEMA/VISIB gels in water at (a) 25°C, (b) 30°C, (c) 45°C, (d) 55°C, and (e) 65°C.

The other equation can be used to calculate the diffusion coefficient D for $Mt/M_\infty \leq 0.8$ (refs. 29 and 30):

$$\frac{M_t}{M_\infty} = \left(\frac{4}{\pi^{0.5}}\right) \times \left(\frac{Dt}{L^2}\right)^{0.5} \quad (4)$$

where t is the time, and L, the initial thickness of the dried sample.

Caffeine-release Experiment

The dry gels were equilibrated in 30 mg caffeine/10 mL of deionized water at 25°C for 1 day to load caffeine into the gels. The caffeine-release experiments were carried out by transferring previously incubated drug gels into 10 mL of deionized water at 37°C. The gels were repeatedly removed and transferred into 10 mL fresh deionized water at each fixed time interval. The amount of released caffeine was analyzed at 272 nm by an ultraviolet spectrophotometer (JASCO V-530).

Uniaxial Compression Experiment

Water-swollen gels produced from different compositions were tested with a universal tester (LLOYD LRX), and the crosshead speed was 1 mm/min. The following equation can be used to calculate the shear modulus of the gels[49,50]:

$$\tau = F/A_0 = G(\lambda - \lambda^{-2}) \quad (5)$$

where τ is the compression stress; F, the compression load; A_0, the undeformed cross-sectional area of the swollen gels; λ, the compression strain (L/L_0); and L_0, the undeformed sample length. At low strains, a plot of the shear stress versus $-(\lambda - \lambda^{-2})$ will yield a straight line whose slope is the shear modulus (G). The effective crosslinking density (ρ_x) can then be calculated from the shear modulus and swelling ratio (Q) as follows[49,50]:

$$\rho_x = GQ^{1/3}/RT \quad (6)$$

where R is the gas constant (8.48×10^4 g cm mol^{-1} K^{-1}), and T, the absolute temperature (298 K).

RESULTS AND DISCUSSION

Although the swelling behavior of HEMA hydrogels has been widely studied by many reseachers,[28–34] the series of HEMA/VSIB copolymeric hydrogels was found to be lacking in the literature. The effect of VSIB on the swelling behavior of the HEMA/VSIB copolymeric hydrogels is described here.

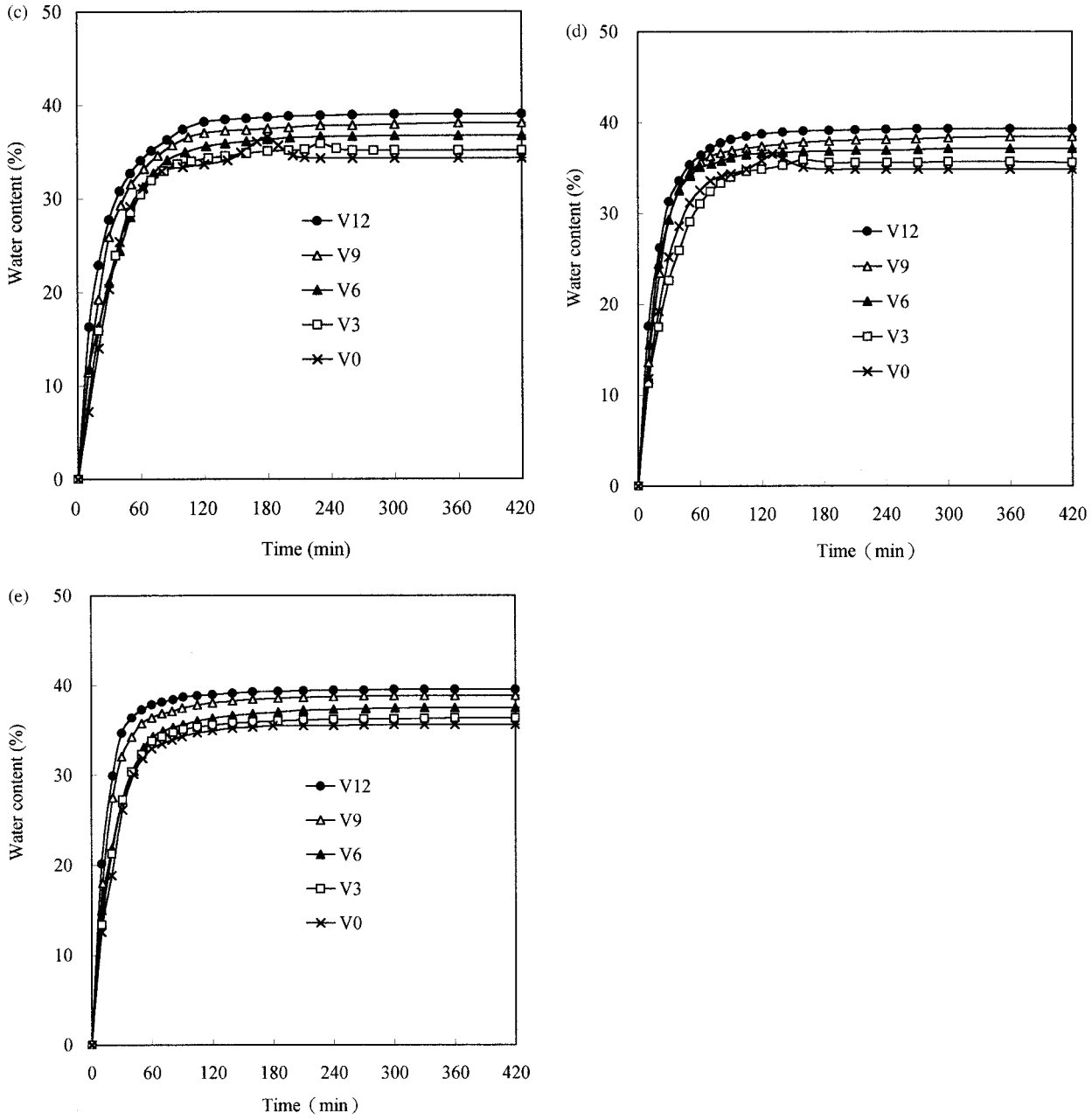


Figure 2 (*Continued from the previous page*)

Characterization of the HEMA/VSIB Copolymeric Gels

The characteristics, shown in Table I for the HEMA/VSIB copolymeric gels prepared in ethanol aqueous solution with various feed compositions, indicate that the appearances of the gels are transparent. In previous research,[45] the appearance of a PHEMA gel prepared in water was opaque. This phenomenon may be caused by phase separation during polymerization of PHEMA in water. The HEMA monomer is liquid at room temperature and has a solubility parameter (δ_m) between 8.0 and 12.0. However, the solubility parameter of water is 23.4, which causes phase separation between HEMA and water during the process of polymerization. For this article, we used alcohol, whose solubility parameter is 12.7, as a polymerization solvent, and successfully prepared a series of homogeneous gels in an alcohol aqueous solution. The equilibrium water contents of the HEMA/VSIB

copolymeric gels increased with increasing VSIB content in the hydrogels (also see Fig. 1). This is because VSIB is a hydrophilic monomer, and the more VSIB in the copolymeric gels, the greater the affinity of the gel.

Effect of Temperature on Water Content for HEMA/VSIB Gels

The effect of temperature on the equilibrium water content, for a series of the HEMA/VSIB gels, is shown in Figure 1. The results show that the sample V0, PHEMA, exhibits a minimum water content at 45°C. This behavior conforms to the result reported by Warren and Prins.[51] This phenomenon can be explained by the binding water caused by the hydrogen-bonding force between the water and the polymeric chain when the temperature is below 45°C. The hydrogen-bonding force decreases with an increase of the temperature. Then, the binding water turns to nonbinding water, free water that can be moved rapidly out of the polymeric networks, and the water content of sample V0 will decrease to the minimum value at 45°C. However, the entropy of water and the polymeric chain will be increased with increase in the temperature. When the temperature is above 45°C, the dispersion force of water molecules is greater than is the attraction force of water and the polymer chain. The free water, the nonbinding water, will be moved from the surrounding into the hydrogel. Hence, the water content of V0 will be reincreased when the temperature is above 45°C. The phenomenon was also observed in the present HEMA/VSIB gels.

Effect of VSIB Content on Water Content

The water contents, as a function of time for the HEMA/VSIB copolymeric gels in the deionized water at various temperatures, are shown in Figure 2(a–e). The results indicate that the equilibrium water contents increase with increasing VSIB content at various temperatures. The result is due to the hydrophilicity of the sulfonic group ($—SO_3^-$) in VSIB. Because VSIB is a hydrophilic monomer, the higher the VSIB content, the greater is the affinity of the hydrogels with water and the higher is the water content of the gels. This is similar to the result obtained from PNIPAAm/VSIB copolymeric gels.[47]

Effect of Temperature on Overshooting Phenomenon

Figure 2(a) also shows that the dynamic water content of the PHEMA gel (V0) exhibits a water uptake over the equilibrium value. This phenomenon is called "overshooting." The overshooting phenomenon disappears at higher VSIB content or at higher temperature (65°C; see Table II). Hence, the overshooting phenomenon may be affected by the temperature. Figure 3 shows the fractional water content, Mt/M_∞, of the PHEMA gels (V0) as a function of time at various temperatures. The results indicate that the overshooting ratios of PHEMA gels decrease with increasing the temperature, which is a result similar to that obtained by Shieh and Peppas.[28] This can be attributed to molecular chain relaxation. Water diffuses into the network before the chains of the molecule have enough time to relax (diffusion is faster than is relaxation), and the Mt/M_∞ curve reaches a maximum, the overshoot value. When

Table II Analysis of Equilibrium Water Contents and Overshooting Ratios for HEMA/VSIB Copolymeric Hydrogels at Various Temperatures

Sample No.	Temperature (°C)	Water Content (%)	Overshoot (%)	Time[a] (min)
V0	25	37.43	7.6	250
	30	36.15	11.6	240
	45	34.32	6.6	180
	55	34.85	4.8	130
	65	35.63	No[b]	—
V3	25	38.65	No	—
	30	36.91	1.1	240
	45	35.16	2.0	230
	55	35.64	0.8	160
	65	36.38	No	—
V6	25	39.80	No	—
	30	38.94	No	—
	45	36.72	No	—
	55	37.11	No	—
	65	37.52	No	—
V9	25	41.20	No	—
	30	40.54	No	—
	45	38.07	No	—
	55	38.43	No	—
	65	38.97	No	—
V12	25	42.66	No	—
	30	41.87	No	—
	45	39.06	No	—
	55	39.31	No	—
	65	39.55	No	—

[a] Time: the time occurred at maximum overshoot.
[b] No: nonobservable.

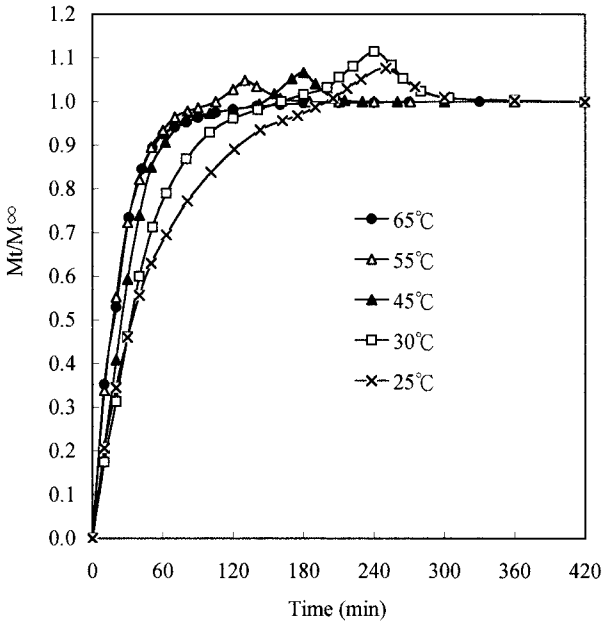


Figure 3 Water uptake of the PHEMA hydrogels in water as a function of time at various temperatures.

the chain does finally relax, the water is forced out of the network, and Q eventually reaches its equilibrium value. This overshooting value, the maximum overshooting time, and the equilibrium time decrease with increase in the temperature (results are shown in Tables II and III), because, with increase in the temperature, both the entropy of the polymeric chain will increase and the relaxation motion of the polymeric chain will be quickened. Thus, the equilibrium time of the polymeric chain shortens as the temperature increases. However, in previous research,[45] the overshooting ratio of PHEMA gel prepared in water was 77.5% (at 25°C) and was larger than that of the gel prepared in a water/alcohol solution. This difference may be caused by the phase separation and the loose structure of the PHEMA gel prepared in water which make the relaxation of the molecular chain slow down.

Figure 4 shows the Mt/M_∞ of the sample V3 copolymeric gel as a function of time at various temperatures. The overshooting phenomenon was not significant and disappeared at temperatures above 55°C. This result implied that the hydrophilic zwitterionic component, VSIB, in the HEMA gel could suppress its overshooting (also see Fig. 5). From the above results, the overshooting phenomenon for a hydrogel is controlled by the amount of the strong hydrophilic component and temperature, aside from the nature of the hydrogel itself.

Investigation of Water Diffusion in Xerogels

Alfrey et al.[52] distinguished three classes of diffusion, based on the rate of diffusion relative to the polymer relaxation rate: (1) Case I, or Fickian diffusion, in which the rate of diffusion is low relative to the relaxation rate, where $n \leq 0.5$; (2) Case II, or relaxation-balanced diffusion, in which the diffusion is very fast relative to the relaxation rate, where $n \geq 1.0$; and (3) non-Fickian, or anomalous, diffusion, which occurs when the diffusion and relaxation rates are comparable, where $n = 0.5$–1.0. The characteristic constant of the gel, k, and the characteristic exponent of the mode transport of the penetrant, n, are calculated through eq. (3). Then, the diffusion coefficient, D, is calculated through eq. (4).

Table III shows n, k, and D for a series of HEMA/VSIB copolymeric gels at various temperatures. The results shown in Table III indicate that the swelling exponents, n, for V0 at various temperatures are between 0.58 and 0.94. This evidence indicates that the swelling transport mechanism for PHEMA is non-Fickian transport nearing the Case II transport. Additionally, the swelling exponents, n, for the HEMA/VSIB copolymeric gels (V3–V12) at various temperatures are between 0.53 and 0.80. These results showed that all the swelling transport mechanisms for HEMA/VSIB copolymeric gels are described by non-Fickian transport nearing the Fickian transport. Hence, we can infer from the above results that the swelling transport mechanism will be transformed from non-Fickian transport to Fickian diffusion transport as the PHEMA gel contains a hydrophilic or water-soluble polymer, that is, the VSIB segment in the HEMA/VSIB copolymeric gel would affect the transport mode of the PHEMA gel. When more VSIB content is introduced into the copolymeric gels, the larger hydrophilic force of the copolymeric gels accelerates the relaxation rate. Hence, the transport mode of the HEMA/VSIB copolymeric gels approximate Case I, Fickian diffusion. In addition, the D value increased with increasing temperature, that is, the diffusion rate was faster and the equilibrium time was shorter at higher temperature.

Effect of Salt Concentration on the Water Content

The effect of the salt concentration on the water content for a series of the HEMA/VSIB copolymeric gels is discussed in this paragraph. Figure 6 shows the water contents as a function of the concentration in different monovalent cation salt

Table III Analysis of Transport Mechanism of Water Transport in HEMA/VSIB Copolymeric Hydrogels at Various Temperatures

Sample No.	Temperature (°C)	n[a]	k[b]	D[c] $\times 10^7$ (cm^2/s)	Equilibrium Swelling Time (min)
V0	25	0.70	0.042	2.60	420
	30	0.89	0.022	3.16	420
	45	0.94	0.024	4.78	215
	55	0.71	0.067	5.28	185
	65	0.58	0.092	6.36	180
V3	25	0.68	0.039	2.72	420
	30	0.80	0.032	3.85	360
	45	0.70	0.056	5.03	260
	55	0.63	0.074	6.00	240
	65	0.67	0.079	6.79	210
V6	25	0.64	0.058	2.83	420
	30	0.72	0.042	4.42	360
	45	0.58	0.08	5.16	260
	55	0.76	0.069	6.48	240
	65	0.54	0.115	7.72	240
V9	25	0.74	0.041	3.32	420
	30	0.72	0.049	4.60	360
	45	0.74	0.054	5.67	300
	55	0.73	0.066	7.09	260
	65	0.65	0.096	8.55	240
V12	25	0.59	0.078	3.85	500
	30	0.58	0.094	5.35	360
	45	0.57	0.107	6.36	300
	55	0.53	0.134	7.95	270
	65	0.53	0.15	8.77	240

[a] n: is kinetic exponent.
[b] K: characteristic constant.
[c] D: diffusion coefficient of water.

aqueous solutions at 25°C. The results indicate that the water contents for the present copolymeric hydrogels almost keep constant values until the salt concentration is over $1.0 \times 10^{-2}\,M$ and then decrease fast when the concentration of salt is higher than $0.1M$. This result indicates that the higher concentration of the salt solution is not aiding swelling for the present hydrogel. This phenomenon is also called the salt screen effect. This behavior and explanation were described in our previous report.[53] Figure 6 also indicates that the rapidly decreasing water content is suppressed by the addition of the VSIB monomer into HEMA gels at the range of the salt concentration from 0.1 to $1.0M$. This phenomenon can be accounted for by the nature of poly(VSIB). Salamone et al.[46] reported that poly(VSIB) is insoluble in deionized water, because the collective positive charges on the polyampholyte attract collective negative charges to form an inner ionically crosslinked network. When the concentration of the salt solution is higher than is the minimum salt concentration (MSC) of poly(VSIB), poly(VSIB) can be dissolved in an aqueous solution. For this reason, when the salt concentration is increased, a part of the positive and negative charges of salt would site-bind on the sulfonate group (SO_3^-), and the quaternary ammonium group (R_4N^+), on VSIB. The charges will be neutralized by counterions in the aqueous solution. This occurrence will reduce the degree of the ionically crosslinked network of VSIB and remove the entanglement of molecular chains and expand the molecular chain.

According to the aforesaid reason, the MSC of poly(VSIB) in a LiCl aqueous solution is $0.50M$.

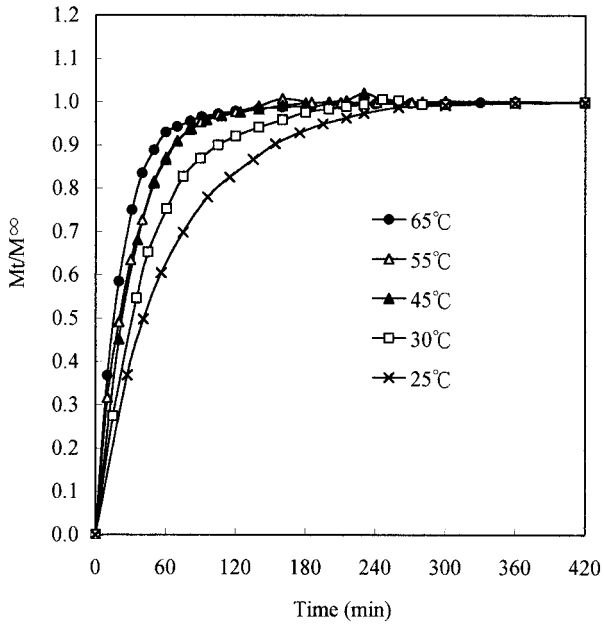


Figure 4 Water uptake of the 3 mol % HEMA/VSIB gels in water as a function of time at various temperatures.

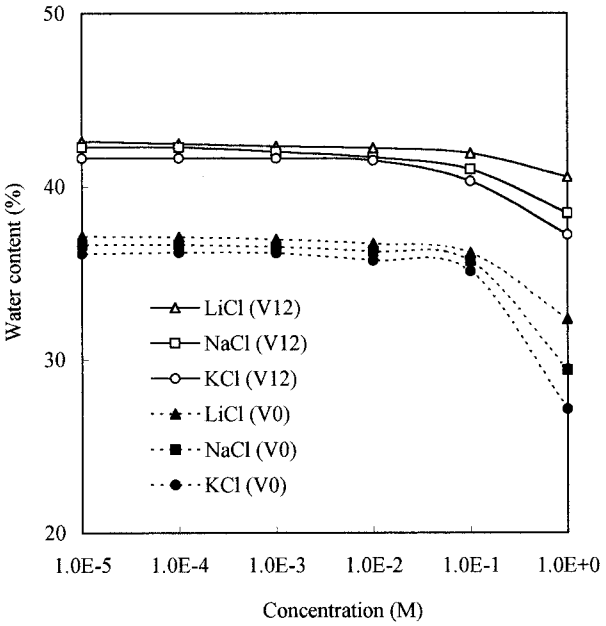


Figure 6 Water contents of PHEMA (V0) and HEMA/VSIB (V12) gels in different monovalent cation salt aqueous solutions at 25°C.

Hence, when the salt concentration is less than 0.50*M*, the inner ionic ring of VSIB cannot be ruptured and the net charge of the discussed copolymeric gel is still zero. The water content for the present gels, therefore, do not change very much when the salt concentration, LiCl(aq), is changed. On the other hand, the inner ring of VSIB will be opened as the salt concentration is higher than 0.50*M*, and the molecular side chain of VSIB will be expanded and the polymer–solvent interaction will be reduced. This behavior implies that the tendency of a rapidly decreased water content in a concentrated salt solution would be effectively suppressed as VSIB is introduced.

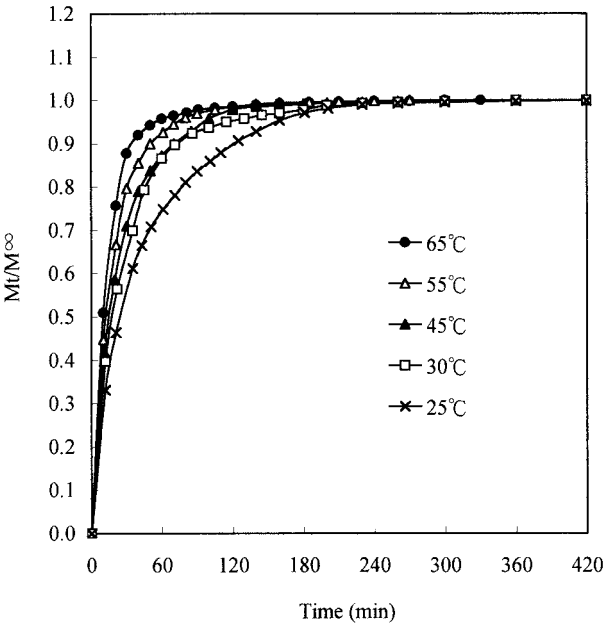


Figure 5 Water uptake of the 12 mol % HEMA/VSIB gels in water as a function of time at various temperatures.

Influence of Different Monovalent Cations with Common Anion (Cl^-) on the Water Content

Figure 6 also shows the equilibrium water contents as a function of the salt concentrations for LiCl, NaCl, and KCl solutions. At a high concentration, the results indicate a decrease in the water contents of sample V0 and V12 in the order $Li^+ > Na^+ > K^+$ for LiCl, NaCl, and KCl, respectively. This is because the hydration radius grows as a result of the smaller cation surrounded with a large amount water. Therefore, the water contents for samples V0 and V12 are higher in the LiCl solution than are those in the NaCl and KCl solutions.

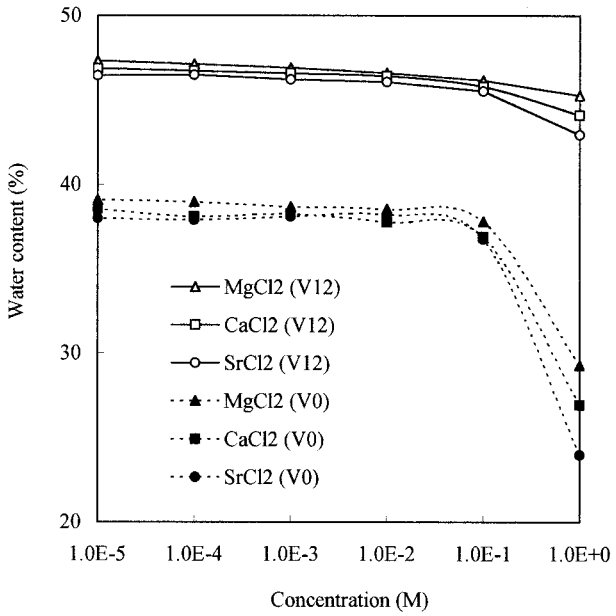


Figure 7 Water contents of PHEMA and HEMA/VSIB gels in different divalent cation salt aqueous solutions at 25°C.

Influence of Different Divalent Cations with Common Anion (Cl^-) on the Water Content

Figure 7 shows the equilibrium water contents for the HEMA/VSIB gels in different divalent cation solutions. The results also indicate a decrease in the water contents of gels in the order $Mg^{2+} > Ca^{2+} > Sr^{2+}$ for $MgCl_2$, $CaCl_2$, and $SrCl_2$, respectively, and have a similar tendency as that of these gels in the LiCl, NaCl, and KCl solutions when the salt concentration is higher than the MSC of poly(VSIB). This is also because their hydration radius grows as a result of the cation. Besides, the rapidly decreased water contents for PHEMA gels at the higher salt concentration will be more effectively suppressed as VSIB is added to the copolymeric gels.

Influence of Different Halide Ions with Common Cation (K^+) on the Water Content

The influence of different halide ions with a common cation (K^+) on the water content for the present copolymeric hydrogels was investigated. The results are shown in Figure 8. For the potassium salts, an increase in the water content of the hydrogel is in the order $F^- < Cl^- < Br^- < I^-$ for KF, KCl, KBr, and KI, respectively. For the potassium salts, Figure 8 shows that the water contents of these gels in the KF and KCl solutions exhibit a decrease with increasing salt concentration. An anion with a small charge/radius ratio is easily bound on the quaternary ammonium group (R_4N^+) of VSIB. This is because the ion with the smaller charge density can be easily polarized during the ionization of salt near to and bound on the quaternary ammonium group (R_4N^+) of VSIB. Therefore, the larger anion can easily infiltrate into the ionically crosslinked network and expand the molecular chain. Hence, as the anion size of the external salt solution is increased, the anti-polyelectrolyte's swelling behavior of the hydrogels is more obvious.

From the above results, we find that the anion effect is larger than is the cation effect in the presence of a common anion (Cl^-) with different cations (see Figs. 6 and 7) and a common cation (K^+) with different anions (Fig. 8) for the hydrogels. These results are similar to our previous reports on NIPAAm/DMAAPS[52] and NIPAAm/VSIB[47] gel systems and consistent with the Pearson principle.[54]

Influence of Different Acidic Ions with Common Cation (Na^+) on the Water Content

The influence of different acidic ions (ClO_4^-, NO_3^-, and CH_3COO^-) with a common cation (Na^+) on

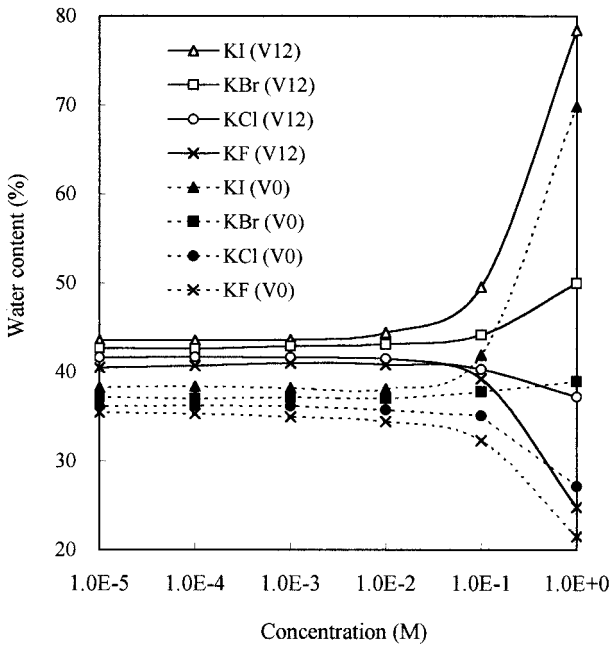


Figure 8 Water contents of PHEMA and HEMA/VSIB gels in different halide ion salt aqueous solutions at 25°C.

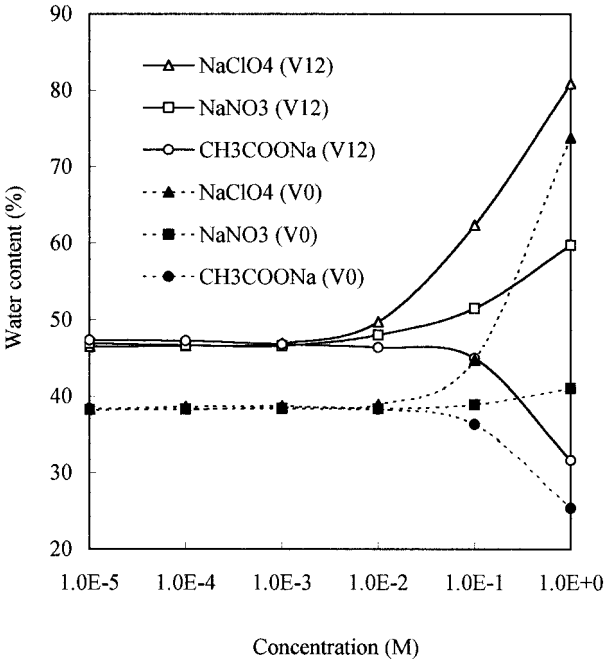


Figure 9 Water contents of PHEMA and HEMA/VSIB gels in different acidic ion salt aqueous solutions at 25°C.

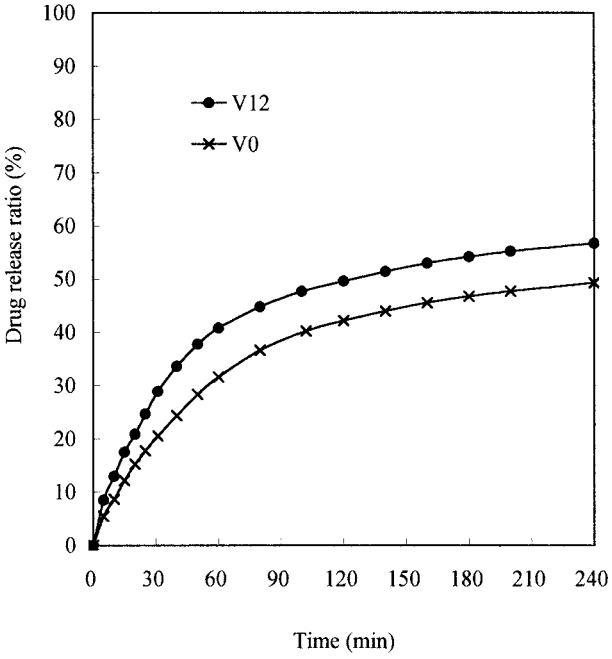


Figure 10 Caffeine-release profile for PHEMA and HEMA/VSIB gels at 37°C.

the water content for the samples V0 and V12 is shown in Figure 9. The results shown are similar to the swelling behavior of the hydrogels in monovalent and divalent chloride salt solutions. The results indicate that the swelling behavior of the gels is similar as to that in Figure 8. The result, observed from Figure 9, indicates that an increase in the water content of the hydrogel is in the order $CH_3COO^- < NO_3^- < ClO_4^-$ for CH_3COONa, $NaNO_3$, and $NaClO_4$, respectively. This tendency is consistent with the NIPAAm/VSIB gel systems.[47]

Behavior of Release Caffeine for HEMA/VSIB Hydrogels

Figure 10 shows the release profile of caffeine for PHEMA (V0) and HEMA/VSIB copolymeric gels (V12), which swelled at 25°C in the caffeine solution and deswelled at 37°C in deionized water. The results show that the fractional release is directly proportional to their water contents. This is because the higher water contents of hydrogels create larger surface areas to release the drug. Sample V12 also has a higher release rate at the initial release stage. From the release curves of the gels, it can be found that the drug is continuously released from the gels. Hence, the HEMA/VSIB copolymeric gels are probably used as a sustained-release drug carrier.

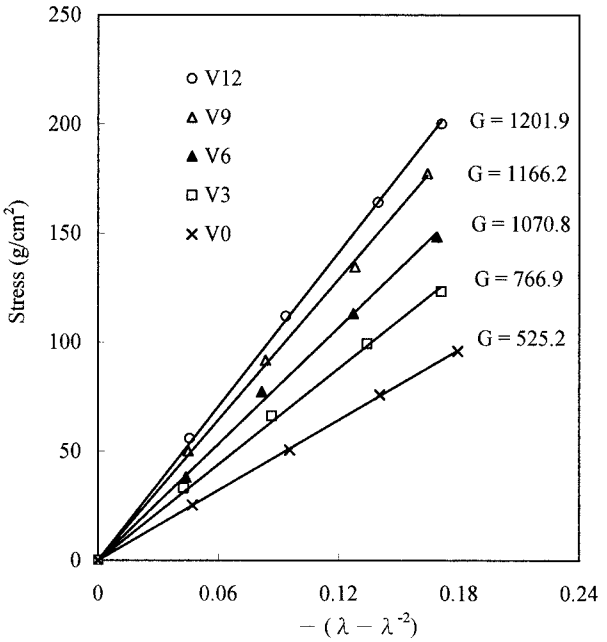


Figure 11 Compression curves for HEMA/VSIB gels crosslinked with NMBA by copolymerization–crosslinking, where $\lambda = L/L_0$.

Table IV Shear Moduli and Crosslinking Densities of HEMA/VSIB Hydrogels

Sample No.	Swelling Ratio Q (g/g) 25°C	$Q^{1/3}$	Shear Modulus G (g/cm^2)	Crosslinking Density $\rho_x \times 10^5$ (mol/cm^3)
V0	0.65	0.87	525.2	1.80
V3	0.69	0.88	766.9	2.68
V6	0.73	0.90	1070.8	3.81
V9	0.78	0.92	1166.2	4.24
V12	0.89	0.96	1201.9	4.58

Effect of VSIB Content on Gel Strength and Crosslinking Densities for HEMA/VSIB Gels

The stress–strain curves for a series of HEMA/VSIB hydrogels at the swollen state at 25°C are shown in Figure 11. The slope of the straight line is the shear modulus (G), and the value represents the gel strength of the HEMA/VSIB gels. The crosslinking densities of hydrogels calculated from eq. (6) are listed in Table IV. The results shown in Figure 11 indicate that the HEMA/VSIB gels have higher G values than those of the PHEMA gel (V0). This is because the rigidity of the imidazole ring on VSIB made the gel become stronger. Hence, addition of more VSIB in the gels enhances the gel strength of the HEMA/VSIB copolymeric gels. The data shown in Table IV also indicate that the crosslinking densities of the hydrogels increase with an increasing amount of VSIB in the hydrogels. This is because poly(VSIB) is insoluble in deionized water and forms an inner ionically crosslinked network.[46] Hence, the crosslinking densities of the HEMA/VSIB copolymeric gels are higher than are those of the PHEMA gels, as can also be explained by eq. (6). Because the values of $Q^{1/3}$ are nearly equal to 0.9 for all gels, the crosslinking densities of the gels are directly proportional to their shear moduli. Hence, the shear moduli for the HEMA/VSIB gels are largely determined by their crosslinking densities.

CONCLUSIONS

We successfully prepared a series of homogeneous gels by copolymerization of HEMA and VSIB in an alcohol aqueous solution. The experimental results indicated that the equilibrium water contents of the HEMA/VSIB copolymeric gels increased with increasing VSIB contents in hydrogels and exhibited a minimum value at 45°C. The addition of a hydrophilic zwitterionic component, VSIB, in the HEMA gel could suppress the phenomenon of overshooting, which is the HEMA gel's unique characteristic. In different salt solutions, the water contents for the hydrogels were affected when the salt concentration was higher than that of the MSC of poly(VSIB). At the same time, the rapidly decreasing water content of the PHEMA gel was suppressed by the addition of the VSIB monomer into the HEMA gels. We also found that the anion effect was larger than was the cation effect in the presence of a common anion (Cl^-) with different cations and a common cation (K^+) with different anions for the hydrogels. Finally, the experimental results also indicated that the addition of VSIB could improve the fractional release of the drug and the gel strength for HEMA/VSIB copolymeric hydrogels.

The authors appreciate the financial support of Tatung University.

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