Effect of the Intercalation Agent Content of Montmorillonite on the Swelling Behavior and Drug Release Behavior of Nanocomposite Hydrogels

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ABSTRACT: A series of novel dual functional nanocomposite hydrogels were prepared from *N*-isopropylacrylamide (NIPAAm), acrylic acid (AA) that is neutralized 50 mol % by sodium hydroxide (SA50), and montmorillonite (MMT). MMT was intercalated with three different contents of intercalation agent of (3-acrylamidopropyl) trimethyl ammonium chloride (TMAACl). Investigation of the effect of intercalated MMT with three contents of intercalation agent (TMAACl) in the present nanocomposite hydrogels on the swelling and drug release behaviors is the main purpose in this study. The microstructure was identified by X-ray diffraction (XRD). Results showed that the swelling ratio for the present nanocomposite hydrogels decreased with an increase in the content of the intercalation agent. The gel strength of the present gels did not change obviously with an increase in the content of intercalation agent. XRD results indicated that exfoliation of MMT was achieved in the dry and swollen gel state. Finally, the drug release behaviors for these gels were accessed also. J Appl Polym Sci 94: 74–82, 2004

Key words: montmorillonite; *N*-isopropylacrylamide; nanocomposite hydrogel; drug release

INTRODUCTION

Hydrogels are cross-linked, three-dimensional hydrophilic polymeric networks that swell but do not dissolve when brought into contact with water. There are some hydrogels that sometimes undergo a volume change in response to a change in surrounding conditions such as temperature,[1,2] pH,[3,4] and solvent composition.[5–7] Poly-*N*-isopropylacrylamide (NIPAAm) hydrogel exhibits a volume phase transition phenomenon at about 33°C[8]; this temperature is defined as critical gel transition temperature (CGTT).

For NIPAAm gel, the amide group would form a stronger hydrogen bond with water when the temperature is below the CGTT. This occurrence makes the gel swell in water. When the temperature is above the CGTT, the hydrophobic force of the gel increases, the gel collapses, and the bound water in the gel is released. Because NIPAAm gel has this swell-deswell behavior, it can be widely used in many fields such as extraction,[9] a drug delivery system,[10,11] and enzyme-activity control.[12] From our studies, adding a hydrophilic monomer, such as acrylic acid (AA), into NIPAAm gel can increase the CGTT of copolymeric gels from 33 to 37°C.[13,14]

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Montmorillonite (MMT) is a kind of loose-layer silicate.[15] When MMT / polymer is synthesized, the polymer chains entering the space between the layers by diffusion or shear stress effect intercalation polymerization.[16–19] MMT, which is a hydrophilic, swollen natural clay, lacks affinity with the hydrophobic organic polymer.[20] In general, natural clay has been treated by long alkylchain ammonium salt to replace Na^+ and Ca^{2+} ions in the clay and render it hydrophobic as an organoclay.

MMT, intercalated by short alkylchain ammonium salt using one equivalent cation exchange capacity (CEC) of MMT and incorporated into the hydrogels was reported in our previous studies.[21,22] The objective of this study was to further investigate the effect of the content of the intercalation agent on intercalated MMT on the swelling and drug release behaviors such as swelling ratio, microstructure, gel strength, and release of different ionic drugs for the present nanocomposite hydrogels.

EXPERIMENTAL

Materials

NIPAAm (Wako Chemical Co., Osaka, Japan) was recrystallized in *n*-hexane before use. AA was purchased from Tokyo Kasei Industries, Ltd. (Tokyo, Japan). The CEC of the MMT was 114 mEq / 100 g of clay. (3-Acrylamidopropyl)trimethyl ammonium chlo-

ride (TMAACl) as intercalation agent was purchased from Tokyo Kasei Industries, Ltd. *N*,*N*′-methylenebisacrylamide (NMBA) as cross-linking agent and ammonium persulfate as an initiator were purchased from Tokyo Kasei Industries, Ltd. *N*,*N*,*N*′,*N*′-tetramethylethylenediamine (TEMED) as an accelerator was obtained from Fluka Chemical Co. (Buchs, Switzerland). Caffeine, crystal violet (CV), and phenol red as model drugs also were obtained from Fluka Chemical Co. All solvents and other chemicals were of analytical grade.

Purification of the MMT

Thirty grams of MMT was suspended in 1000 mL of NaCl solution with a concentration of 1*M*. The suspension solution was stirred for 24 h at 70°C, and the suspension solution containing Na^+-MMT was centrifuged. The purified MMT was washed several times with deionized water until no chloride was detected in the filtrate by one drop of 0.1*N* $AgNO_3$ solution. Finally, the purified MMT was dried at 35°C and stored in a desiccator.

Intercalation of MMT

Intercalation of the TMAACl

Five grams of the purified MMT were dispersed into 400 mL of deionized water. Three different amounts of TMAACl (based on the CEC of MMT) were, respectively, dispersed into 100 mL of deionized water and then poured into the hot MMT / water solution and stirred for 1 h at 70°C. A white precipitate formed and was isolated by filtration and then washed several times with a hot water / ethanol (50 / 50) mixture until no chloride was detected in the filtrate by one drop of 0.1*N* $AgNO_3$ solution. The intercalated MMTs (designated as 0.5CEC, 1CEC, and 2CEC) were then dried for several days at 35°C and stored in a desiccator.

Measurement of the cec

The 0.1-g of purified MMT was dispersed into 30 mL of 1*N* solution of ammonium acetate for 24 h at room temperature. To this solution, 30 mL of ethanol was added and stirred for 2 h, and then 10 mL of NaCl solution with a concentration of 10 wt % was added to wash out ammonium ions for three times. After the suspension solution was centrifuged, only the top portion of solution was collected to measure CEC of the MMT by the Kjeldahl method.

Kjeldahl method

Five milliliters of H_3BO_3-indicator solution was added to a flask and attached to a condenser of a distillation apparatus with the end of the condenser under the surface of the H_3BO_3. Five milliliters of 10*N* NaOH and 5 mL of sample were added to the funnel of the apparatus. When distillate was no longer produced, distillation was stopped by opening the steam bypass tube, the end of the condenser was rinsed, and NH_4^+-N in the distillate was determined by titration with 0.001*N* H_2SO_4. The CEC of the MMT was calculated by eq. (1):

$$0.001\text{N } H_2SO_4*(V_s - V_b) = C*5 \quad (1)$$

where V_s and V_b are the titration volume for the sample and blank experiment and *C* is the concentration of the ammonium ion in solution.

Boric acid-indicator solution

Twenty grams of pure boric acid (H_3BO_3) was placed in a 1-L flask marked to indicate 950 mL, about 500 mL of water was added, and the flask was heated and swirled until the H_3BO_3 dissolved. The solution was cooled and 20 mL of mixed indicator solution, prepared by dissolving 0.099 g of bromocresol green and 0.066 g of methyl red in 100 mL of ethanol, was added. Then, 0.1*N* NaOH was added cautiously until the solution assumed a reddish purple tint (pH, ~ 5.0), and the solution was made up to 950 mL by addition of water. The solution was mixed thoroughly before use.

Measurement of zeta potential

Thirty milligrams of the MMT and intercalated MMT was first dispersed into 100 mL of water and a Zeta Meter System 3.0^+ (Staunton, USA) was used to measure their zeta potentials. The zeta potentials of MMT, 0.5CEC, 1CEC, and 2CEC were −24.7 mV ± 2%, −24.2 mV ± 1%, −21.3 mV ± 2%, and −19.5 mV ± 2%, respectively. This result showed that the negative charge density of MMT decreased with an increase in the content of intercalation agent.

Preparation of the SA50

SA50 was prepared as reported previously.[13–14]

Preparation of hydrogels (in-situ polymerization)

A fixed molar ratio of NIPAAm (95 mol %) and SA50 (5 mol %) was dissolved in 10 mL of deionized water. To this solution, MMT and intercalated MMT and 5 mol % NMBA as a cross-linking agent were well mixed overnight at room temperature. Finally, 1 mol % ammonium persulfate (APS), and 1 mol % TEMED as redox initiator were added, and then the mixture was injected immediately into the space between two

TABLE I
The Feed Compositions and Characteristics of the Nanocomposite Hydrogels

Sample codes	NIPAAm (g)	SA50 (g)	MMT ⟨TMAAC1-MMT⟩ (g)	Swelling ratio (g/g)	Yield (%)	G^*10^2 (MPa)
MMT0	1.075	0.1482	0	9.106	97.26	8.61
MMT1	1.075	0.1482	0.0134	8.91	96.11	12.25
MMT5	1.075	0.1482	0.0669	8.19	94.63	14.91
MMT8	1.075	0.1482	0.1339	7.70	93.24	17.85
MMT12	1.075	0.1482	0.2010	7.65	96.75	18.26
MMT17	1.075	0.1482	0.2678	7.51	95.52	17.96
0.5CEC1	1.075	0.1482	⟨0.0134⟩	8.82	95.22	11.03
0.5CEC5	1.075	0.1482	⟨0.0669⟩	8.05	96.31	12.41
0.5CEC8	1.075	0.1482	⟨0.1339⟩	7.54	95.76	15.42
0.5CEC12	1.075	0.1482	⟨0.2010⟩	7.47	97.64	19.26
0.5CEC17	1.075	0.1482	⟨0.2678⟩	7.40	94.53	20.07
1CEC1	1.075	0.1482	⟨0.0134⟩	8.74	92.35	11.81
1CEC5	1.075	0.1482	⟨0.0669⟩	7.99	93.46	15.42
1CEC8	1.075	0.1482	⟨0.1339⟩	7.43	93.62	15.96
1CEC12	1.075	0.1482	⟨0.2010⟩	7.34	95.26	20.41
1CEC17	1.075	0.1482	⟨0.2678⟩	7.29	93.27	20.62
2CEC1	1.075	0.1482	⟨0.0134⟩	8.49	93.55	12.15
2CEC5	1.075	0.1482	⟨0.0669⟩	7.59	95.37	16.12
2CEC8	1.075	0.1482	⟨0.1339⟩	7.27	92.58	18.01
2CEC12	1.075	0.1482	⟨0.2010⟩	6.84	95.32	18.60
2CEC17	1.075	0.1482	⟨0.2678⟩	6.54	92.82	21.17

glass plates. Polymerization was performed at 8°C for 1 d. After the gelation was completed, the gel membrane was cut into disks, 10 mm in diameter, and immersed in an excess amount of deionized water for 3 d to remove the residual unreactive monomer. Swollen polymer gels were dried at 25°C for 1 d, and these samples were further dried in a vacuum oven for 2 d. The feed compositions and characteristics of these nanocomposite hydrogels are listed in Table I.

Equilibrium swelling ratio

The dried gels were immersed in an excess amount of deionized water at different temperatures until swelling equilibrium was attained. The weight of wet sample (W_w) was determined after removing the surface water by blotting with filter paper. Dry weight (W_d) was determined after drying the gel in a vacuum oven for 2 d. The swelling ratio was obtained by weighing the initial and swollen samples at various time intervals. Equilibrium swelling ratio (Q_{eq}) was calculated from eq. (2):

$$Q_{eq} = (W_w - W_d)/W_d \tag{2}$$

Swelling kinetics

The dried gels were immersed in an excess amount of deionized water. The swelling ratio was obtained by weighing the initial and swollen samples at various time intervals. The amount of water sorbed W_t was reported as a function of time, and the equilibrium sorption at infinitely long time was designated as W_∞. Equation (3) was used to calculate the diffusion coefficient D for $W_t / W_\infty \leqq 0.8$.[23]

$$\frac{W_t}{W_\infty} = \frac{4}{\sqrt{\pi}} \times \left(\frac{D \times t}{L^2}\right)^{1/2} \tag{3}$$

where t is the time and L is the initial thickness of the dry gel. To investigate the diffusion model of the gel, the initial swelling data were fitted to the exponential heuristic in eq. (4) for $W_t / W_\infty \leqq 0.6$[24,25]:

$$W_t/W_\infty = Kt^n \tag{4}$$

where K is a characteristic constant of the dry gels and n is a characteristic exponent of the mode transport of the penetrate.

Physical properties measurement

The gel strength of these samples was measured by a uniaxial compression experiment with a universal tester (LLOYD LRX, Lloyd Instruments Ltd., Foreham, UK). The following eq. (5) was used to calculate the shear modulus:

$$\tau = F/A = G\,(\lambda - \lambda^{-2}) \tag{5}$$

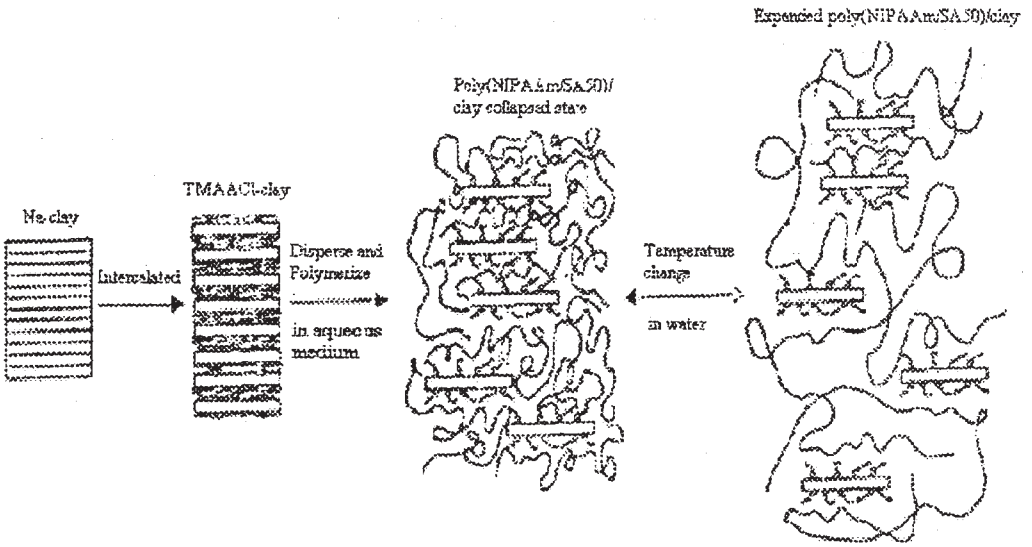

Figure 1 Schematic illustration of the formation of the nanocomposite hydrogels and the swelling process.

where τ is compression stress, F is compression load, A is cross-sectional area of swollen gels, and λ is compression strain (L / L_0). At low strains, a plot of shear stress versus $-(\lambda - \lambda^{-2})$ yields a straight line in which its slope is shear modulus (G).

Drug release experiment

The dry gels were equilibrated in 30 mg of drug / 10 mL of deionized water at 25°C for 2 d to load the drug into the gels. The drug release experiment was performed by transferring previously incubated drug gels into 10 mL of deionized water or 0.9 wt % saline solution at 37°C. The gels were removed repeatedly and transferred into 10 mL of fresh deionized water or saline solution at each fixed time interval. The release drug was analyzed at 272, 431, and 589 nm for caffeine, phenol red, and CV, respectively, by an ultraviolet (UV) spectrophotometer (JASCO V530; JASCO, Tokyo, Japan).

X-ray diffraction analysis

Powder X-ray diffraction (XRD) analyses were performed using a Siemens D5000 diffractometer (Munich, Germany) with Cu radiation (40 kV, 30 mA). The scanning speed and the step size were 3° / min, respectively. The structure of the clay was determined at different states of the nanocomposite synthesis. The clay powders were mounted on a sample holder with a large cavity and a smooth surface was obtained by pressing the powders with a glass plate. Analysis of these nanocomposite gels was performed by spreading the mixture on a gel membrane disc (50 mm in diameter and 0.5 mm thick) used as sample holder. XRD data were processed using Origin 6.0 software, Siemens, Munich, Germany.

Partition coefficient determination

Partition coefficients (Kd) were determined by the solution depletion technique using a UV-spectrophotometer to measure the solution concentration. The hydrogels that had been preswollen in deionized water were held to equilibrium in a drug solution at 25°C. The partition coefficient Kd was calculated by using eq. (6) from a decrease in the solute concentration of the external solution[26]:

$$Kd = (C_o - C_s)Vs/(C_s^* V_m) \quad (6)$$

where C_o and C_s are initial and final solute concentrations in solution, V_s is the solution volume, and V_m is the hydrogel volume.

RESULTS AND DISCUSSION

Preparation of the nanocomposite hydrogels

Because MMT is a hydrophilic material, it should be readily uniformly dispersed in aqueous medium. However, large interactions on the surface of MMT make it easy to agglomerate. To overcome this problem, we have successfully used a short alkylchain intercalation agent TMAACl to intercalate MMT and to render it to be more uniformly dispersed into aqueous medium as described in our previous report.[23] Hence, in this work we have successfully prepared nanocomposite hydrogels in aqueous medium by using three intercalated MMTs at low temperature. Figure 1 shows a schematic illustration of the formation

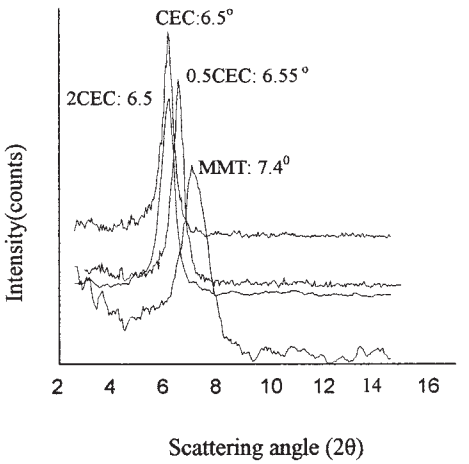

Figure 2 XRD patterns of MMT and TMAACL-MMT.

of the nanocomposite hydrogels and the swelling process.

Identification of NIPAAm / SA50 nanocomposite hydrogels

Figure 2 is a typical diffraction pattern of Na^+-MMT, with a peak corresponding to a basal space of 12 Å (2θ = 7.4°). After intercalation with different contents of TMAACl, this peak was shifted to a lower angle, corresponding to a basal space of 13.5 Å (2θ = 6.55°), 13.6 Å (2θ = 6.5°), and 13.6 Å (2θ = 6.5°) for gels of 0.5CEC, 1CEC, 2CEC, respectively. This shows that TMAACl had intercalated the space between the layers during the cation-exchange process, adopting a lateral bilayer structure, and the basal space increased with an increase in the content of intercalation agent. When the amount of the intercalation agent was increased to two times the CEC of MMT, i.e., 2CEC, the basal space did not further increase. This shows that the cations of MMT were completely exchanged by TMAACl. Figure 3 shows the diffraction patterns of various nanocomposite hydrogels in dry and swollen states. The results in Figure 3 indicate that the characteristic diffraction peak was not observed in the dry composite samples and swollen samples. This evidence shows that the MMT and TMAACl-MMT in the nanocomposite hydrogels were exfoliated completely.

Effect of intercalated MMT with different CECs on the properties of the nanocomposite hydrogels

The fundamental properties such as equilibrium swelling ratio, gel strength, and drug release for the present nanocomposite hydrogels prepared from NIPAAm / SA50 / MMT or TMAACl-MMT were investigated.

Effect on equilibrium swelling ratio

Some characteristics of the NIPAAm / SA50 gels with MMT and TMAACl-MMT are shown in Table I. The results in Table I show that the equilibrium swelling ratios decrease with an increase of the content of MMT or TMAACl-MMT in the gels. This is because the original hydrophilic MMT, intercalated by TMAACl, becomes a hydrophobic chain: it makes NIPAAm / SA50 nanocomposite hydrogels become slightly hydrophobic and, therefore, the swelling ratios of the gels decrease. Similar results were observed in our previous reports.[21,22]

Effect on the gel strength

The gel strength can be assessed by the shear modulus (G) measured from uniaxial compression experiments. The results, shown in Table I, indicate that the G values of the present gels were enhanced by incorporation of intercalation agent in the gel systems.

Effect on swelling kinetics

The swelling ratios, as a function of time, for these gels in deionized water are shown in Figure 4. The n, K, and D values calculated from eqs. (3) and (4), are listed in Table II. The results show that the diffusion coefficients for these gels in deionized water are not obviously affected by increase of intercalation agent content. According to the classification of diffusion mechanism presented by Alfrey et al.,[26] the results shown in Table II indicate that the transport mechanisms of these nanocomposite hydrogels all belong to Fickian diffusion.

Effect of temperature on swelling ratio

The effect of temperature on equilibrium swelling ratio for the present gels is shown in Figure 5. The

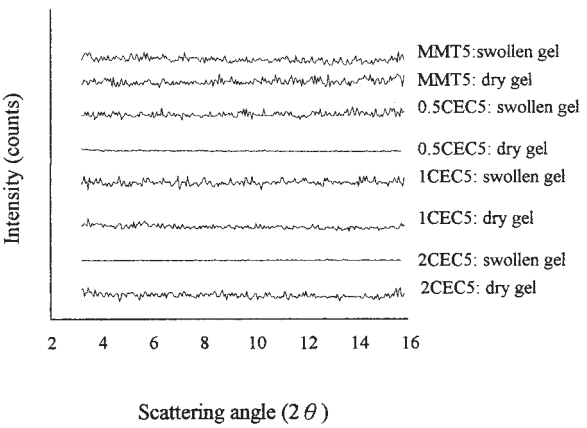

Figure 3 XRD patterns of the nanocomposite hydrogels.

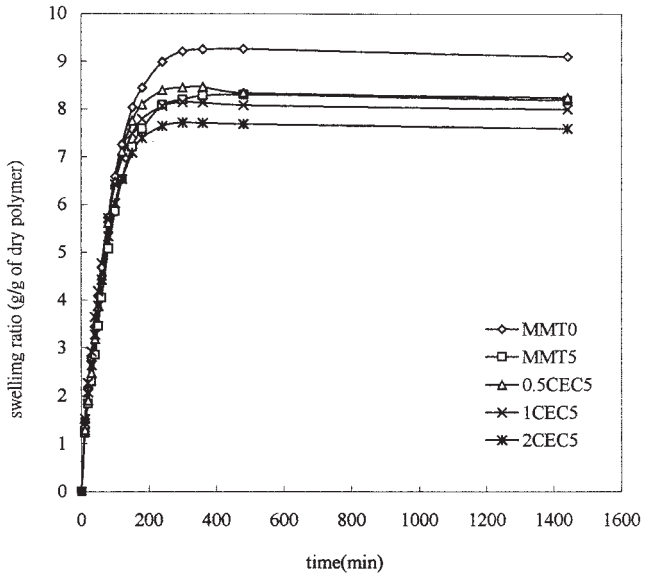

Figure 4 Swelling ratio as a function of time for the nanocomposite hydrogels.

results indicate that the higher the temperature, the lower the swelling ratio. However, the gel transition temperature did not obviously shift with an increase in CEC of the intercalated MMT. This could be because MMT and TMAACl-MMT did not hydrogen bond with NIPAAm chains. Although the CGTT did not obviously change, the hydrogels still showed excellent thermal response over a wide range of clay loading. The CGTT for these present hydrogels is

TABLE II
Initial Diffusion Coefficient of Water *D*, Kinetic Exponent *n*, and Characteristic Constant *k* for the Nanocomposite Hydrogels in Deionized Water at 25°C

Sample codes	*n*	$K*10^2$	$D*10^7$ (cm^2 sec)
MMT0	0.41	0.095	0.9
MMT1	0.39	0.095	0.9
MMT5	0.38	0.104	0.9
MMT12	0.41	0.112	1.6
MMT17	0.39	0.110	1.6
0.5CEC1	0.44	0.097	1.6
0.5CEC5	0.40	0.102	1.6
0.5CEC8	0.41	0.109	1.6
0.5CEC12	0.37	0.117	1.6
0.5CEC17	0.32	0.110	0.9
1CEC1	0.42	0.096	1.6
1CEC5	0.42	0.096	1.6
1CEC8	0.37	0.118	1.6
1CEC12	0.34	0.122	1.6
1CEC17	0.34	0.128	0.9
2CEC1	0.43	0.089	1.6
2CEC5	0.37	0.096	1.6
2CEC8	0.38	0.111	1.6
2CEC12	0.39	0.114	1.6
2CEC17	0.39	0.115	1.6

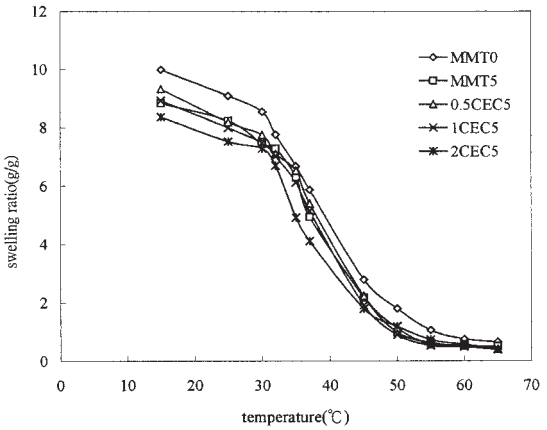

Figure 5 Effect of temperature on equilibrium swelling ratio for the gels in deionized water.

about 37°C. Because NIPAAm is the main component in the present copolymeric gels, the swelling ratio decreases with an increase of temperature.

Effect on fractional release of caffeine, CV, and phenol red in deionized water or saline

The investigation of the charge effect on the drug release behavior for ionic thermosensitive hydrogels was studied in a previous report.[27] The results indicated that the drug release behavior for ionic thermosensitive hydrogels is related to its ionicity and drug types. In this study, the fractional releases of caffeine, CV, and phenol red in deionized water or saline solution for NIPAAm / SA50 / MMT or TMAACl-MMT nanocomposite hydrogels at 37°C are shown in Figures 6 -11, respectively. Because MMT bears negative charges on the surface, the hydrogel is an anionic gel.

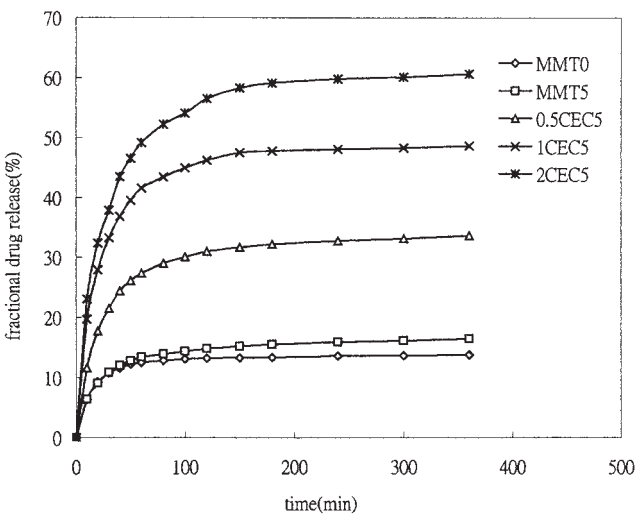

Figure 6 Caffeine release profiles during loading at 25°C and releasing at 37°C in deionized water.

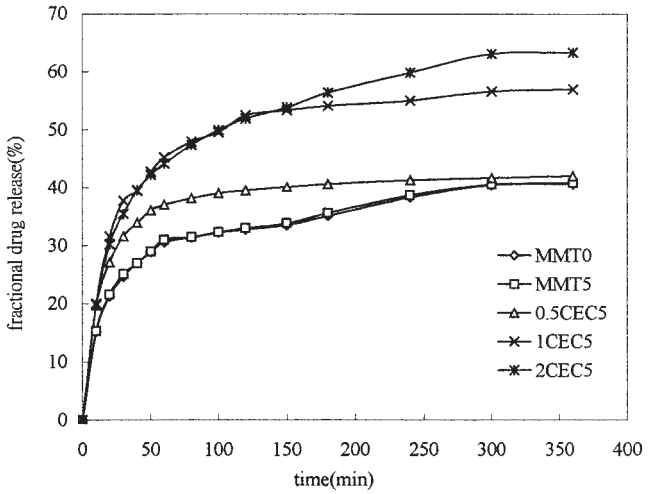

Figure 7 Caffeine release profiles during loading at 25°C and releasing at 37°C in saline.

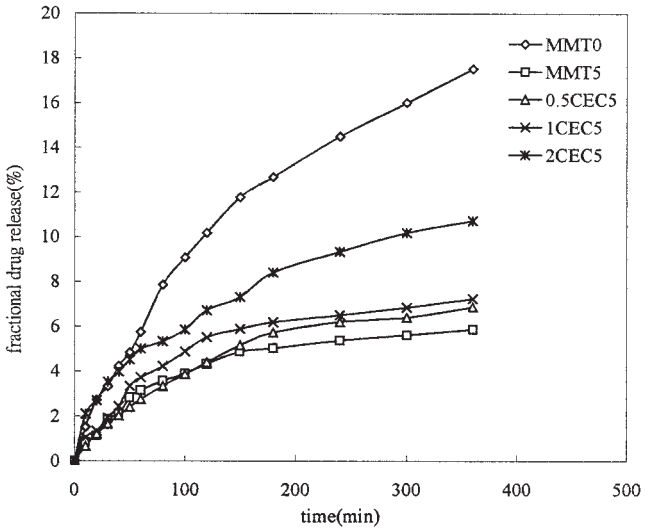

Figure 9 CV release profiles during loading at 25°C and releasing at 37°C in saline.

The fractional drug releases in these gels are shown in Table III.

The results in Figure 6 show the fractional drug release of uncharged caffeine for these hydrogels in deionized water at 37°C: fractional drug release of these nanocomposite hydrogels increased with an increase of intercalation agent content, i.e., 2CEC5 > 1CEC5 > 0.5CEC > MMT5 > MMT0. To examine this behavior, the interaction between the caffeine and hydrogels was measured through the partition coefficient (*Kd*). Because the larger the *Kd*, the stronger the interaction between the drug and hydrogel. The values of *Kd*, in Table IV, decrease with an increase in the intercalation agent content. Hence, the interaction between caffeine and hydrogel decreases, and the fractional release of caffeine increases with an increase of the intercalation agent content. The fractional release of caffeine for these gels in saline solution, shown in Figure 7, is larger than in deionized water (also see Table III). This result also can be explained by the value of *Kd*. Table IV shows that *Kd*'s for these gels in saline solution were smaller than those in deionized water.

When the charge of the drug solute and hydrogel are different, electrostatic attraction exists between them. Hence, the cationic solutes strongly bind to the anionic gels and are difficult to release from the gel with free water. So, the fractional release of CV in these gels is lower. The results in Figure 8 indicate that because the negative charges on the surface of MMT are partially neutralized by the cations, the fractional release of CV drug for these nanocomposite hydrogels in deionized water increases with an increase in the

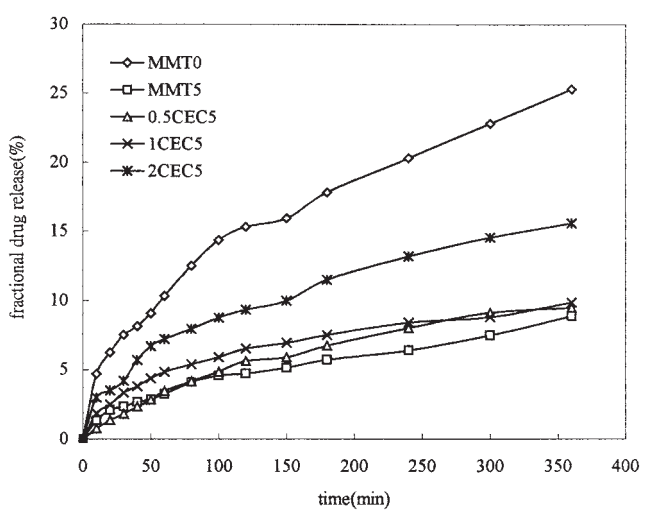

Figure 8 CV release profiles during loading at 25°C and releasing at 37°C in deionized water.

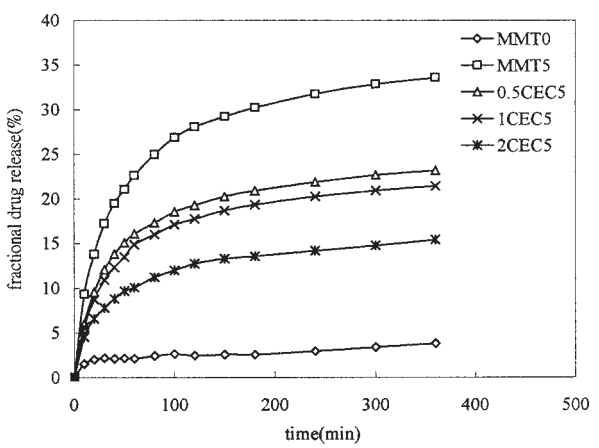

Figure 10 Phenol red release profiles during loading at 25°C and releasing at 37°C in deionized water.

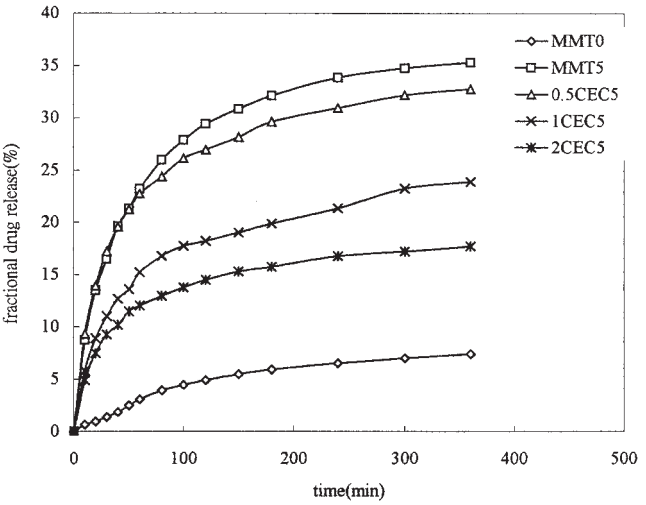

Figure 11 Phenol red release profiles during loading at 25°C and releasing at 37°C in saline.

content of intercalation agent, i.e., MMT0 > 2CEC5 > 1CEC5 > 0.5CEC > MMT5. Because the CV is difficult to release from the hydrogels in deionized water, we proposed to use the ion exchange technique to improve the drug release behavior. However, the results, shown in Figure 9, indicate that the CV release did not increase in saline solution (also see Table IV).

In addition, when the charge of the drug solutes and hydrogels are the same, the drug release fraction of gels is higher. This is because charge repulsion exists between the drug solutes and gels. The solute is difficult to load into the gel and is easily released from the gels. The results for anionic phenol red releasing from anionic gels in deionized water are shown in Figure 10. They show that the fractional release of phenol red from these nanocomposite hydrogels decreased with an increase in intercalation agent content, because the stronger the repulsion force is between drug and hydrogel, the larger is the fractional drug release. So, it made the fractional drug release decrease. The fractional release of anionic phenol red solutes in saline solution, shown in Figure 11, are larger than those in deionized water. The results indicate that because anionic drug solutes are attracted by the cations (Na^+), the fractions of phenol red release are larger in the presence of saline than in the presence of deionized water.

TABLE IV
The Partition Coefficient (*Kd*) for Nanocomposite Hydrogels in Caffeine Solution

Sample codes	*Kd* in deionized water	*Kd* in saline solution
MMT0	4.21	3.62
MMT5	3.93	3.57
0.5CEC5	3.68	0.94
1CEC5	0.31	0.27
2CEC5	0.24	0.21

From the forgoing results, we find that the drug release behavior for NIPAAm / SA50 / MMT or TMAACl-MMT nanocomposite hydrogels is affected by the intercalated MMT with different content of intercalation agent, charge of drug solute, and ionic strength of surroundings. These results conform to our previous study.[27]

CONCLUSION

NIPAAm / SA50 with fixed molar ratios of NIPAAm (95 mol %) and SA50 (5 mol %) nanocomposite hydro-

TABLE III
The Loading Amount and Drug Release Fraction of the Model Drugs in the Hydrogels

Drug	Sample codes	Drug release fraction at 360 min in deionized water	Drug release fraction at 360 min in saline solution
Caffeine	MMT0	13.74%	40.60%
	MMT5	16.43%	40.83%
	0.5CEC5	33.68%	42.06%
	1CEC5	48.65%	56.98%
	2CEC5	60.61%	63.38%
CV	MMT0	25.32%	17.52%
	MMT5	8.87%	5.88%
	0.5CEC5	9.48%	6.87%
	1CEC5	9.87%	7.24%
	2CEC5	15.6%	10.74%
Phenol red	MMT0	3.77%	7.39%
	MMT5	33.59%	35.32%
	0.5CEC5	23.20%	32.76%
	1CEC5	21.44%	23.88%
	2CEC5	15.40%	17.71%

gels were synthesized successfully in this study. From the foregoing discussion, some conclusions can be drawn as follows: the swelling ratio of these nanocomposite hydrogels decreased with an increase of the content of the intercalation agent. The gel strength and gel transition temperature of these gels did not obviously change as the content of intercalation agent increased. The XRD patterns showed that the MMT or TMAACl-MMT, in the dry composite samples or in the swollen samples, were completely exfoliated. In drug release behavior, results showed that the fractional release of caffeine in the hydrogels was not affected by the ionicity of the hydrogels. Because the negative charges on the surface of MMT are partially neutralized by the cations, the CV release fractions increased with an increase of the content of the intercalation agent. However, the result of phenol red (anionic solutes) release in these hydrogels was contrary to CV release.

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