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Rapid temperature/pH response of porous alginate-*g*-poly(*N*-isopropylacrylamide) hydrogels

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Abstract

To improve the swelling and deswelling rate, comb-type macroporous hydrogels were prepared. The temperature-sensitive poly(*N*-isopropylacrylamide) (PNIPAAm) was grafted on the surface or bulk of the pH-responsive alginate. The larger surface area in pores and free chain mobility by comb-type graft copolymer reached its equilibrium swollen state within a minute. The swelling ratio of porous hydrogel in equilibrium state was over fifteen times greater than that of nonporous hydrogels. The increase of surface area by pores caused water molecules to transfer easily in and out of the matrix, resulting in a rapid deswelling. The degree of change in swelling ratio during deswelling might be affected by the phase transition behavior of PNIPAAm attached on only the surface of the pore rather than PNIPAAm grafted into mainchain of alginate. Surface-grafted alginate/PNIPAAm gels had a suitable mechanical strength without collapsing during the repeatable shrinkage and expansion due to swelling and deswelling, whereas bulk-grafted gels easily collapsed.

Keywords: Alginate; *N*-isopropylacrylamide; Porous hydrogel

1. Introduction

Hydrogels are hydrophilic three-dimensional polymer networks capable of absorbing a large volume of water or other biological fluid. Stimuli-sensitive hydrogels have the capability to change their swelling behavior, permeability or mechanical strength in response to external stimuli, such as small changes in pH, ionic strength, temperature and electromagnetic radiation [1–4]. Because of these useful properties, hydrogels have numerous applications, and they are particularly used in the medical and pharmaceutical fields [1–2,5].

Conventional hydrogels are limited by their slow swelling and deswelling rates [6], and new methods to prepare hydrogels have been investigated to enhance the swelling and deswelling rates. One approach was to synthesize comb-like hydrogels by graft copolymerization. The grafted hydrogel showed advantageous swelling kinetics in comparison with conventional hydrogels, owing to the free mobility of the grafted chains [1,7–9]. Another method used was to prepare a hydrogel that contained pores in the matrix. The formation of a porous structure facilitated the migration of water through the large surface area contained within the pores. Several reports in the literature describe the preparation of porous hydrogels, including the incorporation of surfactants during hydrogel preparation and their subsequent extraction [10–12], hydrogel preparation above its lower critical solution temperature (LCST) [13–15], preparation using freeze-drying, gas forming [16], and by other means [6,17–19]. Therefore, it can be anticipated that the preparation of comb-type graft hydrogels containing macropores would enhance the kinetics of the swelling-deswelling process because of the synergistic effect of the two types of hydrogel present. Unfortunately, to date, there have been no reports on porous comb-type hydrogels.

The thermosensitive hydrogel, poly(*N*-isopropylacrylamide) (PNIPAAm), is well known as the best candidate material for this task, owing to its LCST behavior around 32 °C in aqueous solution. In water, PNIPAAm chains hydrate to form an expanded structure when the temperature is kept below the LCST, with the PNIPAAm chains forming

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a more compact structure by dehydrating when heated above the LCST [1,20]. For pH-sensitive hydrogels, alginate can be used to form the mainchain, because of the carboxyl groups present in the alginate mainchain. Alginate is also useful for preparing hydrogels owing to the following properties: (i) it has a relatively inert aqueous environment within the matrix, (ii) it has a high gel porosity that allows for high diffusion rates of macromolecules, and (iii) its dissolution and biodegradation under normal physiological conditions enables it to be used as a matrix for the entrapment and delivery of proteins, drugs and cells [1,21–23]. In particular, porous hydrogels composed of alginate mainchains may overcome the main disadvantage of hydrogels composed of PNIPAAm, in that they are mechanically weak [18].

The goal of this study was to prepare porous alginate/PNIPAAm comb-type graft hydrogels using NaCl particles as a porogen. The difference in swelling behavior is discussed by considering bulk-grafting and surface-grafting PNIPAAm hydrogels onto the alginate. The effect of the grafted PNIPAAm and the porosity of the hydrogel are taken into account when discussing the degree of swelling.

2. Experimental

2.1. Materials

The *N*-isopropylacrylamide (NIPAAm) (Aldrich Chemicals, Milwaukee, WI, USA) used was purified by recrystallization from *n*-hexane/toluene (Duksan Pure Chemicals, Seoul, Korea). Sodium alginate (mannuronate/gluronate (*M*/*G*) ratio of the alginate = 1.56) and 2-aminoethanethiol hydrochloride (AESH) were purchased from Aldrich Chemicals. The molecular weight distribution of the alginate was determined using gel permeation chromatography (GPC, Waters Model 510 HPLC pump, Milford, MA, USA) in water using the Millennium software program. The number-average (M_n) and weight-average (M_w) molecular weights were 339,000 and 1,073,000, respectively. 1-Ethyl-(3-3-dimethylaminopropyl) carbodiimide hydrochloride (EDC) and *N*-hydroxysuccinimide (NHS) were purchased from Sigma Chemicals (St. Louis, MO, USA). *N*,*N*′-azobisisobutyronitrile (AIBN) (Aldrich Chemicals) was recrystallized from methanol (Duksan Pure Chemicals), and *N*,*N*-dimethylformamide (DMF) (Duksan Pure Chemicals) was purified by distillation. The sodium chloride, calcium chloride ($CaCl_2$), tetrahydrofuran (THF) and ethyl ether (Duksan Pure Chemicals) were used as purchased without any further purification. The water used in the experiments was first treated using a reverse osmosis system (Sambo Glove, Ansan, Korea), and then further purified using a Milli-Q Plus system (Waters, Millipore, MA, USA).

2.2. Synthesis of semi-telechelic PNIPAAm-NH_2

Amino semi-telechelic PNIPAAm was synthesized by radical polymerization using AESH as the chain transfer agent, and AIBN as an initiator. The synthesis and characterization were performed using the same procedure as described in our previous work [1]. To quantitatively determine the incorporation of terminal amino groups of PNIPAAm-NH_2, non-aqueous potentiometric titration method was used [8]. Semi-telechelic PNIPAAm-NH_2 (0.2 g) was dissolved in 20 ml acetic acid, and titrated with 0.1 M perchloric acid–acetic acid standard solution using crystal violet as an indicator.

2.3. Preparation of macroporous alginate hydrogels

To prepare macroporous alginate hydrogels, the alginate was dissolved in water to prepare a 5 wt% (w/w) aqueous solution. Then, NaCl crystals (diameter = 100–300 μm) corresponding to 25–50 wt% of the solute were added into the solution. This solution was homogeneously mixed at room temperature, poured into a petri-dish and freeze-dried. To crosslink the alginate, the sample containing the NaCl crystals was immersed in 5 wt% aqueous $CaCl_2$ solution for 20 min at room temperature, and then washed with water. During this time, the NaCl crystals were removed from the matrix, and pores formed in the sites occupied by the NaCl crystals. The sample containing the newly-formed pores was freeze-dried to support the pore structure. Fig. 1 schematically describes the procedure in preparing the macroporous hydrogels including the surface- and bulk-grafted hydrogels.

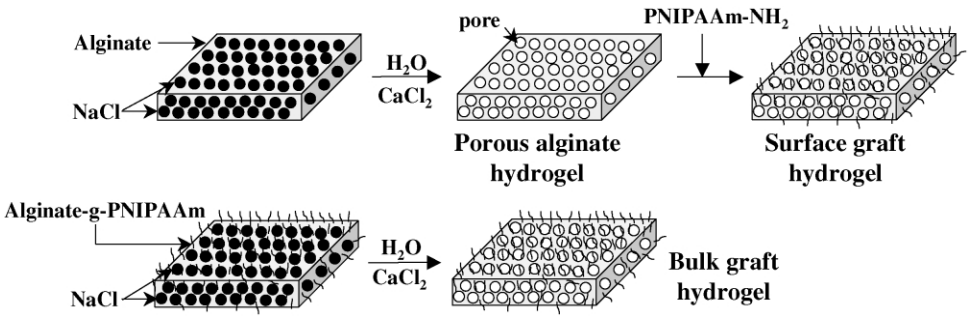

Fig. 1. Schematic illustration of the preparation of porous hydrogels.

Table 1
The composition and designation of each sample

Hydrogel type	Sample code	Added NaCl weight ratio[a] (wt%)	Weight ratio (wt%)	
			Alginate	PNIPAAm-NH_2
Alginate matrix	A-0	0	100	0
	A-25	25		
	A-50	50		
Surface graft	S-0	0	50	50
	S-25	25		
	S-50	50		
Bulk graft	B-0	0	50	50
	B-25	25		
	B-50	50		

[a] (Weight of NaCl/total weight of alginate and PNIPAAm) × 100.

2.4. Preparation of macroporous alginate-g-PNIPAAm-NH_2 hydrogels—bulk graft

Alginate and PNIPAAm-NH_2 (3 wt%) were dissolved in water at room temperature. EDC and NHS were added to the solution to form amide bonds between the alginate carboxyl groups and the PNIPAAm-NH_2 amino groups. The solution had an alginate/PNIPAAm weight ratio of 1:1, and an alginate/EDC/NHS molar ratio of 2:2:1 with reference to the alginate carboxyl group. The mixed solution was continuously stirred overnight at room temperature. After precipitation, using a THF–hexane solution (4:1), the reactant was following by a Soxhlet extraction with methanol, dialyzed for two days in water, and then freeze-dried. The procedure used to generate macroporosity was the same as that described above (see Table 1).

2.5. Preparation of PNIPAAm-NH_2 surface-grafted hydrogels on macroporous alginate matrix—surface graft

To graft PNIPAAm-NH_2 onto the macroporous alginate matrix, the porous alginate matrix ($1.0 \times 1.0\ cm^2$) was immersed in the PNIPAAm-NH_2 solution (5 wt%). EDC and NHS were added to the solution at room temperature. The solution had an alginate/PNIPAAm weight ratio of 1:1, and an alginate/EDC/NHS molar ratio of 2:2:1, with reference to the alginate carboxyl group. The PNIPAAm solution containing the porous matrix was slowly shaken overnight at room temperature. After the surface graft, any unreacted PNIPAAm-NH_2 and alginate were removed using Soxhlet's extractor with methanol for three days, and lyophilized.

2.6. Evaluation of cross-linking

To measure the ionically bound calcium ions, the hydrogels were treated with a 0.1N HCl solution for liquefying the hydrogels. Then, the amount of Ca^{2+} ions incorporated in the carboxyl groups of alginate in the hydrogels was determined by measuring atomic absorbance at 422.7 nm using the NO-C_2H_2 gas flame method on an atomic absorption analyzer (SpectraAA 220 FS, Varian, Victoria, Austalia). A calibration curve was obtained using $CaCl_2$ standard solution with an appropriate dilution.

2.7. Morphologies of the hydrogels

The morphologies of hydrogels were studied using a field emission scanning electron microscope (FE-SEM, JEOL-6340F, Kyoto, Japan) using an operating voltage of 5 kV. Specimens were fixed on brass holders and coated with Pt prior to SEM observation. The porosity of the hydrogels was measured using image analyzer (Bum-Mi Universe Co., Ltd., Seoul, Korea).

2.8. Measurement of graft yield and swelling ratio

The graft yield, based on the weight change, was calculated using the following equation

$$\text{Graft yield(wt\%)} = [(W_2 - W_1)/W_1] \times 100 \quad (1)$$

where W_1 is the weight of alginate before grafting, and W_2 is the total weight after grafting PNIPAAm-NH_2 onto alginate mainchain.

A swelling study was conducted on the porous alginate/PNIPAAm-NH_2 hydrogels to observe the behavior as functions of the temperature and pH of the swelling medium. The swelling ratio was calculated using the following formula

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

where, W_s is the weight of hydrogel in the swollen state at a particular temperature, and W_d is the dry weight of the hydrogel. To measure the swelling ratio, pre-weighed dry samples were immersed in water. After wiping off the excessive water on the samples' surface using moistened filter paper, the weight of the swollen samples was measured in the temperature range 20–50 °C, and in the pH range

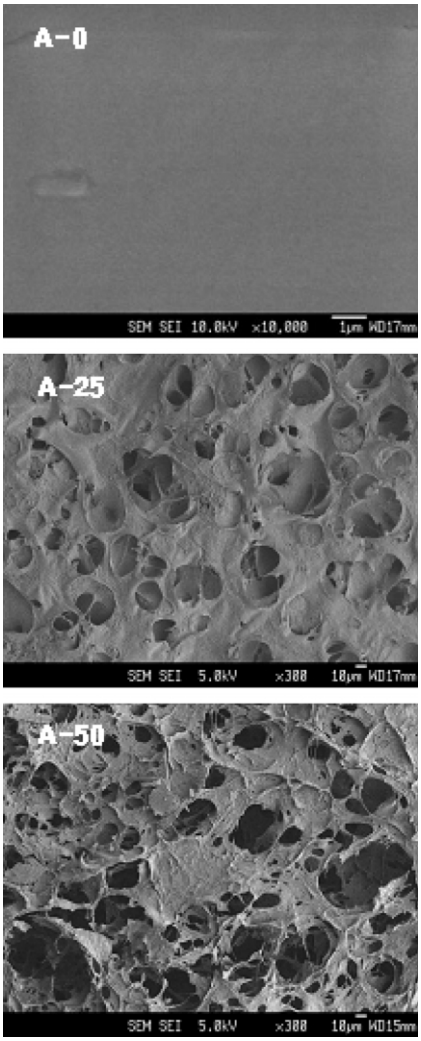

Fig. 2. Surface morphologies of the alginate matrix with various NaCl weight ratios as shown in Table 1.

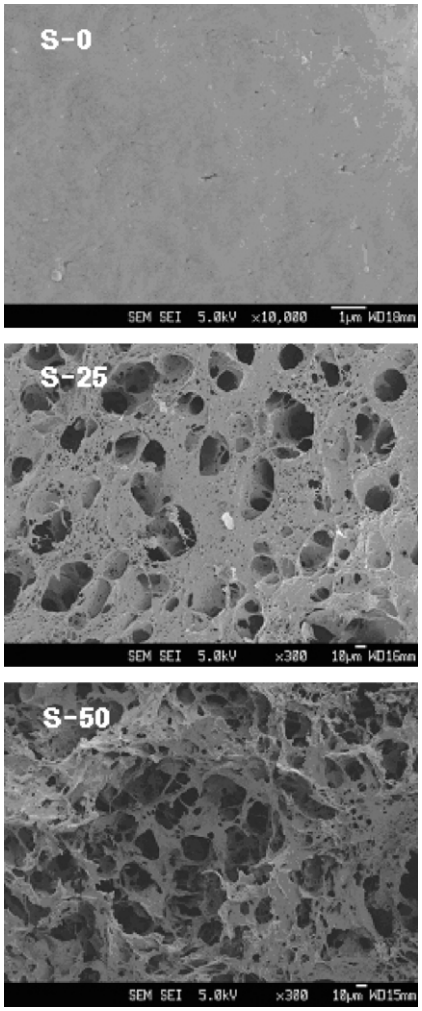

Fig. 3. Surface morphologies of the surface-grafted hydrogels with various NaCl weight ratios as shown in Table 1.

from 2 to 7. The swelling ratio was monitored until there was no further change in weight in the solution.

2.9. Measurement of the deswelling, reswelling and pulsatile kinetics

The deswelling kinetics were measured using a rapid increase in temperature of the samples from the equilibrated swollen state at 25 °C by immersion in hot water at 45 °C. The reswelling kinetics were determined by transferring the deswelled sample from the solution at 45 °C to that at 25 °C. During the deswelling and reswelling processes, the weight change of the hydrogels was recorded at five-minutes intervals. The pulsatile swelling behavior was observed in deionized water maintained at alternate temperatures of 25 and 45 °C, and in buffer solutions with pH values between 2 and 7. The weight of the hydrogels in the different temperature and pH solutions was measured every 5 min.

3. Results and discussion

3.1. Preparation of macroporous hydrogels

To obtain free and mobile grafted chains, a comb-type hydrogel graft composed of alginate and PNIPAAm-NH_2 was prepared composed of the amide bonds formed between the carboxyl group of the alginate and the amino groups of the PNIPAAm-NH_2.

The macroporous hydrogels were synthesized using the same salt-leaching method that has frequently been employed in the preparation of scaffold for tissue engineering. Macropores were formed from NaCl particles that did not react with the functional groups or chemicals. The porosity and particle size of the hydrogel were regulated by the number and size of the NaCl particles. Usually, NaCl content exceed the saturation concentration, and it existed as solid particles in the mixing solution. Some NaCl was dissolved in the mixing solution, and was recrystallized as solid particles in the matrix during solvent evaporation. Excess and recrystallized NaCl particles were washed out

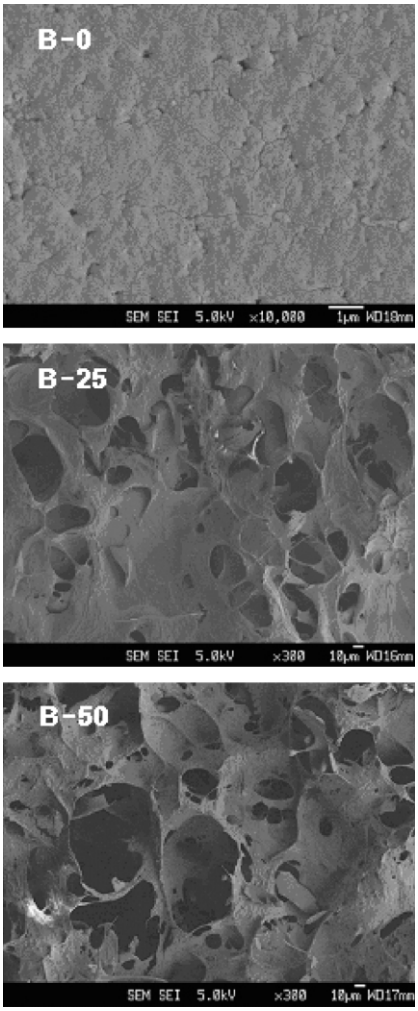

Fig. 4. Surface morphologies of the bulk-grafted hydrogels with various NaCl weight ratios as shown in Table 1.

Table 2
Graft yield and porosity of alginate, surface, and bulk-grafted hydrogels

Sample code	Graft yield (wt%)	Porosity[a] (%)	
		Surface	Cross-section
A-0	–	–	–
A-25	–	42.74	46.00
A-50	–	51.08	58.51
S-0	7.45	–	–
S-25	8.64	38.16	40.64
S-50	20.13	53.21	53.00
B-0	77.12	–	–
B-25	77.12	45.54	46.75
B-50	77.12	50.95	52.73

[a] Porosity was obtained by estimating the area between the pore zone and the matrix zone using the image analyzer program.

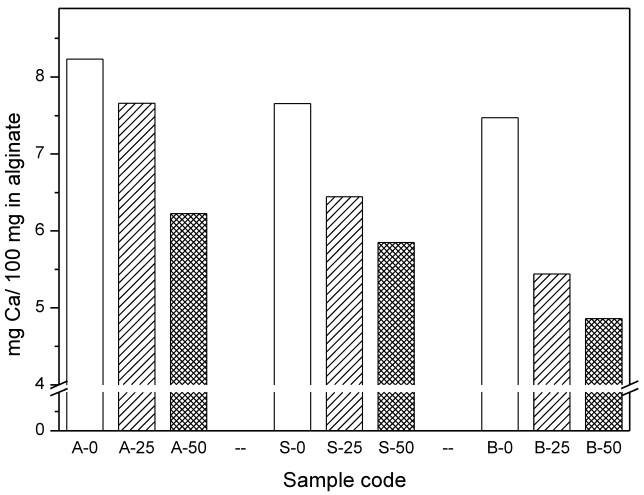

Fig. 5. Ca^{2+} ions contents incorporated in the carboxyl groups of alginate in hydrogels (atomic absorbance at 422.7 nm using the NO-C_2H_2 gas flame method on an atomic absorption analyzer).

either during, or after the crosslinking process of the matrix. From this procedure, macropores formed in the spaces previously occupied by the NaCl particles.

3.2. Surface morphology, graft yield and cross-linking density of the hydrogels

Figs. 2–4 show the surface morphology of the hydrogels. Macropores were observed in the hydrogels prepared by the salt-leaching method, whereas hydrogels prepared without using NaCl had a dense surface without any pores. From this result, it was deduced that macroporous hydrogels could be successfully prepared using the salt leaching technique, and that the porosity depended on the mass of salt added, as shown in Table 2.

To covalently graft the PNIPAAm on the carboxyl groups of alginate, amino-terminated PNIPAAm was prepared by radical polymerization using AESH, as a chain transfer agent. The efficiency of PNIPAAm possessing the amino end groups was 91%, which was determined by comparing the molecular weight of PNIPAAm measured from GPC with the amino-group contents obtained from titration assay. Table 2 shows the graft yield and porosity of alginate, surface- and bulk-grafted hydrogels. Particularly in the surface grafts, the weight ratio of NaCl particles in the alginate matrix significantly affected the grafting reaction of the PNIPAAm on the porous surface of alginate matrix, indicating that the graft yield increased with the porosity of hydrogels due to the increase of the area of surface on which the PNIPAAms were attached.

Fig. 5 shows the Ca^{2+} ion content bounded on the carboxyl groups of the alginate in the hydrogel. Sample A-0 possesses relatively high Ca^{2+} ion content rather than samples S-0 and B-0 due to the absence of grafted PINPAAm. Also, samples A-0, S-0 and B-0 without salts have more Ca^{2+} incorporated in the alginate of hydrogel

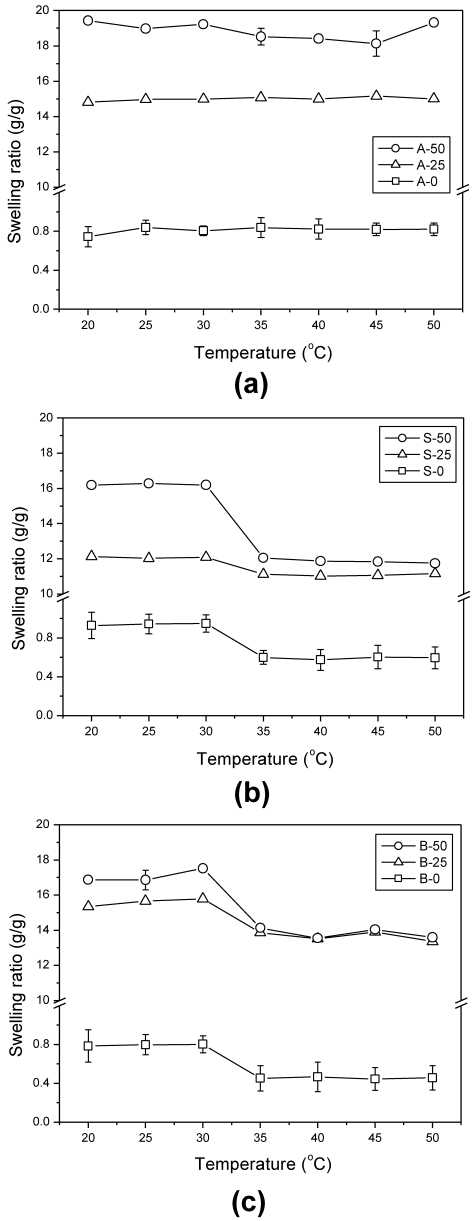

Fig. 6. Swelling ratio of (a) alginate hydrogels (A-0, A-25 and A-50), (b) surface graft hydrogels (S-0, S-25 and S-50) and (c) bulk graft hydrogels (B-0, B-25 and B-50) as a function of temperature in distilled water (pH 5.4).

than with NaCl particles because Na^+ ions affect on reducing the number of cross-linkable guluronate carboxyl groups. It means that Na^+ ions released from NaCl particles upon immersing the hydrogels containing NaCl particles in $CaCl_2$ aqueous solution to cross-link interrupt the formation of calcium-alginate hydrogels due to ion exchange reaction between Ca^{2+} and Na^+. For this reason, the amount of Ca^{2+} ions in the alginate rapidly decreases when there exists NaCl in calcium-alginate hydrogels.

3.3. Temperature/pH-dependant swelling behavior

Fig. 6 shows the temperature-dependant swelling of the hydrogels when the temperature of the aqueous media increased from 20 to 50 °C. The swelling ratio of the surface and bulk-grafted hydrogels decreased dramatically between 30 and 35 °C, whereas the swelling ratio of the alginate hydrogels that did not contain PNIPAAm was not affected by the temperature change. This effect arose because of the temperature-responsive properties of PNIPAAm around the LCST (32 °C).

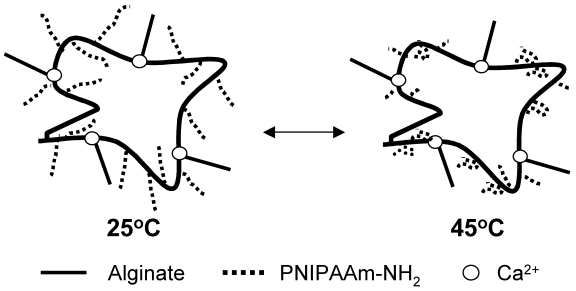

Fig. 7. Schematics of alginate/PNIPAAm-NH_2 come-type graft hydrogel according to the change of temperature.

The temperature sensitivity of the hydrogels was dependent upon the porosity and PNIPAAm content of the hydrogel. In this case, the pores enhanced the uptake of water during swelling and deswelling when compared with the nonporous hydrogels. The dimensions of all porous hydrogels did not change so much during the temperature sensitive swelling measurement because alginate that did not have the temperature sensitivity was used as a framework of hydrogel. Thus, it was considered that swelling/deswelling kinetics of the hydrogels were dependent upon the intrinsic thermal behavior of grafted PNIPAAm with free end side, as shown in Fig. 7.

Fig. 8 shows that the swelling ratio of the alginate, and the surface and bulk-grafted hydrogels continuously increases, regardless of the existence of pores, as the pH value of the solution increases. This was mainly attributed to the carboxylic acid groups of the alginate network. Below the pK_a value of alginate (pK_a of guluronic acid residue is 3.2, and that of mannuronic acid residue is 4), the carboxylic acid groups transform into the ionized form (COO^-) as the pH value of the buffer solution increases. The electrostatic repulsion between the ionized groups causes the hydrogels to swell [1,21–23].

3.4. Swelling–deswelling–reswelling kinetics

Fig. 9 shows the swelling–deswelling–reswelling kinetics of the alginate and surface and bulk-grafted hydrogels. Note that the macroporous hydrogels reached their equilibrium swollen state within 1 min, whereas the swelling of a conventional hydrogel would take at least several hours to reach the equilibrium state [1,6]. Also, the swelling ratio of the macroporous hydrogels at the equilibrium state was over 15 times greater than that of the nonporous hydrogels, because the porous hydrogels had reservoirs formed by the vacant pore volume.

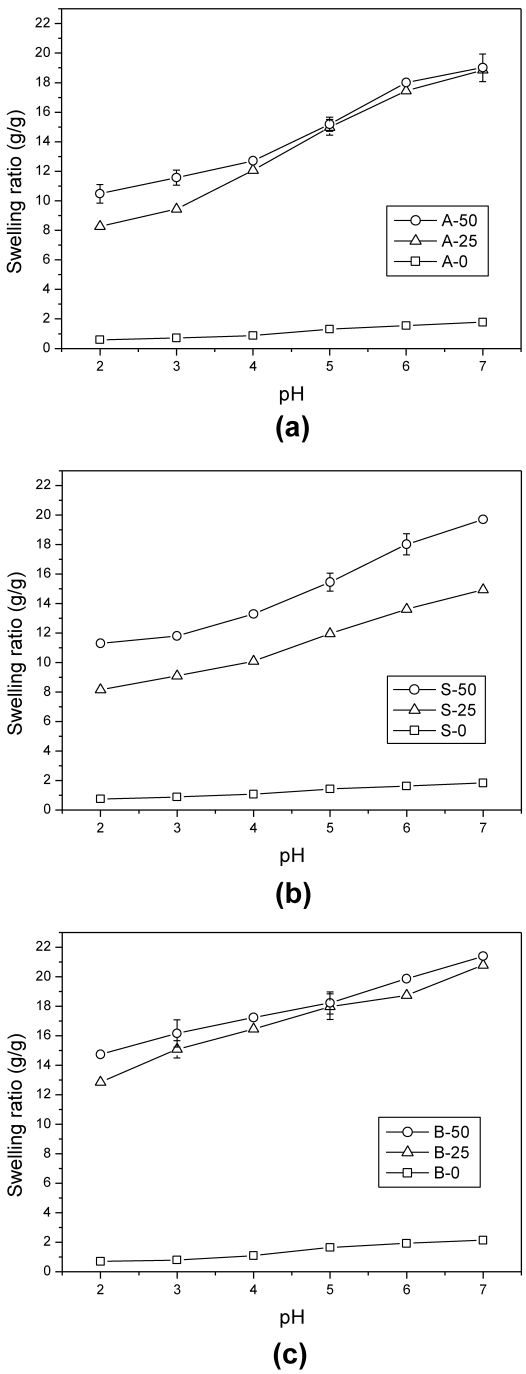

Fig. 8. pH-dependent swelling behavior of (a) alginate hydrogels (A-0, A-25 and A-50), (b) surface-grafted hydrogels (S-0, S-25 and S-50) and (c) bulk-grafted hydrogels (B-0, B-25 and B-50) at 25 °C.

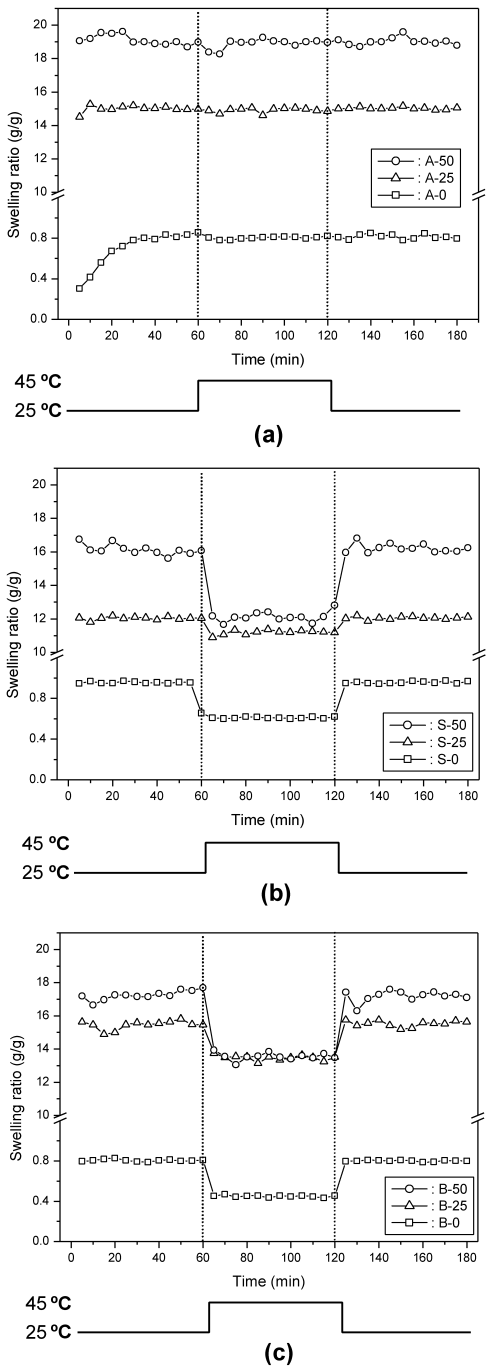

Fig. 9. Swelling–deswelling–reswelling kinetics of (a) alginate hydrogels (A-0, A-25 and A-50), (b) surface-grafted hydrogels (S-0, S-25 and S-50) and (c) bulk-grafted hydrogels (B-0, B-25 and B-50) in distilled water (pH 5.4).

In regard to the deswelling kinetics, during the initial deswelling stage, the conventional gels undergo phase separation and shrink in surface area. The skin forms a dense layer and entraps water inside the gels, preventing heat and mass transfer from the aqueous medium to the inner part of the hydrogel [9]. However, in the case of the porous hydrogels, it was possible for the water molecules to rapidly transfer through the macropores into the innermost matrix, even though phase separation had occurred on the surface, and this resulted in a rapid deswelling.

As shown in Fig. 9(a), the alginate matrix that did not contain PNIPAAm exhibited a rapid swelling to reach the equilibrium state. However, the swelling ratio was not affected by a change in temperature owing to the absence of PNIPAAm. On the other hand, the surface- and bulk-grafted

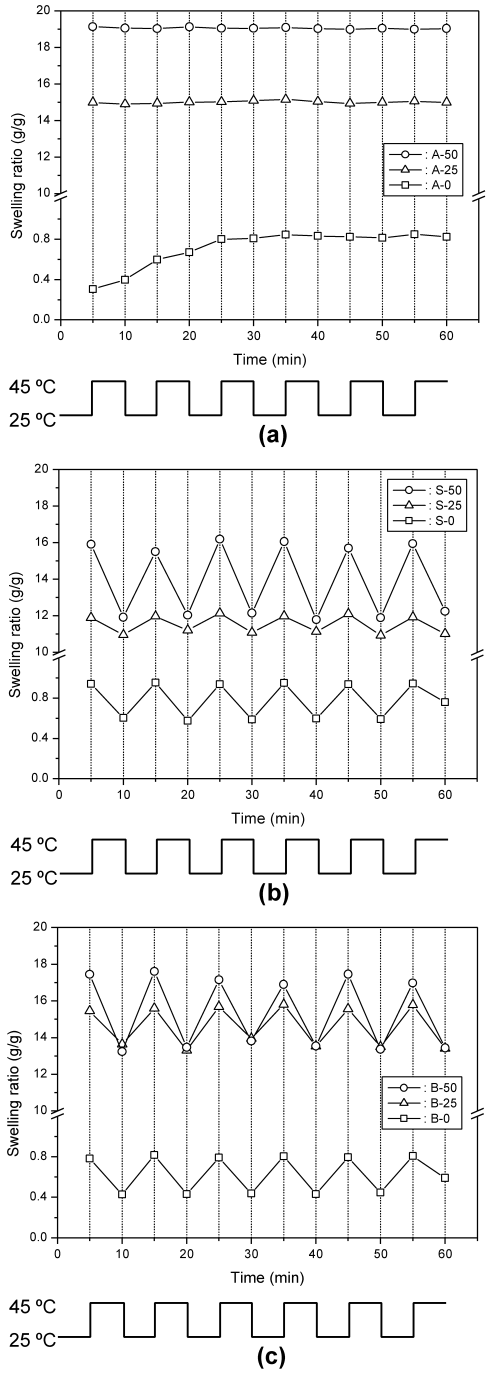

Fig. 10. Pulsatile swelling behavior of (a) alginate hydrogels (A-0, A-25 and A-50), (b) surface-grafted hydrogels (S-0, S-25 and S-50) and (c) bulk-grafted hydrogels (B-0, B-25 and B-50) in response to temperature changes between 25 and 45 °C in distilled water (pH 5.4).

hydrogels that had macropores showed a drastic decrease in their swelling ratios during the deswelling process. The nonporous surface- and bulk-grafted hydrogels showed sensitivity to temperature change because of the presence of PNIPAAm. However, the degree of swelling of the nonporous graft hydrogels was much smaller than that of the porous hydrogels.

Fig. 9(b) and (c) show the more acute volume shrinkage

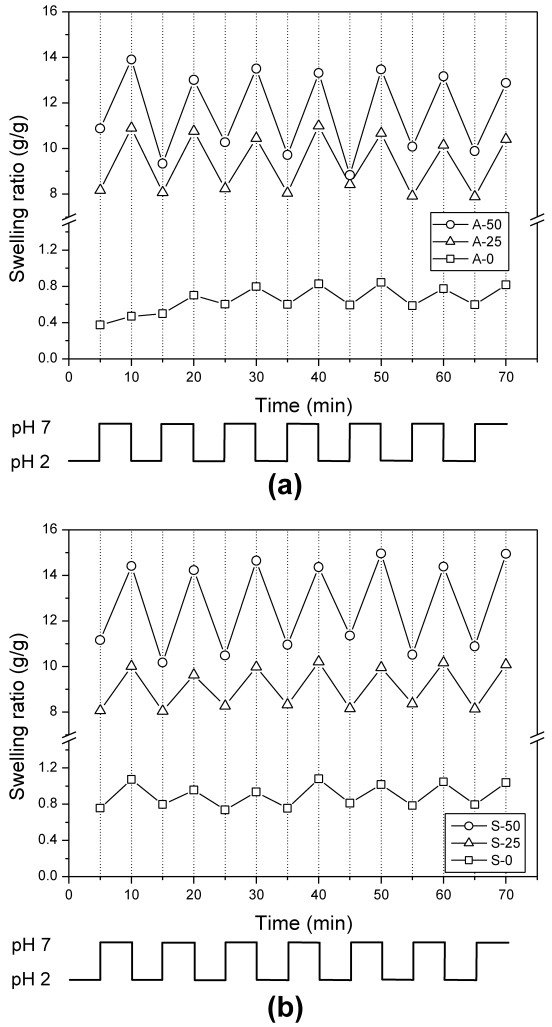

Fig. 11. Pulsatile swelling behavior of (a) alginate hydrogels (A-0, A-25 and A-50) and (b) surface-grafted hydrogels (S-0, S-25 and S-50) in response to pH changes between pH 2 and 7 at 25 °C.

in the deswelling behavior of the PNIPAAm grafted porous hydrogels. It is assumed that the PNIPAAm content and the porosity (see Table 2) of the porous hydrogels affected the degree of change in the swelling ratio.

The bulk-grafted hydrogels (B-0, B-25 and B-50) have the grafted PNIPAAm both on surface and in bulk states. However, PNIPAAm content on the surface of B-0 is smaller than that of B-25 and B-50 which are more porous, even though the bulk-grafted hydrogels contain the same PNIPAAm content. Thus, a small amount of PNIPAAm on the surface in B-0 is responsible for a slight change of swelling ratio, compared with B-25 and B-50. In addition, the porous hydrogel sample S-50, showed an enhanced degree of change in its swelling ratio in comparison with sample S-25, because it had more PNIPAAm attached to its surface of pores. Sample S-50 showed sharper change of swelling ratio than that of sample B-25, even though the content of grafted PNIPAAm on the alginate was relatively small. Also, sample B-50 showed a similar degree of transition as sample S-50, because of the similar porosity

of the two hydrogels. Thus, it was found that the degree of change in the swelling ratio during deswelling was affected by the phase transition behavior of the PNIPAAm attached only on surface of pore rather than PNIPAAm grafted onto the alginate mainchain.

In the reswelling process, the swelling ratio rapidly recovered back to the initial equilibrium state. This indicates that the alginate/PNIPAAm graft gels have a suitable mechanical strength to undergo a reversible shrink process, owing to the strong hydrogel formed, supported by the alginate mainchain and crosslinked by Ca^{2+} ions. For this reason, there was no recorded volume change during the volume–phase transition of PNIPAAm.

3.5. Pulsatile stimuli—responsive swelling behavior

In this study, the swelling ratio of the macroporous hydrogels reached an equilibrium swollen state within about 1 min. However, we were unable to measure the swelling ratio over a 1 min period, and thus, the pulsatile swelling ratios were investigated over 5 min owing to the difficulty obtaining the shorter time measurements.

A step-wise swelling behavior was observed in water in temperatures alternating between 25 and 45 °C, as shown in Fig. 10. The swelling process proved to be repeatable, in accordance with the temperature changes. The porous hydrogels rapidly responded to temperature change, whereas the swelling ratio of the porous alginate was unchanged during the swelling and deswelling processes. Both nonporous and porous PNIPAAm grafted hydrogels exhibited fast swelling/deswelling behavior. However, the porous hydrogel was superior to the nonporous hydrogel in the magnitude of its swelling ratio during the swelling and deswelling processes. Fig. 11 shows the pulsatile swelling behavior of the hydrogels at 25 °C with alternating solution pH values between 2 and 7. The swelling ratio was also measured in five-minutes steps. After 5 min, a pH-dependent pulsatile swelling behavior was observed, caused by the carboxyl groups of the alginate. The surface-grafted hydrogel exhibited a similar degree of pulsatile swelling ratio as the alginate, even though PNIPAAm had been grafted on the carboxyl groups of the alginate.

The bulk-grafted hydrogel dissolved into the solution at pH 7 after several pulsatile measurements, and thus, we could not measure the swelling ratio after this. On the other hand, the surface-grafted hydrogel maintained its original shape. This can be explained by crosslinking of the bulk-grafted hydrogel by Ca^{2+} that had occurred after grafting, because the prior association of PNIPAAm-NH_2 with the alginate carboxyl groups would have prevented any crosslinking occuring. As shown in Fig. 5, the crosslinking density of surface-grafted hydrogel was higher than bulk-grafted hydrogel because the PNIPAAm graft was performed after the crosslinking process. Also, it was a well-known fact that in alkaline solution calcium alginate, crosslinked sodium alginate, is decomposed into sodium alginate because of the exchange reaction between Ca^{2+} and Na^{+}. The dissociation of carboxyl groups in calcium alginate is suppressed at lower pH values [22]. Thus, the dissolution of calcium alginate was reduced at pH 2 owing to the presence of the neutral carboxyl groups [1].

4. Conclusion

We have prepared hydrogels composed of temperature-sensitive PNIPAAm and pH-responsive alginate that have macropores and a comb-type grafted structure. The porous hydrogels rapidly reached their equilibrium swelling and deswelling states, and from their large surface area and free chain mobility, showed a fast response to changes in pH and temperature. Both the surface- and bulk-grafted hydrogels showed a change in swelling ratio at temperature around 32 °C arising from the PNIPAAm LCST behavior. From their increased volume of grafted PNIPAAm and pore surface area, the swelling behavior of porous hydrogels displays sharper volume phase transition than nonporous hydrogels. The swelling ratio was particularly affected by the phase transition behavior of the PNIPAAm that was attached only on the surface of the pores. In the pH-sensitive swelling behavior, the swelling ratio increased with increasing pH value because of the presence of the carboxyl groups of the alginate, regardless of the presence of the PNIPAAm graft. Also, the alginate/PNIPAAm graft gels showed suitable mechanical strength without collapsing during repeatable shrinkage and expansion changes, whereas conventional porous hydrogels did not sustain their pore structures. Thus, this type of porous hydrogel will be useful as a rapid stimuli-responsive drug delivery system, or as a biomimetic actuator in biomedical fields.

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