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Polymer 46 (2005) 8098–8106
polymer
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Synthesis of thermosensitive poly(*N*-alkylacrylamide) gels and core–shell type gels

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Received 17 March 2005; received in revised form 17 June 2005; accepted 21 June 2005
Available online 27 July 2005

Abstract

When the poly(acrylic acid) (PAA) gel-1,8-diazabicyclo-[5,4,0]-7-undecene salt (DAA) was placed in *N*-methyl-2-pyrrolidone containing an excess of alkylamine and triphenylphosphine, selective amidation took place from the outside to give the corresponding poly(*N*-alkylacrylamide) gel containing a C3 alkyl chain through a DAA–poly(*N*-alkylacrylamide) type gel capsule consisting of a hydrophilic unreacted core part and an amidated shell layer. The amidation proceeded by a reaction mechanism similar to the unreacted-core model. Thermal properties of the resulting poly(*N*-alkylacrylamide) gels such as deswelling behavior and equilibrium swelling ratio in water as a function of temperature were measured. The release of methyl orange from a poly(*N*-alkylacrylamide) gel and the gel capsule was also examined. PAA–poly(*N*-alkylacrylamide) type gel capsules containing a PAA core part and thermosensitive poly(*N*-alkylacrylamide) shell layer, prepared by the neutralization of DAA–poly(*N*-alkylacrylamide) type gel capsules, showed on–off chemical release characteristics in response to stepwise temperature changes across the LCST.
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Keywords: Thermosensitive gel; Poly(*N*-alkylacrylamide) gel; Core–shell type gel

1. Introduction

Poly(*N*-isopropylacrylamide) (PNIPA) gel is a well known thermosensitive or smart gel which has lower critical solution temperature (LCST) in the temperature range of 32–34 °C [1–3]. It swells in water at temperatures (T_1) below LCST and shrinks at temperatures (T_2) above the LCST and its properties change greatly when the water temperature is changed in a stepwise manner, between the two operating temperatures (T_1 and T_2). PNIPA gels can be used in a variety of applications such as extraction [4], absorption [5], drug-delivery [6], and enzyme immobilization [7], since they show a relatively rapid and large volume change as the results of a small temperature change around the LCST, many literature references and information are available, and the monomer *N*-isopropylacrylamide (NIPA) used in its preparation is commercially available. However, certain applications may be restricted because the operating temperatures are limited by the LCST. Thus, the question arises as to whether PNIPA gel is the best thermosensitive polymer gel. Thermosensitive polymer gels with different LCST based on the PNIPA gel are needed for practical use. Ito [8] reported on a detailed study of the LCST of soluble poly(*N*-alkylacrylamide)s and poly(*N*,*N*-dialkylacrylamide)s, and changes in the LCST with the length of the alkyl chain contained in the polymer. Data concerning the LCST and swelling behavior of poly(*N*-alkylacrylamide) gels has been reported previously [6,9b]. Since the LCST of poly(*N*-alkylacrylamide)s and related gels depends primarily on their chemical structure, the LCST for linear poly(*N*-alkylacrylamide)s is in essential agreement with that of the corresponding gels. However, the swelling behavior of gels is strongly affected by the network structure of the gel itself as well as the chemical structure. Since poly(*N*-alkylacrylamide) gels with the same network structure are not prepared by the polymerization of the corresponding monomers, it is not possible to systematically study the relative thermosensitivity of poly(*N*-alkylacrylamide) gels.

In a recent study, we reported on the heterogeneous

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0032-3861/$ - see front matter © 2005 Elsevier Ltd. All rights reserved.
doi:10.1016/j.polymer.2005.06.081

reaction of the poly(acrylic acid) gel (PAA)-1,8-diazabicyclo-[5,4,0]-7-undecene (DBU) salt (DAA) with reagents such as alkyl halides [10] and isopropylamine (IPA) [11], and on the acetylation of poly(2-hydroxylethyl acrylate) gel [12]. A nearly quantitative esterification or amidation occurred, starting from the outside of the gel, to give a new core–shell type gel (gel capsule) consisting of an unreacted core gel which was hydrophobic that was encapsulated by a chemically reacted shell (Fig. 1).

In a previous communication [13], a series of poly(*N*-alkylacrylamide) gels containing C3 alkyl chains with the same network structure was prepared by the amidation of DAA with alkylamines such as *n*-propylamine (NPA), IPA, cyclopropylamine, allylamine (AA), and a mixture of NPA and IPA using triphenylphosphine (TPP) as an activating agent. The reaction of DAA with alkylamines proceeded equally well, irrespective of the structure of the alkylamines. In this paper, we report on the synthesis of poly(*N*-alkylacrylamide) gels and novel gel capsules consisting of a hydrophilic core gel and thermosensitive or hydrophobic shell containing alkyl chains, produced by the quantitative amidation of DAA with various alkylamines using TPP (Fig. 2). The swelling–deswelling behavior and LCST of the resulting poly(*N*-alkylacrylamide) gels and gel capsules are discussed.

2. Experimental

2.1. Materials

Acrylic acid and solvents were distilled prior to use. Commercial alkylamines were used as purchased. *N*,*N*′-methylenebisacrylamide, DBU, TPP, and Methyl Orange were used without further purification. Cylindrical DAA (length and diameter; about 5 mm) was prepared via a two-step procedure involving the copolymerization of acrylic acid with 0.5 mol% of *N*,*N*′-methylenebisacrylamide in Teflon tubes (internal diameter; 6 mm) and neutralization of the resulting gel with excess DBU in methanol, as described in the previous reports [10a].

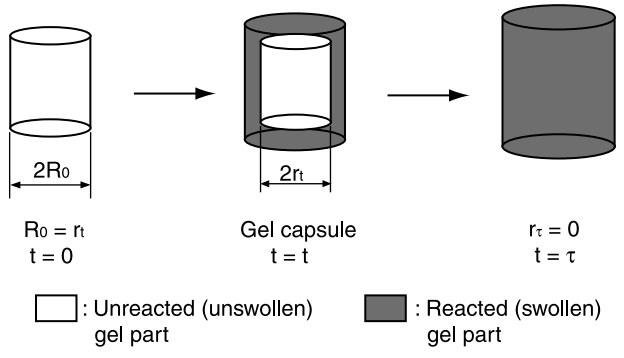

Fig. 1. Reaction of a gel through a core–shell type gel (gel capsule) consisting of an unreacted core gel and reacted shell layer.

2.2. Apparatus

IR spectra were obtained on a Perkin–Elmer model IR-700 spectrophotometer. UV spectra were obtained on a Shimadzu model UV mini 1240 spectrophotometer.

2.3. Amidation of DAA [11,13]

In a typical amidation of DAA, a mixed solution (50 ml) of IPA (2.0 mol l^{-1}) and TPP (1.0 mol l^{-1}) in *N*-methyl-2-pyrrolidone (NMP) was charged into a 50 ml cylindrical cell in a water bath at 80 °C. A cylindrical DAA was dipped into this solution. R_0 and r_t values of the sample, the radii of shells and cores after $t=t$ minutes, respectively, were periodically determined by a digital video camera (Sonny, DCR-TRV950). After the disappearance of the core, the resulting gel was washed with an acetic acid solution in methanol, to remove unreacted substances and by-products in a Soxhlet extractor. The sample was then dried carefully and slowly, and finally dried in vacuo at 80 °C to constant weight. The gel contained no free carboxylic acid, as evidenced by the back-titration with a triethylamine solution in methanol–aqueous HCl solution. The degree of amidation was 99%, calculated from A_{ester}/A_{amide}, where A_{ester} and A_{amide} are the absorption at 1755 and 1650 cm^{-1}, respectively. The results of the amidation of various alkylamines are summarized in Table 1.

2.4. Synthesis of DAA–poly(N-alkylacrylamide) type gel capsules and PAA–poly(N-alkylacrylamide) type gel capsules [11b]

A typical synthesis of DAA–poly(*N*-alkylacrylamide) type gel capsules was as follows. 200 ml of a mixed solution of TPP (1.0 mol l^{-1}) and IPA (2.0 mol l^{-1}) in NMP was charged into a 300 ml Erlenmeyer flask in a water bath at 80 °C. Dozens of DAA samples ($2R_0=5.0$ mm) were soaked in this solution, until the thickness of the shell layer ($1-r_t/R_0$) became 0.10 after 55 min of soaking. The gels were removed from the solution and placed in a large quantity of methanol to terminate the reaction. The resulting DAA–poly(*N*-alkylacrylamide) type gel capsules were washed with methanol in a Soxhlet extractor. They were dried in vacuo at 60 °C to constant weight. The DAA–poly(*N*-alkylacrylamide) type gel capsules that were prepared by this procedure are listed in Table 2.

The gel capsules were neutralized with an acetic acid solution in methanol in a Soxhlet extractor for 2 days, and then washed with methanol in a Soxhlet extractor. The resulting PAA–poly(*N*-alkylacrylamide) type gel capsules were dried carefully and slowly, and finally dried in vacuo at 60 °C to constant weight.

2.5. Measurement of swelling–deswelling rate

A sample was placed in a 50 ml cylindrical cell at the

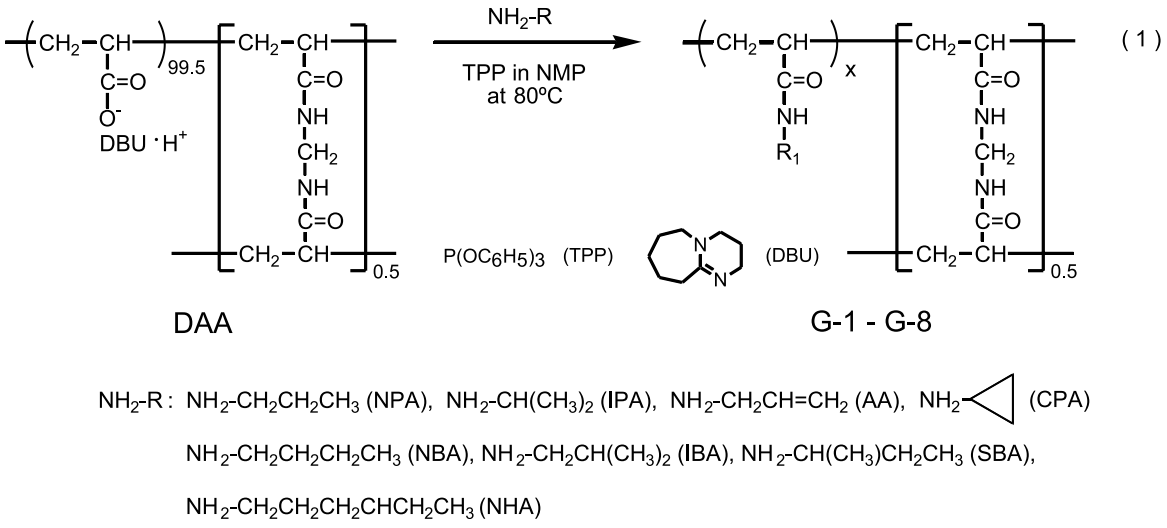

Fig. 2. Synthesis of a poly(*N*-alkylacrylamide) gel via the reaction of DAA with various alkylamines.

desired temperature. The change in external radius (R_t'/R_0'), where $2R_0'$ and $2R_t'$ are the external radii of the gel stored in water at 80 °C and the gel swollen or deswollen after $t=t$ minutes, respectively, was recorded using the digital video camera system described above.

2.6. Measurement of equilibrium swelling ratio

A sample was immersed in water at the desired temperature (the initial temperature was 50 °C). The equilibrium swelling ratio was measured using a previously reported method [6]. The relationship $(W_s+W_p)/W_p$ was used, where W_s and W_p are the weights of absorbed water and dried polymer, respectively.

2.7. Chemical release from the poly(N-alkylacrylamide) gel

The dried gel capsule was dipped in a saturated aqueous solution of methyl orange and allowed to swell for 1 day at 15 °C. The sample was then placed in 50 ml of water at a fixed temperature. The absorbance of the solution at 468.5 nm (A_t) was measured after t minutes by means of a UV spectrophotometer.

2.8. Chemical release from the gel capsule [11b]

The gel capsule was dipped into a solution (0.1 mmol l^{-1}) of methyl orange in methanol–acetone mixture (1:1) and allowed to swell for 1 day at 30 °C. After drying, the shell layer was selectively washed with acetone in a Soxhlet extractor and dried again. The sample was then placed in 50 ml of water. The A_t value was measured, as the temperature was changed stepwise between 15 and 40 °C at 6-h intervals.

3. Results and discussion

3.1. Amidation of DAA with alkylamines

A series of poly(*N*-alkylacrylamide)s could be readily synthesized by the amidation of poly(acrylic acid) with alkylamines, rather than by the polymerization of the corresponding monomers. The quantitative amidation of poly(acrylic acid) is very important in the synthesis of a thermosensitive poly(*N*-alkylacrylamide) because unreacted acrylic acid units and by-products greatly affect the LCST [11]. However, quantitative amidation is difficult

Table 1
Synthesis of poly(*N*-alkylacrylamide) by the reaction of DAA with alkylamine

Run no.	Gel	Alkylamine	Solvent	τ (min)	CA[a] (mol%)
1	G-1	NPA	NMP	1100	99
2	G-2	IPA	NMP	1060	99
3	G-3	AA	NMP	1030	99
4	G-4	CPA	NMP	1080	99
5	G-5	NBA	NMP	1080	
6	G-6	SBA	NMP	1120	
7	G-7	IBA	NMP	1060	
8	G-8	NHA	NMP	1120	

Reaction of DAA was carried out in a solution of TPP (1.0 mol l^{-1}) and alkylamine (2.0 mol l^{-1}) in a solvent (50 ml) at 80 °C.
[a] CA: content of *N*-alkylacrylamide unit, calculated by back-titration.

Table 2
Synthesis of DAA–poly(*N*-alkylacrylamide) type gel capsules by the amidation of DAA with some alkylamines

Run No	Gel capsule	Alkylamine	Solvent	Time (min)	r_t/R_0
9	GC-1	NPA	NMP	55	0.90
10	GC-2	IPA	NMP	55	0.90
11	GC-3	AA	NMP	55	0.90
12	GC-4	NHA	NMP	55	0.90

Reaction of DAA was carried out in a solution of TPP (1.0 mol l^{-1}) and alkylamine (2.0 mol l^{-1}) in a solvent (50 ml) at 80 °C.

to achieve. Previous papers [11,13] reported that the heterogeneous reaction of DAA with IPA using TPP proceeded according to a reaction mechanism that was similar to the unreacted-model [14]; the reaction from the outer region gave a copolymer gel of NIPA with phenyl acrylate through a gel capsule that consisted of an unreacted DAA core and a reacted shell (Fig. 1). The content was dependent on the IPA concentration used, although the apparent rate was independent of the concentration. When a concentration of IPA solution higher than 1.0 mol l^{-1} was used, the amidation proceeded quantitatively. Based on these results, the amidation of a cylindrical DAA (length the same as the diameter; about 5 mm) with various alkylamines (2.0 mol l^{-1}) such as NPA, IPA, AA, CPA, *n*-butylamine (NBA), *sec*-butylamine (SBA), isobutylamine (IBA), and *n*-hexylamine (NHA) was carried out in NMP using TPP at 80 °C (Fig. 2). When DAA was placed in NMP containing an excess amount of alkylamine and TPP, swelling occurred and the gel was divided into a swollen outer shell and an unswollen inner cylindrical core. The characteristics of reaction are the same as that of DAA with IPA [11]. Typical rates of disappearance of the core are shown in Fig. 3. The rate was not affected by the type of alkylamine used because the reaction rate is independent of the concentration. The core disappeared after about 1100 min. The complete reaction with various alkylamines such as NPA, IPA, AA, CPA, NBA, SBA, IBA, and NHA gave samples denoted as G-1, G-2, G-3, G-4, G-5, G-6, G-7, and G-8, respectively (Table 1). Poly(*N*-allylacrylamide) gel cannot be prepared by the polymerization of *N*-allylacrylamide because the radical copolymerization of acryl group and allyl group in *N*-allylacrylamide occur competitively. This is a clear advantage of this synthetic method described herein.

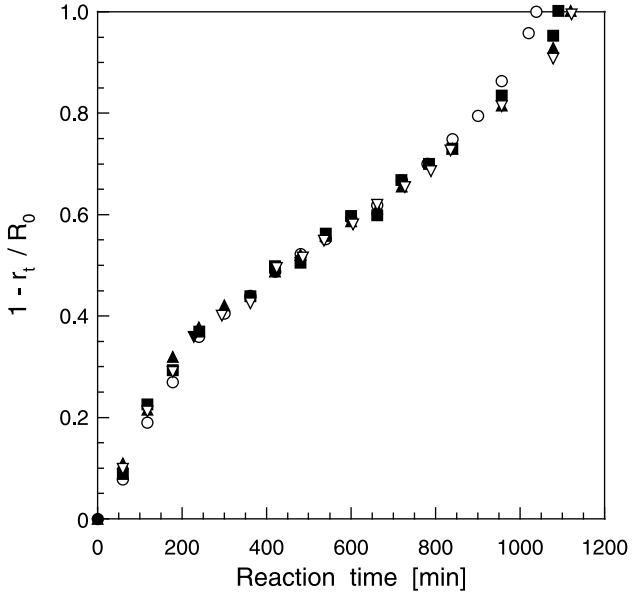

Fig. 3. Typical amidation of a DAA gel with various alkylamines; (■) IPA; (▽) NPA; (○) AA; (▲) CPA.

3.1.1. Characterizations of the amidated gels

IR spectra of typical amidated gels are shown in Fig. 4. The spectrum of the obtained gels showed strong absorptions at 3300 cm^{-1} (N–H, stretching), 1650, 1545

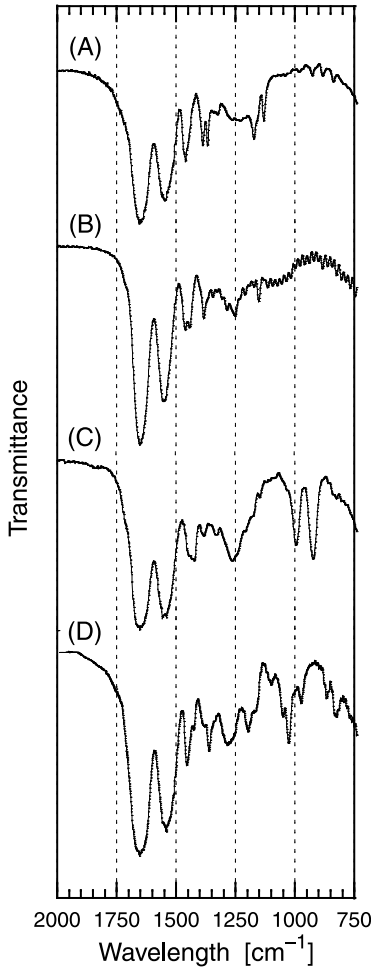

Fig. 4. IR spectra (KBr) of (A) G-2, (B) G-1, (C) G-3, and (D) G-4.

(amides I and II), and no absorption around 1710 cm^{-1} (C=O of carboxylic acid) or 1755 cm^{-1} (C=O of phenyl ester) was detected. The neutralization analysis showed that the amidated gels contain no carboxylic acid groups. Samples G-1, G-2, G-3, G-4, and G-8 showed characteristic absorptions at 1459, 1384, and 1153 cm^{-1} (*n*-propyl group), 1385, 1346, 1173, and 1131 cm^{-1} (isopropyl group), 1422, 1263, 996, and 923 cm^{-1} (allyl group), 1456, 1362, and 1026 cm^{-1} (cyclopropyl group), and 1458, 1378, and 1278 cm^{-1} (*n*-hexyl group), respectively. These results indicate that the amidation was nearly quantitative, giving the corresponding poly(*N*-alkylacrylamide) gels.

3.1.2. Thermal swelling–deswelling behavior of the amidated gels

Poly(*N*-alkylacrylamide)s containing C2–C3 alkyl chains are known to show LCST behavior [8]. However, the swelling behavior of gels is dependent on the network structure. It is difficult to prepare different structures of gels with the same network structure by the polymerization method of a monomer. On the other hand, the gels obtained using this synthetic method had the same network structure because the same lot of DAA was used and a cleavage reaction or crosslinking reaction hardly occurred as a side reaction. This, therefore, permits the effect of alkyl groups in the poly(*N*-alkylacrylamide) gels on the equilibrium swelling ratio to be examined. Equilibrium swelling ratio for G-1–G-4 was measured in water over a wide temperature range. G-8 did not swell in water because it contains hydrophobic *n*-hexyl groups. The $(W_w + W_p)/W_p$ values for G-1–G-4, where W_w and W_p are the weights of absorbed water and dried gel, respectively, was 1.4–2.2, that is, these gels were barely swollen in water at temperatures above the LCST (Fig. 5). When the temperature was lower than the LCST, the gels underwent swelling as they absorbed water, and the equilibrium-swelling ratio increased drastically. Samples G-1, G-2, G-3, and G-4 showed an LCST at about 21, 31, 35, and 43 °C, respectively. These LCSTs were in relative agreement with those of the corresponding soluble polymers [8]. A remarkable feature of the gels is their higher thermosensitivity, compared to the corresponding gels prepared by direct polymerization. The transition occurred within a narrow temperature range (3–4 °C). The equilibrium-swelling ratio is nearly constant at temperatures below the transition. It is well-known that copolymerization gels of NIPA with a comonomer such as butyl methacrylate [9a], phenyl acrylate [11a], sodium acrylate [15], *N*,*N*-dimethylacrylamide [16], *N*-isopropylmethacrylamide [17], or other monomers [18] showed different LCST values from PNIPA gels, and that the LCST is very sensitive to the presence of small amounts of comonomers or impurities. The change in LCST becomes larger with increasing content of comonomer units in the copolymer gel, and the content can become so high that the gel cannot show a high thermosensitivity. These results suggest that the poly(*N*-alkylacrylamide) gels prepared by this method were of high purity. When gels stored in water at 80 °C were placed in water at 15 °C, the deswollen gels began to swell from the outside using the expression R_t'/R_0', where R_0' and R_t' are the external radii of the gel deswollen at 80 °C, the gel swelled in water at 15 °C for *t* minutes, respectively (Fig. 6). All the gels swelled slowly but maintained their cylindrical shape, and reached the equilibrium swelling ratio after 45 h, where they did not swell at a temperature above the LCST. The equilibrium swelling ratio ($R_t'/R_0' = 2.0$) of G-1 (molecular formula of monomer unit: $C_6H_{11}NO$) was the same as that of G-2 (molecular formula of monomer unit: $C_6H_{11}NO$),

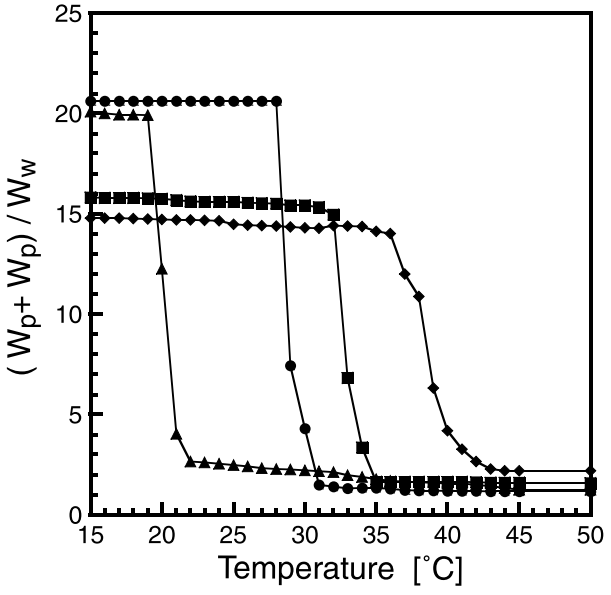

Fig. 5. Equilibrium swelling ratio of poly(*N*-alkylacrylamide) gels in water as a function of temperature; (▲) G-1; (●) G-2; (■) G-3; (♦) G-4.

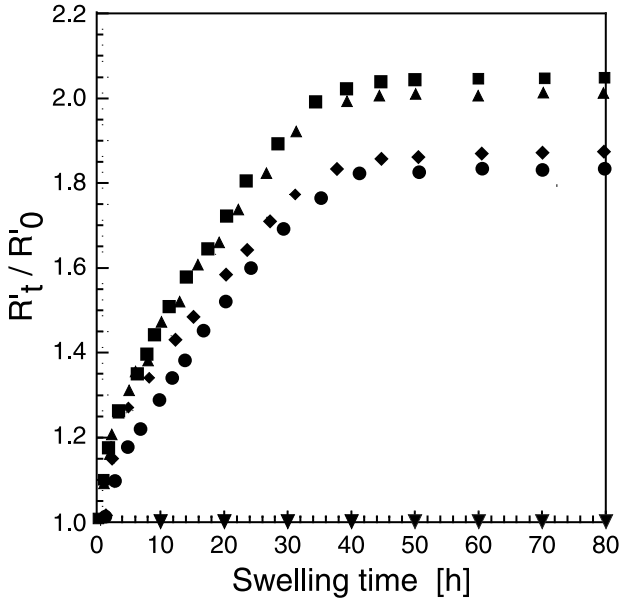

Fig. 6. Swelling of poly(*N*-alkylacrylamide) gels in water at 15 °C; (▲) G-1; (■) G-2; (●) G-3; (♦) G-4; (▼) G-1 (at 40 °C).

and higher than those ($R'_t/R'_0 = 1.75$) for G-3 and G-4 (molecular formula of monomer unit: C_6H_9NO). This results are consistent with the data shown in Fig. 5.

The deswelling of G-1, G-2, and G-3 swollen in water at 15–20 °C was carried out at various temperatures above their LCSTs. When the swollen G-2 gel was dipped in water, a dense skin layer, which functions as a permeability barrier of water is produced. The shrinkage force is so strong that water and chemicals can be ejected from the gel, that is, a squeeze effect. The deswelling rate for G-2 increased with increasing water temperature because the shrinkage force became stronger (Fig. 7(A)). Typical pictures in the deswelling of G-1 are shown in Fig. 8. In the case of G-1, no skin layer was initially formed in water at 21–30 °C. Accordingly, the initial deswelling rate was very fast. A skin layer was immediately produced at temperatures above 35 °C. The rate decreased with increasing water temperature, and the skin layer became so tough that the deswelling was not completed at 50 °C (Fig. 7(B)). When G-3 was left in water at 40 and 45 °C, shrinking occurred, and the resulting skin layer eventually burst because the shrinking face was too strong. Chemical release from G-1 and G-2 swollen in a saturated aqueous methyl orange solution under their LCSTs was examined at various temperatures (Fig. 9). The rate of release of methyl orange from G-2 was the same as that from G-1 at 15 °C. When these gels were dipped in water at 35 °C, the former showed almost the same rate as the latter, although the diffusion was inhibited by the resulting skin layer. At a temperature higher than 35 °C, the former rate was accelerated with increasing shrinkage force, while the latter rate was slowed down and the resulting skin layer completely inhibited the release of dye. These results indicate that the thermal properties of poly(*N*-alkylacrylamide) gels such as swelling–deswelling behavior and the LCST were substantially affected by their chemical structures. These differences are interesting in terms of the design of novel functional polymers.

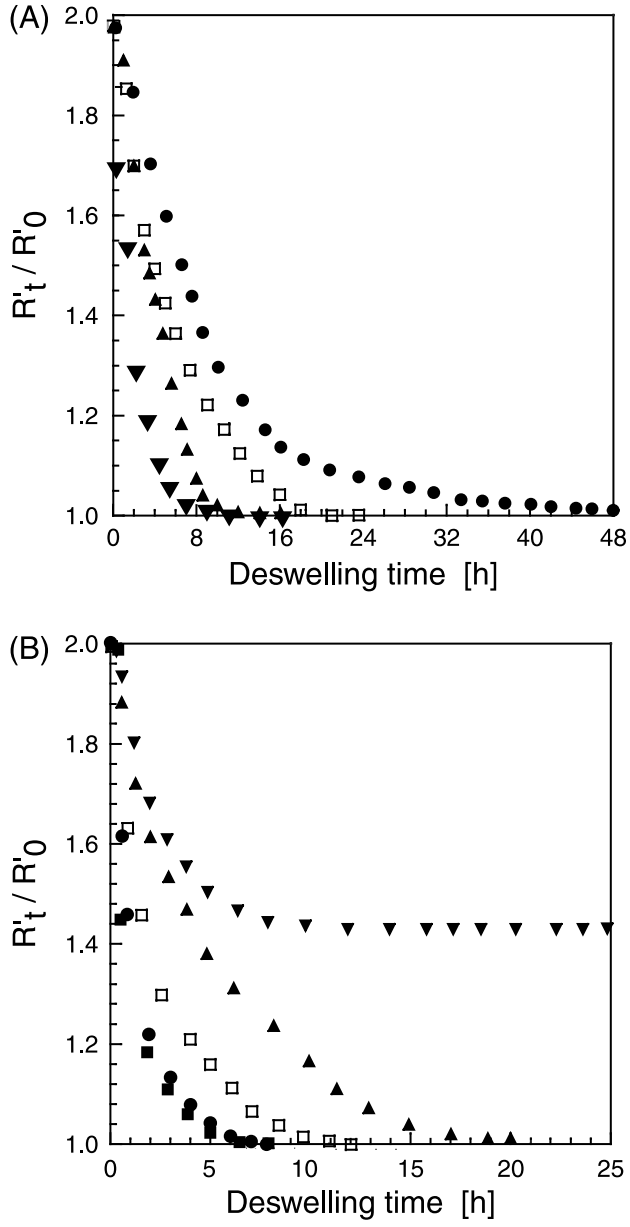

Fig. 7. Deswelling of poly(*N*-alkylacrylamide) gels previously swollen in water at various temperatures. (A) G-2; (●) 25→32 °C; (□) 25→35 °C; (▲) 25→40 °C; (▼) 25→50 °C. and (B) G-1; (■) 15→25 °C; (●) 15→30 °C; (□) 15→35 °C; (▲) 15→40 °C; (▼) 15→50 °C.

3.2. Synthesis of gel capsule

Gel capsules GC-1, GC-2, GC-3, and GC-4 [DAA-poly(*N*-alkylacrylamide) type gel capsules, $r_t/R_0 = 0.90$] were synthesized by the amidation of DAA with alkylamines such as NPA, IPA, AA, and NHA using TPP in NMP at 80 °C for 55 min (Table 2). The neutralization of DAA-poly(*N*-alkylacrylamide) type gel capsules (GC-1, GC-2, and GC-3) with methanol containing a small amount of acetic acid in a Soxhlet extractor gave the corresponding PAA–poly(*N*-alkylacrylamide) type gel capsules (GC-5, GC-6, and GC-7) consisting of a hydrophilic PAA core and a thermosensitive poly(*N*-*n*-propylacrylamide) shell, a poly(*N*-isopropylacrylamide) shell, and a poly(*N*-allylacrylamide) shell, respectively.

3.2.1. Thermal swelling behavior of gel capsule

The DAA–poly(*N*-alkylacrylamide) type gel capsules (GC-1, GC-2, and GC-3) with thermosensitive shell layers are swollen in water at a temperature below their LCSTs, and the shell layers cannot be differentiated from the well-swollen gel capsules. The swelling behavior of typical gel capsules was observed in water at 50 °C (Fig. 10). At a temperature above their LCSTs, the gel capsules are not swollen, since the shell layer became hydrophobic. However, GC-2 underwent rapid swelling in water. GC-1 burst within a few hours, although the poly(*N*-*n*-propylacrylamide) shell layer depressed the swelling of the core. Therefore, the DAA core is too hydrophilic to disturb the

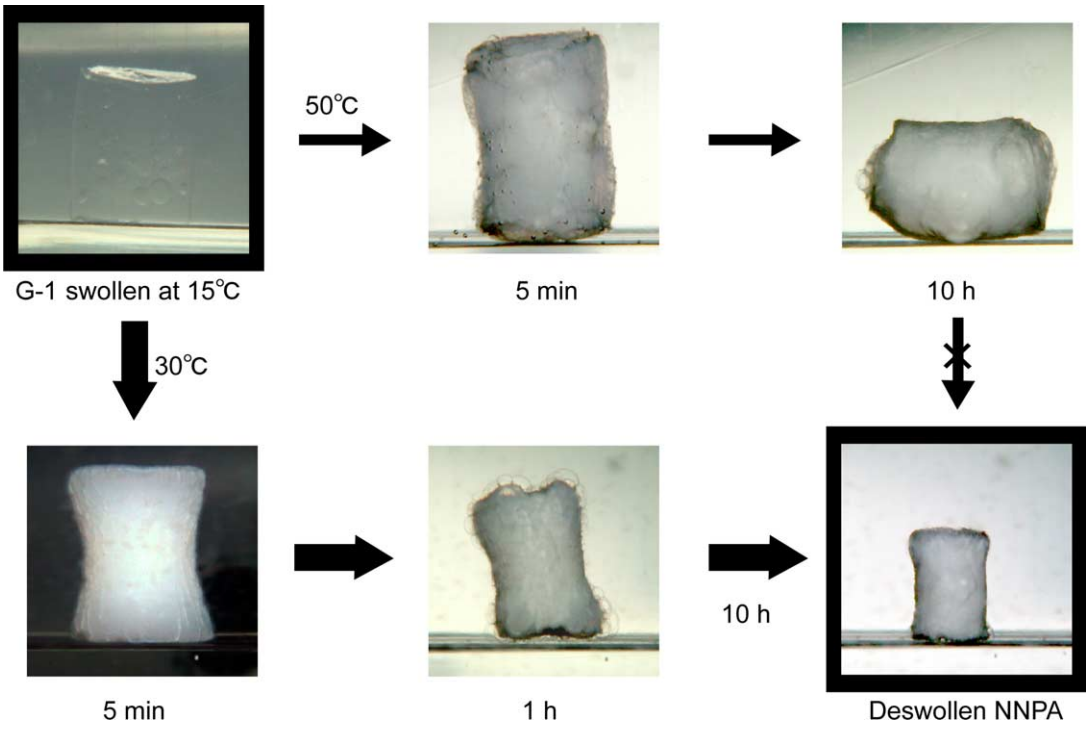

Fig. 8. Typical pictures of the deswelling of G-1.

transition of the thermosensitive poly(*N*-alkylacrylamide) shell layer from hydrophilicity to hydrohobicity. The hydrophobic poly(*N*-*n*-hexylacrylamide) shell layer in GC-4 was able to depress the swelling of the core parts, and the gel capsule underwent only limited swelling in water. This is in contrast to a gel capsule [EGC, $r_t/R_0 = 0.80$] prepared by the esterification of DAA with *n*-hexyl bromide, which consists of a hydrophilic unreacted core part and poly(*n*-hexyl acrylate) shell layer which swelled rapidly and burst within a few hours [10d]. Although the structure of the former shell layer is strikingly similar to the latter shell layer, this difference between amide and ester may be attributed to the strong hydrogen bond of amido groups in the *N*-*n*-hexylacrylamide units.

On the other hand, the PAA–poly(*N*-alkylacrylamide) type gel capsules (GC-5, GC-6, and GC-7) prepared by the neutralization of the corresponding DAA–poly(*N*-alkylacrylamide) type gel capsules swelled only slightly, since the shell layer became hydrophobic at a temperature above the LCST, where the shell layer as well as the core part swelled at a temperature below the LCST. The difference between the two gel states; the swelling state and the deswelling state, was so large that the properties of the shell layer would be expected to change dramatically in response to temperature changes. When a PAA–poly(*N*-alkylacrylamide) type gel capsule with methyl orange in the core part was placed in water, the swelling of the shell layer at 15 °C caused the dye in the core to diffuse through the shell layer and to be release outside. However, the dye was not released when the shell layer was not swollen at 40 °C. Accordingly, at lower temperatures, the release of dye reached a state of 'on' and then a state of 'off' at the higher temperatures. Furthermore, the dye was released from the gel capsule in water when the temperature was changed stepwise between 15 and 40 °C at 6-h intervals (Fig. 11). Swelling of the gel capsule and dye release was not detected at 40 °C. When the temperature was reduced to 15 °C after 6-h, the swelling of gel capsule and the release of dye started, in response to the swelling of the shell layer. When the temperature was raised to 40 °C, the shell layer shrank again. This shrinking caused the swelling of the core part and the release of dye to stop. The same changes were found in response to the stepwise temperature changes. The swelling and deswelling phenomenon of the shell layer acted as a switch for drug release. A similar phenomenon was observed in the release of chemicals from a poly(*N*-isopropylacrylamide) gel [9a] and interpenetrating polymer networks (IPN) composed poly(acrylamide-*co*-butyl methacrylate) and poly(acrylic acid) [19]. The deswelling of these gels that had been swelled in water caused the gels to develop a dense surface skin layer, which functioned the same as the shell layer of the gel capsule. In the many cases, chemicals are rapidly squeezed out of the gel and the gel rapidly shrank to the original size, as was observed for the release of methyl orange (Fig. 9). In contrast, when the PAA–poly(*N*-alkylacrylamide) type gel capsule was placed in water at 40 °C, the core size remained unchanged, although the shell shrank immediately. Thus, in this case, the squeeze effect was very small. Therefore, the PAA–poly(*N*-alkylacrylamide) type gel capsule is different from poly(*N*-

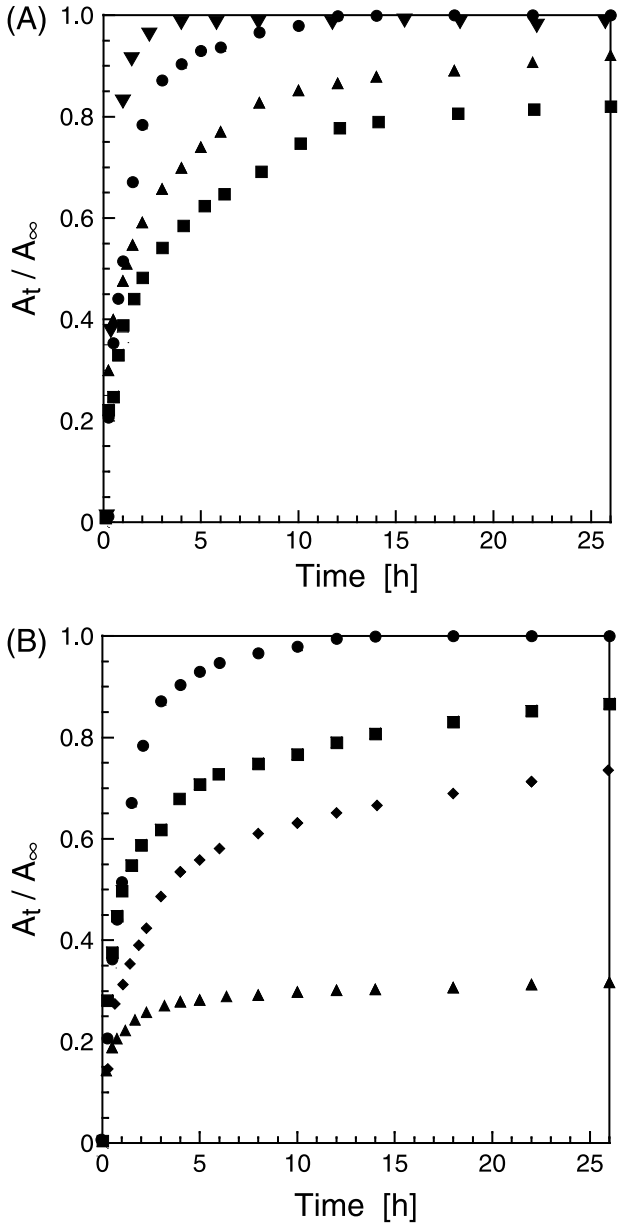

Fig. 9. Chemical release of methyl orange from (A) G-2 and (B) G-1 in water. (A) G-2; (●) 15 °C; (■) 15→35 °C; (▲) 15→40 °C; (♦) 15→50 °C, and (B) G-1; (●) 15 °C; (■) 15→35 °C; (♦) 15→40 °C; (▲) 15→50 °C.

isopropylacrylamide) gel and IPN gels in terms of swelling–deswelling characteristics as a function of temperature. These results suggest that the PAA–poly(*N*-alkylacrylamide) type gel capsule might be useful for use as a novel thermosensitive drug carrier.

4. Conclusion

1. The amidation of DAA with C3–C6 alkylamines proceeded quantitatively at 80 °C in the presence of TPP to give the corresponding poly(*N*-alkylacrylamide) gels with the same network. The reaction was not affected by the type of alkylamine used.
2. The saturated equilibrium swelling ratio of G-1

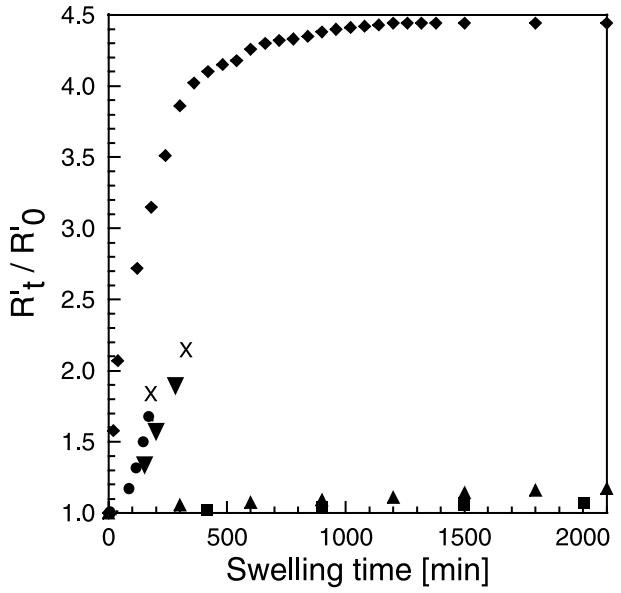

Fig. 10. Swelling behavior of typical gel capsules in water at 50 °C; (▼) GC-1; (♦) GC-2; (▲) GC-4; (■) GC-5; (●) EGC (gel capsule prepared by the esterification of DAA with *n*-hexyl bromide). The X mark denotes the occurrence of burst.

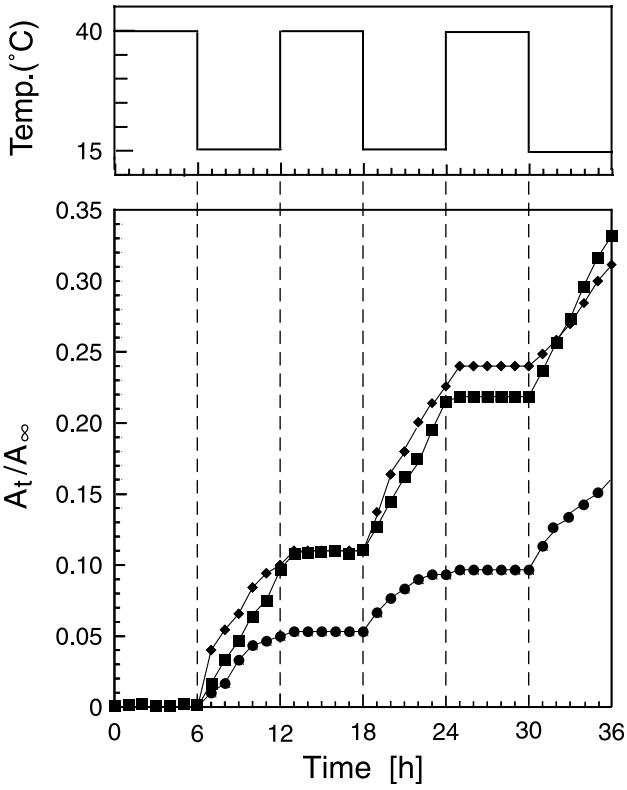

Fig. 11. Methyl orange release profiles from a PAA–poly(*N*-alkylacrylamide) type gel capsule in response to the stepwise change in temperature; (●) GC-5; (■) GC-6; (♦) GC-7.

(molecular formula of monomer unit: $C_6H_{11}NO$) was the same as that for G-2 (molecular formula of monomer unit: $C_6H_{11}NO$), and higher than those for G-3 and G-4 (molecular formula of monomer unit: C_6H_9NO). G-1, G-2, G-3, and G-4 showed LCST at about 21, 31, 35, and 43 °C, respectively.

3. The DAA–poly(*N*-alkylacrylamide) type gel capsules consisting of an unreacted DAA core and an amidated shell were synthesized by the amidation of DAA with alkylamines using TPP at 80 °C for 55 min. The DAA core was so hydrophilic that the thermosensitive poly (*N*-alkylacrylamide) shell layer was barely able to function as a permeability barrier for water when the gel was place in water at a temperature above the LCST.
4. PAA–poly(*N*-alkylacrylamide) type gel capsules were prepared by the neutralization of the corresponding DAA–poly(*N*-alkylacrylamide) type gel capsules. The shell layer functioned as a permeability barrier to chemicals in water at a temperature above the LCST. In addition, the gel capsules showed on–off chemical release characteristics, in response to stepwise temperature changes across the LCST of the shell layer.

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