Temperature/pH-Sensitive Comb-Type Graft Hydrogels Composed of Chitosan and Poly(*N*-isopropylacrylamide)

Sang Bong Lee,[1] Dong In Ha,[1] Seong Kwan Cho,[1] Seon Jeong Kim,[2] Young Moo Lee[1]

[1]*School of Chemical Engineering, College of Engineering, Hanyang University, Seoul 133-791, South Korea*
[2]*Department of Biomedical Engineering, Hanyang University, Seoul 133-605, South Korea*

Received 2 September 2003; accepted 31 December 2003

ABSTRACT: Comb-type graft hydrogels, composed of chitosan and poly(*N*-isopropylacrylamide) (PNIPAAm), were prepared to manifest rapid temperature and pH sensitivity. Instead of directly grafting the NIPAAm monomer onto the chitosan chain, semitelechelic PNIPAAm with carboxyl end group was synthesized by radical polymerization using 3-mercaptopropionic acid as the chain-transfer agent, and was grafted onto chitosan having amino groups. The comb-type hydrogels were prepared with two different graft yields and grafting regions, such as surface- and bulk-grafting, and then compared with a chitosan hydrogel. The synthesis of telechelic PNIPAAm and the formation of amide group were confirmed by using FTIR spectroscopy and gel permeation chromatography. Results from the water state and thermal stability revealed that the introduction of the PNIPAAm side chain disturbed the ordered arrangement of the chitosan molecule, resulting in an increase in the equilibrium water content. Comb-type graft hydrogels showed rapid temperature and pH sensitivity because of the free-ended PNIPAAm attached to the chitosan main chain and the chitosan amino group itself, respectively. In particular, the surface graft hydrogel maintained its dimension at low pH, although the chitosan main chain was not crosslinked, whereas chitosan and bulk graft hydrogel were dissolved as a result of the coating effect of pH-independent PNIPAAm.
 J Appl Polym Sci 92: 2612–2620, 2004

Key words: graft copolymers; hydrogels; stimuli-sensitive polymers; swelling; telechelics

INTRODUCTION

Chitosan, a deacetylated form of chitin, has a subunit of β-(1,4)-2-amido-2-deoxy-D-glucopyranose, being second only to cellulose in the amount produced annually by biosynthesis.[1] Because of its biocompatibility, biodegrability, antibacterial properties, and remarkable affinity to proteins, it has been found to increase applications in areas such as hematology, immunology, wound healing, drug delivery, and cosmetics.[2–5]

In particular, the amino group, which is rare in polysaccharides, of chitosan influences the pH-responsive behavior because pH-sensitive hydrogels usually contain either acid or basic pendent groups in the network.[6–8] The amino group can be used to be a reactive site and also to chemically alter its properties under mild reaction conditions. Thus, to simultaneously impart the temperature sensitivity, *N*-isopropylacrylamide (NIPAAm) molecules were grafted onto the amino groups of chitosan, and because poly(*N*-isopropylacrylamide) (PNIPAAm) exhibits large swelling changes in aqueous media in response to small changes in temperature, it is used in a variety of applications including controlled drug delivery and solute separation.[9–13]

Wang et al.[14,15] studied the semi- and full interpenetrating network (IPN) hydrogels composed of chitosan and PNIPAAm. However, their swelling rates to reach the equilibrium state were relatively slow, thus making it necessary to manipulate the molecular structure for a rapid response to external stimuli. From the perspective of kinetics responding to stimuli, many researchers have investigated the fast response hydrogels. Okano et al.[16,17] synthesized temperature-sensitive hydrogels consisting of PNIPAAm chains grafted onto the backbone PNIPAAm network and also reported comb-type graft hydrogels composed of poly(ethylene oxide) (PEO) graft chains in a PNIPAAm crosslinked network. We also prepared PNIPAAm comb-type graft alginate hydrogels, resulting in rapid swelling and deswelling behaviors.[7,11]

In our previous study, the PNIPAAm-grafted chitosan hydrogels were prepared by the direct grafting method using the NIPAAm monomer and ceric ammonium nitrate (CAN) as a grafting agent.[8] However, the direct grafting method had the disadvantage of excessive formation of homopolymer of PNIPAAm.[8]

Correspondence to: Y. Lee (ymlee@hanyang.ac.kr).
Contract grant sponsor: Brain Korea 21 Program, Hanyang University.
Contract grant sponsor: International Mobile Telecommunications 2000 R&D Project, Ministry of Information and Communication, Republic of Korea.

Journal of Applied Polymer Science, Vol. 92, 2612–2620 (2004)

On the other hand, the PNIPAAm chains of the present study were grafted by forming the amide linkage with chitosan after the NIPAAm monomers were polymerized with carboxylic group in the chain end to graft efficiently and control the grafted regions and chain length of NIPAAm.

Thus, the goal of the present study was to prepare chitosan/PNIPAAm comb-type graft hydrogels that are able to rapidly respond to changes in both temperature and pH. Furthermore, the difference of swelling behaviors is discussed by comparing chitosan alone with the comb-type grafted hydrogels such as surface and bulk grafts.

EXPERIMENTAL

Materials

The *N*-isopropylacrylamide (NIPAAm; Aldrich Chemicals, Milwaukee, WI) used was purified by recrystallization from *n*-hexane/toluene (Duksan Pure Chemicals, Seoul, Korea). Chitosan (degree of deacetylation = 85%) was purchased from Sigma Chemicals (St. Louis, MO) and used after being dissolved in a 2 wt % acetic acid aqueous solution and filtered using a glass filter. 3-Mercaptopropionic acid (MPA) was purchased from Aldrich Chemical and purified by distillation under reduced pressure. *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. 1-Ethyl-(3–3-dimethylaminopropyl) carbondiimide hydrochloride (EDC) and *N*-hydroxy-succinimide (NHS) were purchased from Sigma Chemicals. Sodium hydroxide, tetrahydrofuran (THF), and *n*-hexane (Duksan Pure Chemicals) were used as purchased without any further purification. Water was first treated with a reverse osmosis system (Sambo Glove, Ansan, Korea) and further purified with a Milli-Q Plus system (Waters Chromatography Division/Millipore, Billerica, MA). Other chemicals were reagent grade and used without any further purification.

Synthesis of semitelechelic PNIPAAm

Semitelechelic PNIPAAm, with carboxyl group termination, was synthesized by radical polymerization using MPA as the chain-transfer agent and AIBN as an initiator. Synthesis and characterization were performed by procedures and compositions similar to those described in previous works.[11,16,18] Briefly, NIPAAm (221 mmol) and MPA (6.52 mmol) were dissolved in DMF (50 mL). Dried nitrogen was bubbled into the solution for 30 min before polymerization, which was initiated by AIBN (17.7 mmol) and carried out at 70°C for 6 h. The reactant was precipitated into an excess of diethyl ether and dried in vacuum at room temperature. The dried polymer was repeatedly purified by precipitation in hot water and dissolved in water. The purified product was freeze-dried.

Preparation of PNIPAAm–COOH grafted hydrogels on chitosan film: surface graft

Chitosan was dissolved in 2% acetic acid aqueous solution with 1.5 wt % concentration at room temperature. The chitosan solution was poured into a petri dish and dried at room temperature in a vacuum oven. The formed film was immersed in 0.1*N* NaOH aqueous solution for 3 h to extract the complexed acetic acid molecules from amino groups of chitosan. The hydrogel was washed with distilled water and then dried at 30°C in a vacuum oven.

To graft PNIPAAm–COOH onto the film, the chitosan film was immersed in a 1.5 wt % PNIPAAm aqueous solution, and then EDC and NHS were added to the solution at room temperature. The solution had a chitosan/PNIPAAm feed weight ratio of 1 : 1, and chitosan/EDC/NHS molar ratio of 2 : 2 : 1, with reference to the chitosan amino group, considering the degree of deacetylation. The chitosan film in PNIPAAm solution was slowly shaken overnight at room temperature. After the surface graft, any unreacted PNIPAAm–COOH residues with chitosan amino groups were removed by using Soxhlet's extractor with methanol for 3 days, and dried at 30°C.

Preparation of chitosan-*g*-PNIPAAm hydrogel: bulk graft

Chitosan and PNIPAAm–COOH were simultaneously dissolved in 2% acetic acid aqueous solution with 1.5 wt % concentration at room temperature. EDC and NHS were added to the solution to form amide bonds between the amino groups of chitosan and the carboxyl groups of PNIPAAm–COOH. The solution had a chitosan/PNIPAAm weight ratio of 1 : 1, and chitosan/EDC/NHS molar ratio of 2 : 2 : 1, with reference to the chitosan amino group. The mixed solution was continuously stirred overnight at room temperature. After precipitation with a THF–hexane solution (4 : 1), the precipitant was dialyzed using the cellulose tube (molecular weight cutoff: 12,000; Sigma) in water for 4 days, and then freeze-dried. The procedure used to prepare a bulk graft hydrogel is the same as that of preparing chitosan film as described above.

Measurement of graft yield and swelling behaviors

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 chitosan before grafting and W_2 is the total weight after grafting PNIPAAm–COOH onto the chitosan main chain.

A swelling study was conducted on chitosan/PNIPAAm–COOH hydrogels to observe the behavior as a function of both temperature and pH in the swelling medium. To measure the swelling behaviors, preweighed dry samples were immersed in water. After wiping off the excess water on the samples' surface, the weight of the swollen samples was measured at various time intervals. The swelling ratio and equilibrium water content (EWC) were calculated using the following formulas:

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

$$\text{EWC (\%)} = [(W_s - W_d)/W_s] \times 100 \quad (3)$$

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, after drying the gels in a vacuum oven for 2 days.

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 40°C. The pulsatile swelling behavior was observed in deionized water maintained at alternate temperatures of 25 and 40°C, and in buffer solutions with pH values between 3 and 7. The weight of the hydrogels in the different temperature and pH conditions was measured every 10 min.

Characterizations

FTIR spectroscopy (Model Magna IR 550FTIR, Nicolet Analytical Instruments, Madison, WI) was used to confirm the synthesis of carboxyl-terminated PNIPAAm. In addition, the molecular weight distribution of the telechelic PNIPAAm was determined using gel permeation chromatography (GPC, Waters Model 510 HPLC pump, Waters Chromatography Division/Millipore, Milford, MA) in water using the Millennium software program.

The state of water in the hydrogels was investigated by differential scanning calorimetry (DSC; DSC910, TA Instruments, New Castle, DE) in the temperature range of −20 to 30°C, with a heating rate of 5°C/min under N_2 flow. Amounts of free water and bound water were calculated from the respective melting enthalpies. The following equation assumes that the heat of fusion of free water in the hydrogel (Q_{endo}) is the same as that in ice (Q_f; 79.7 cal/g):

$$W_b\ (\%) = W_t - (W_f + W_{fb}) = W_t - (Q_{endo}/Q_f) \times 100 \quad (4)$$

where W_b is the amount of bound water (%); W_f and W_{fb} are the amounts of free water and freezing bound water, respectively; and W_t is the equilibrium water content [EWC (%)].

To examine thermal stability of hydrogels, chitosan, surface- and bulk-grafted hydrogels were measured using thermogravimetric analysis (TGA, Perkin–Elmer TGA-7, Shelton, CT). Decomposition profiles of TGA were recorded with a heating rate of 10°C/min in nitrogen between 30 and 650°C.

RESULTS AND DISCUSSION

Preparation of semitelechelic PNIPAAm–COOH

In our previous studies, we synthesized the amino-terminated PNIPAAm with 2-aminoethanethiol hydrochloride (AESH) as a chain-transfer agent to prepare the comb-type graft hydrogel with polysaccharide containing the carboxyl groups as pendent groups.[7,10,11] On the other hand, this study discusses the polysaccharide with amino groups. To covalently graft the PNIPAAm on the amino groups of chitosan, semitelechelic PNIPAAm–COOH was synthesized by radical polymerization using MPA as a chain-transfer agent. The procedure for synthesis of the carboxyl group-terminated PNIPAAm is shown in Figure 1.

To confirm the preparation of semitelechelic PNIPAAm–COOH, the existence of COOH groups on the end of chain and molecular weight of PNIPAAm were investigated by using FTIR and GPC, respectively. Figure 2 shows FTIR spectra of NIPAAm monomer, MPA, and PNIPAAm to confirm the polymerization of semitelechelic PNIPAAm–COOH. The FTIR spectrum obtained from telechelic PNIPAAm–COOH [see Fig. 2(c)] shows a significant peak at 1711 cm^{-1}, which represents the carboxylic acid group of MPA [Fig. 2(b)], although the peak in the telechelic PNIPAAm shows very low intensity or somewhat small shoulder attributed to the existence of a small amount of carboxyl group at the end of the NIPAAm polymer. In addition, the characteristic peaks at 1618 cm^{-1} (C═C), 1410 cm^{-1} (CH_2═), and C—H vinyl out-of-plane bending vibrations, observed in the spectrum of the monomer [see Fig. 2(a)], disappeared in telechelic PNIPAAm [Fig. 2(c)]. From the results, we could confirm the synthesis of semitelechelic PNIPAAm–COOH.

The molecular weight distribution of the telechelic PNIPAAm–COOH, determined by GPC apparatus, showed number-average (M_n) and weight-average (M_w) molecular weights of 2100 and 4600, respectively. The ratio of PNIPAAm possessing the carboxyl end groups in the entire PNIPAAm molecules was 97%, which was determined by comparing the molecular weight of PNIPAAm measured from GPC with the carboxyl group contents obtained from titration

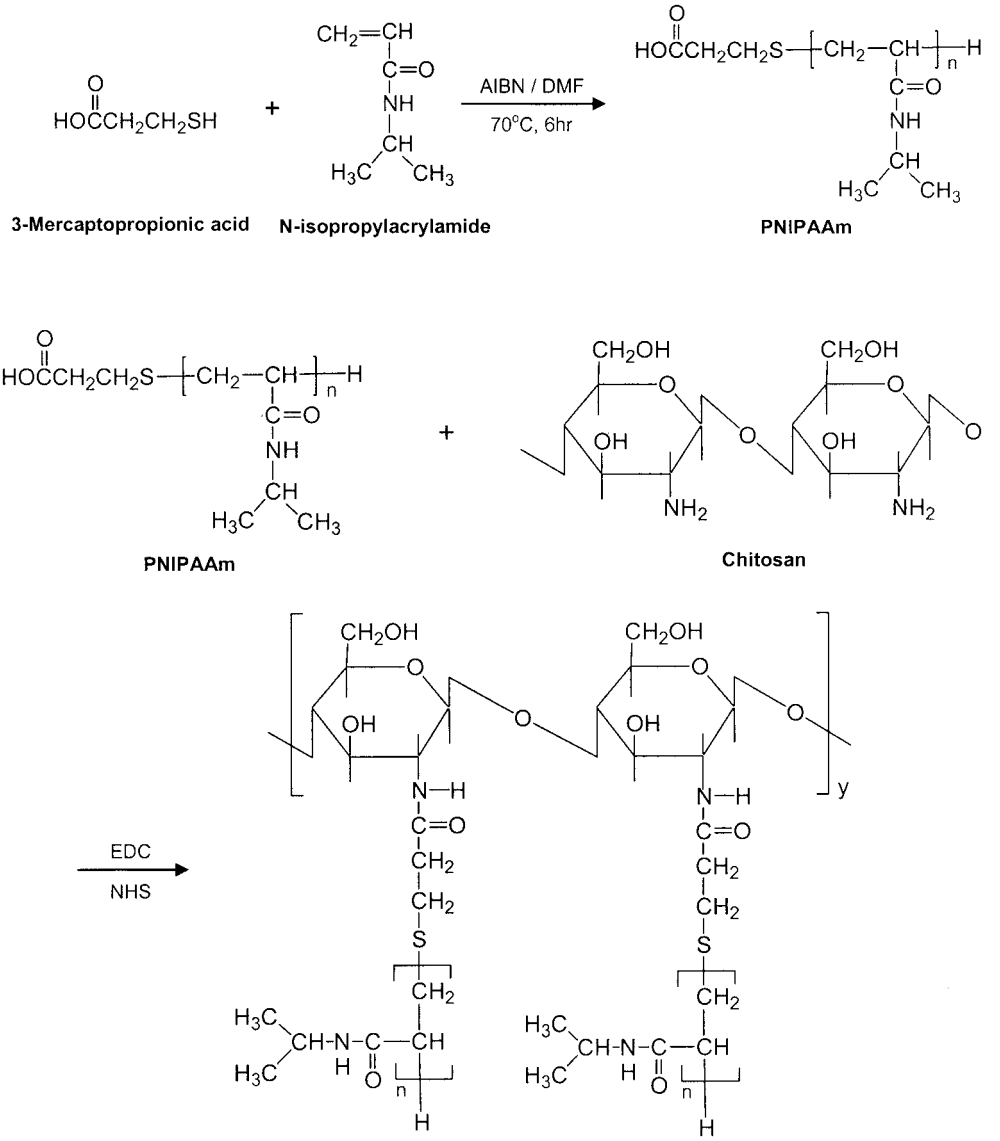

Figure 1 Molecular scheme for preparation of carboxyl group-terminated PNIPAAm and comb-type graft hydrogel.

assay (data not shown). This result accords with that of a previous study, which found that the semitelechelic PNIPAAm had an average of one carboxyl-terminated group per polymer chain.[16]

Preparation and characterization of chitosan and comb-type graft hydrogels

To prepare the comb-type graft hydrogels with free and mobile end chains, the telechelic PNIPAAm–COOH synthesized was grafted onto the chitosan amino groups. FTIR spectroscopic measurement was carried out to confirm the comb-type formation based on the changes in chemical structure of the chitosan-*g*-NIPAAm copolymer. Figure 2 shows the FTIR spectra for PNIPAAm–COOH (c), chitosan (d), and chitosan-*g*-NIPAAm copolymer (e). The FTIR spectrum of chitosan with 85% deacetylation degree indicated that peaks appearing at 1653 and 1598 cm^{-1} could be assigned to a carbonyl stretching vibration (amide I) and N—H bending vibration (amide II) of a primary amino group, respectively. In addition, Figure 2(c), obtained from linear NIPAAm homopolymer, shows characteristic peaks at 1654, 1542, and 1459 cm^{-1}, which can be attributed to the characteristic peaks of amide I, amide II, and methyl group in $-CH(CH_3)_2$, respectively. Thus, in the case of the chitosan-*g*-NIPAAm copolymer [Fig. 2(e)], the formation of amide groups was confirmed by the peak increases of amide I in PNIPAAm–COOH at 1654 cm^{-1} and methylene group in $-CH(CH_3)_2$ at 1459 cm^{-1} and the disappearances of free amino group of chitosan at 1598 cm^{-1} and carboxyl group in PNIPAAm–COOH at 1711 cm^{-1}, attributed to the formation of amide bond-

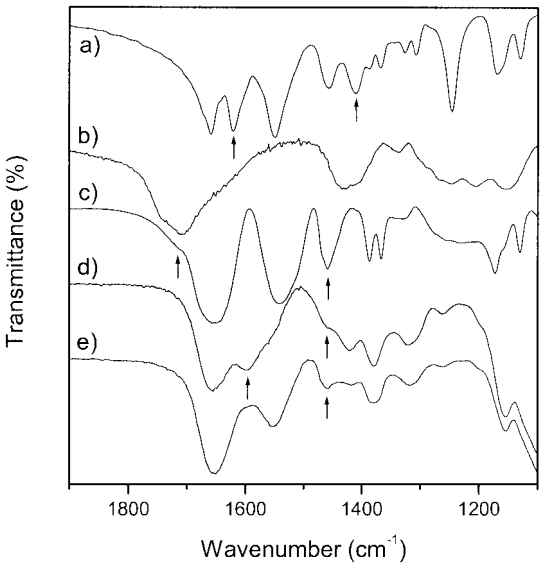

Figure 2 FTIR spectra for (a) NIPAAm monomer, (b) MPA, (c) telechelic PNIPAAm–COOH, (d) chitosan, and (e) PNPAAm-*g*-chitosan.

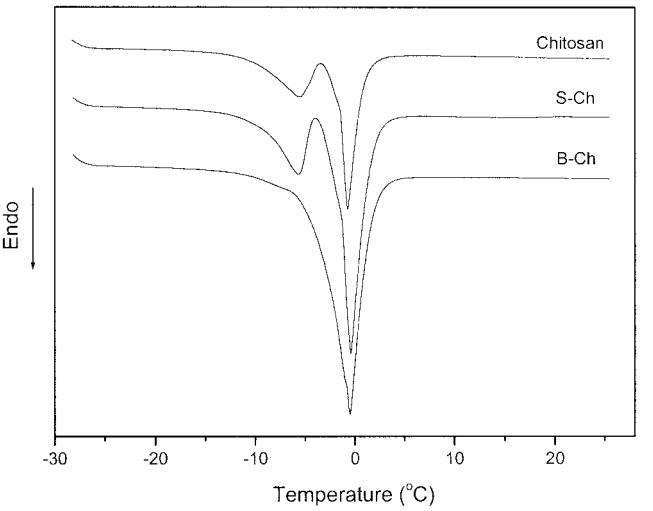

Figure 3 DSC thermograms of hydrogels that were fully swollen in distilled water (pH = 5.4).

ages, compared with chitosan itself and PNIPAAm–COOH.

Table I shows the compositions and graft yields of chitosan and both surface- and bulk-grafted hydrogels. In particular, the comb-type graft hydrogels were prepared with two different grafting regions and graft yields, and then compared with a chitosan hydrogel. In the surface graft, the molecules of PNIPAAm–COOH were grafted onto the surface of hydrogel, attributed to grating the PNIPAAm–COOH chains on the surface of chitosan film, whereas the bulk graft had the grafted regions on both the surface and the inside of the hydrogel. For this reason, surface- and bulk-grafted hydrogels have graft yields of 10.7 and 67.2 wt %, respectively, as shown in Table I. However, in our previous study,[8] when chitosan-*g*-NIPAAm hydrogel was prepared using the direct graft of the NIPAAm monomer onto the amino group of chitosan using CAN as an initiator, the maximum grafting percentage of 48.0% was obtained at 0.5*M* of NIPAAm concentration, 2×10^{-3} *M* of initiator (CAN), and 2 h of reaction time at 25°C. The direct grafting of NIPAAm monomers onto the amino groups of chitosan showed a lower grafting yield and higher formation of NIPAAm homopolymer, compared with the telechelic PNIPAAm grafting method.

Water states and thermal stability

Table I displays the water states of chitosan and both surface- and bulk-grafted hydrogels. The EWC of chitosan hydrogel is 59.5%, which is lower than that of comb-type graft hydrogels. This may mean that introducing the derivatives in the main chain of chitosan influenced the breakdown of the crystalline region because of the presence of bulky groups of the side chain, thus improving the solubility of chitosan.[8] Thus, the PNIPAAm attached on the chitosan may disturb the ordered arrangement of molecules during hydrogel formation, resulting in an increase of EWC in the comb-type graft hydrogel.

To further elucidate the swelling behavior of chitosan/PNIPAAm comb-type hydrogel, the water state of the hydrogels was investigated by DSC. Figure 3 shows DSC thermograms of hydrogels of comb-type graft hydrogels, such as surface and bulk, and chi-

TABLE I
Composition, Water States, and Graft Yield of Hydrogels

Type	Sample code	Weight ratio (wt %)		Water state[a]			Graft yield (wt %)
		Chitosan	NIPAAm	EWC (%)	Free water (%)	Bound water (%)	
Chitosan	Chitosan	100	0	59.5	31.6	27.9	—
Surface graft	S-Ch	50	50	71.8	50.3	21.5	10.7
Bulk graft	B-Ch	50	50	72.8	45.4	27.4	67.2

[a] Samples were fully swollen in distilled water (pH = 5.4) at 25°C for 2 h.

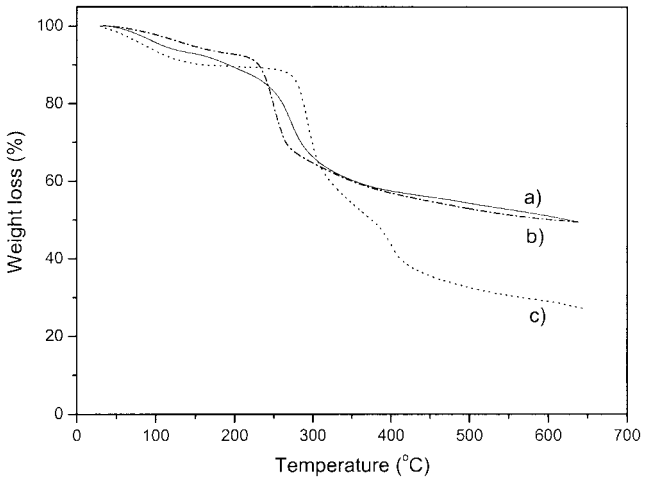

Figure 4 Thermogravimetric analysis of (a) chitosan, (b) surface graft, and (c) bulk graft.

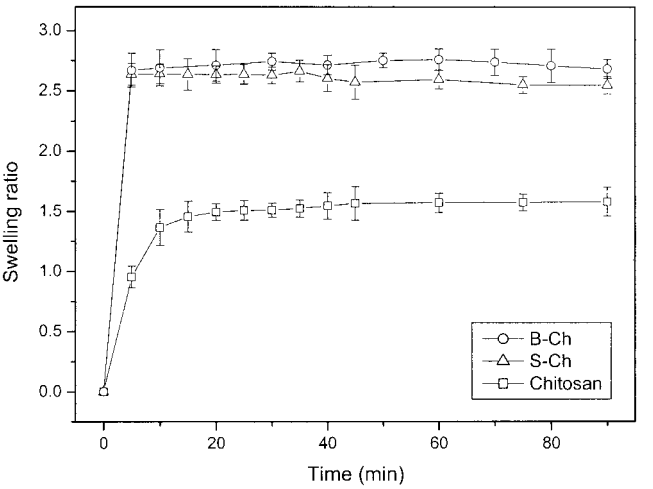

Figure 5 Swelling kinetics of chitosan, surface graft hydrogel, and bulk graft hydrogels in distilled water (pH = 5.4) at 25°C.

tosan hydrogels. The free water had no interaction with polymer chains, whereas the bound water was involved in the hydrogen bonding with polymer. The endothermic peak appeared at around 0 to 10°C and was attributed to the presence of free water in the hydrogels. The fraction of free water in total water was calculated approximately as the ratio of the endothermic peak area for the water-swollen hydrogel to the melting endothermic heat of fusion (79.9 cal/g) for pure water.

As shown in Figure 3, the heat flow plot of chitosan hydrogel is similar to that of surface graft hydrogel, which shows two completely separated peaks, whereas bulk graft hydrogel exhibits the one endothermic peak between −10 and 0°C. Thus, it is found that the surface graft hydrogel has the highest free water content and seems to be affected by the intrinsic thermal behaviors of PNIPAAm chain on the surface and chitosan chain inside the matrix.

Thermal stabilities of chitosan alone and comb-type graft hydrogels were measured using TGA analysis. Figure 4 shows the weight loss curves recorded with a heating rate of 10°C/min in nitrogen between 30 and 650°C. The bulk graft hydrogel shows a faster thermal decomposition, compared with that of chitosan alone, because the introduction of the PNIPAAm inside the matrix decreased thermal stability caused by the breakdown of the crystalline region of chitosan. On the other hand, the thermal degradation profile of surface graft hydrogel is similar to that of chitosan, indicating that the thermal stability of surface graft hydrogel is mainly affected by the chitosan matrix.

Swelling and deswelling kinetics

Figure 5 shows swelling kinetics of chitosan and comb-type graft hydrogels composed of chitosan and telechelic PNIPAAm. In the chitosan/PNIPAAm comb-type graft hydrogels, the swelling ratio reached an equilibrium swelling state within about 5 min, whereas chitosan hydrogels reached an equilibrium swelling state within 40 min. Rapid swelling kinetics of comb-type hydrogels arose from the fast and strong hydration of PNIPAAm graft chain, given that the comb-type grafted chains maintain high mobility as opposed to polymer networks crosslinked on each chain because they were free-end polymer.[1,13] In addition, the swelling ratios of comb-type series are higher than that of chitosan alone because of the attached PNIPAAm chain.

Figure 6 shows the deswelling kinetics of hydrogels

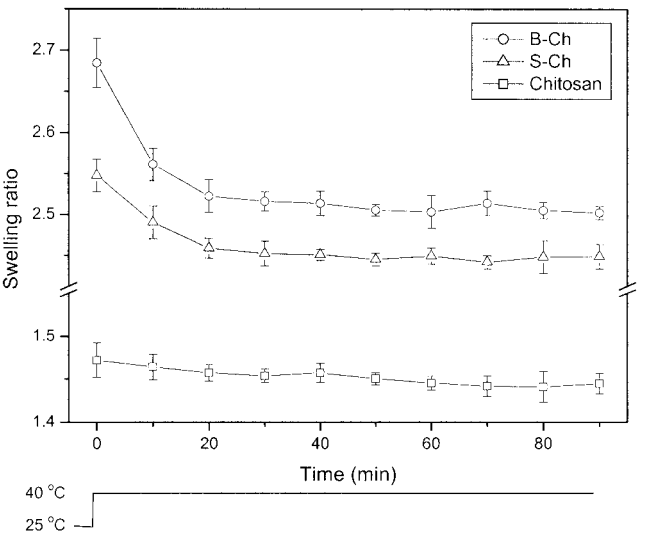

Figure 6 Deswelling kinetics of chitosan, surface graft hydrogel, and bulk graft hydrogels in water at 40°C from the equilibrium swelling state at 25°C.

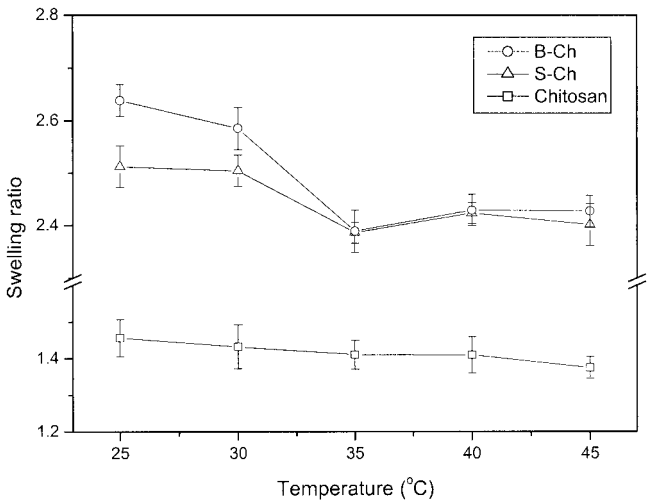

Figure 7 Swelling ratio of chitosan, surface graft hydrogel, and bulk graft hydrogels as a function of temperature in distilled water.

preequilibrated at 25°C by elevating the temperature to 40°C. The comb-type series reach an equilibrium deswelling state within about 20 min, which is a faster deswelling rate than that of previously studied blend hydrogels, composed of the same materials.[11]

The difference between swelling and deswelling rates to reach equilibrium seems to be a consequence of the PNIPAAm gel shrinking slowly because of the formed skin layer, which hindered the heat transfer during the deswelling process. Thus, the porous hydrogel in a morphology and comb-type structure in a molecular design were reported to overcome the skin layer formation.[17] Comb-type graft hydrogels with temperature-sensitive PNIPAAm–COOH chains show a rapid deswelling attributed to the mobility of grafted chains. At temperatures above 32°C, grafted chains are dehydrated, and then a hydrophobic aggregation force is formed between dehydrated grafted chains. These strong aggregation forces contribute to an increase in void volume within a gel, resulting in a rapid release of water. From the results of swelling and deswelling kinetics, we could expect that freely mobile chains in comb-type graft hydrogels are responsible for a fast rate of swelling and deswelling.

Temperature-dependent swelling behavior

Figure 7 shows the temperature-dependent swelling behavior of the hydrogels when the temperature of the aqueous media increased from 25 to 45°C. The swelling ratio of the surface- and bulk-grafted hydrogels dramatically decreased between 30 and 35°C, whereas the swelling ratio of the chitosan hydrogel that did not contain PNIPAAm was not affected by the temperature change. This effect could be expected in that the temperature sensitivity of PNIPAAm was attributed to the dissociation of ordered water molecules surrounding hydrophobic *N*-isopropyl groups in PNIPAAm. As a result, comb-type hydrogels composed of chitosan and PNIPAAm underwent a volume phase transition in water at around the lower critical solution temperature (LCST) of PNIPAAm (32°C) because PNIPAAm chains hydrate to form expanded structures in water when the solution temperature is below its LCST but becomes a compact structure by dehydration when heated to temperatures above the LCST.

Note that the swelling ratio changes in temperature-dependent swelling may result from the component of the backbone network. Okano[9] also synthesized the comb-type graft hydrogels with PNIPAAm as a backbone, reporting that the swelling behavior was dependent on the dimensional change upon the temperature stimulus. However, this study showed that the dimensions of all hydrogels changed only slightly during the temperature-sensitive swelling measurement because chitosan, which did not have the temperature sensitivity, was used as a framework for the hydrogel. Thus, it was considered that swelling/deswelling kinetics of the hydrogels was dependent on the intrinsic thermal behavior of grafted PNIPAAm with free end side. The temperature sensitivity of the hydrogels was dependent on the PNIPAAm content of the hydrogel. Among the hydrogels, bulk graft hydrogel with 67% graft yield of PNIPAAm showed the most drastic volume phase transition among the hydrogels.

A stepwise swelling behavior was observed in temperatures alternating between 25 and 40°C, as shown in Figure 8. The swelling process proved to be repeatable, in accordance with the temperature changes. The

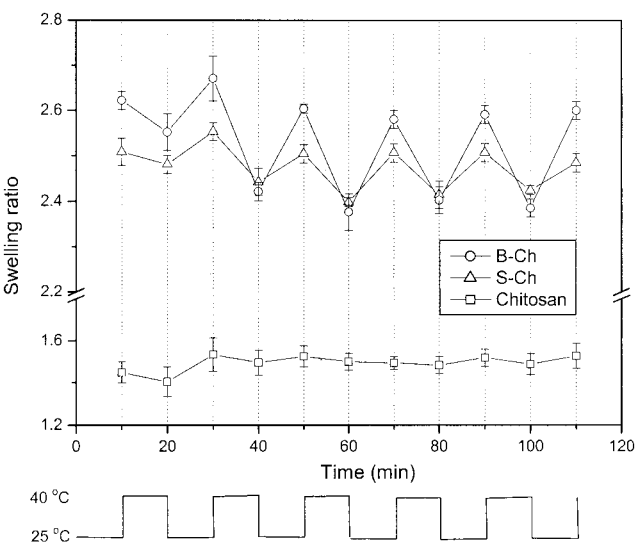

Figure 8 Pulsatile temperature-dependent swelling behaviors of chitosan, surface graft hydrogel, and bulk graft hydrogels in distilled water.

comb-type hydrogels rapidly responded to temperature change, whereas the swelling ratio of the chitosan alone was unchanged during the swelling and deswelling processes. Comb-type graft hydrogels respond to temperature change more rapidly than blend hydrogels, as shown in our previous study.[11]

pH-dependent swelling behavior

Figure 9 shows pH-sensitive characteristics of hydrogels, which are investigated by swelling test under various pH values ranging between 3 and 9. The pH sensitivity is mainly affected by chitosan amino groups, which constitute a weak base with an intrinsic pK_a of about 6.5; that is, the chitosan hydrogels swelled at low pH because of the ionic repulsion of the protonated amine groups, and collapsed at high pH because of the influence of unprotonated amine groups. As the pH value of the buffer solution increases, ionized NH_3^+ groups become NH_2 groups, and the resulting neutralization of ionic groups causes the hydrogels to be precipitated. As shown in Figure 9, the swelling ratio of hydrogels continuously decreased with increasing pH values.

The swelling ratios of chitosan and bulk graft hydrogel could not be measured below pH values of 6 and 7, respectively, because they were dissolved in the buffer solution before reaching its equilibrium swelling state attributed to the absence of crosslinking. On the other hand, the surface-grafted hydrogel maintained its original shape, even at pH 3. This can be explained by the coating effect on the surface of chitosan film by PNIPAAm, which is not pH sensitive. In the bulk graft hydrogel, although NIPAAm is grafted both on and in the chitosan film, the water molecules are easily permeated into the film because of the relatively loose molecular structure caused by PNIPAAm side chain inside the hydrogels.

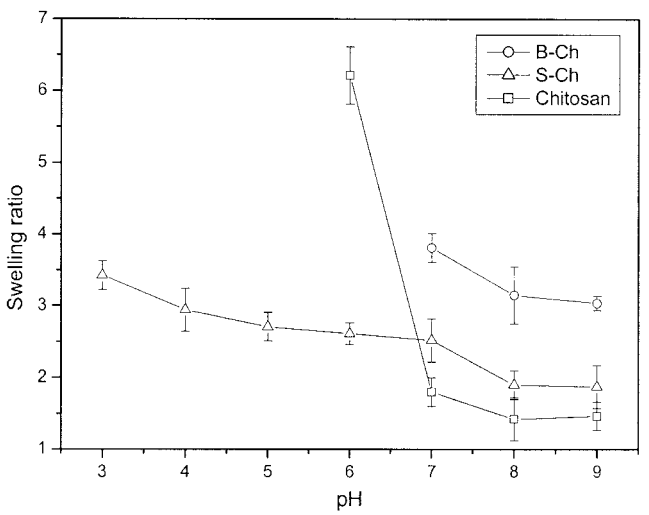

Figure 9 pH-dependent swelling behaviors of chitosan, surface graft hydrogel, and bulk graft hydrogels at 25°C.

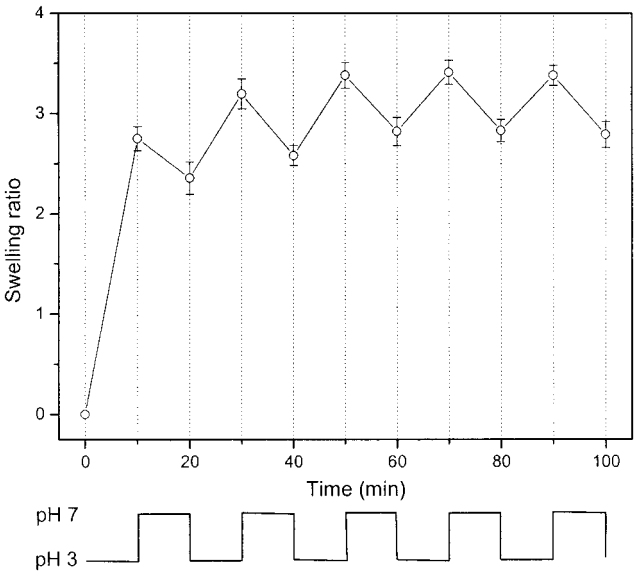

Figure 10 Pulsatile pH-dependent swelling behaviors of surface graft hydrogel at 25°C.

Figure 10 shows the pulsatile swelling behavior of the hydrogels at 25°C with solution pH values alternating between 3 and 7. The swelling ratio was also measured in 10-min steps. After 10 min, a pH-dependent pulsatile swelling behavior was observed, attributed to the amino groups of the chitosan. However, the only surface-grafted hydrogel exhibited a pulsatile swelling behavior because of the dissociation of hydrogels such as chitosan and bulk graft under low pH condition. In addition, the swelling process proved to be repeatable and rapidly responded to changes in pH.

CONCLUSIONS

To prepare the comb-type graft hydrogels composed of chitosan and poly(*N*-isopropylacrylamide) (PNIPAAm), semitelechelic PNIPAAm with a carboxyl end group was synthesized by radical polymerization and grafted with chitosan amino groups, instead of directly grafting the NIPAAm monomer onto the chitosan chain. The synthesis of telechelic PNIPAAm was confirmed by FTIR, with number- and weight-average molecular weights of 2100 and 4600, respectively. Results from the water state reveal that the EWC of comb-type graft hydrogels is higher than that of chitosan alone. In addition, the thermal stability of bulk graft hydrogel was relatively low and that of surface graft hydrogel is similar to that of chitosan. In the swelling/deswelling behaviors, comb-type graft hydrogels without graft regions and yields showed rapid temperature and pH sensitivity because of the free-ended PNIPAAm attached to the chitosan main chain and the chitosan amino group itself,

respectively. The stepwise swelling behavior confirmed that the swelling process was repeatable, in accordance with the temperature and pH changes. In particular, the surface graft hydrogel maintained its dimension even at low pH, although the chitosan main chain was not crosslinked.

S.B.L. and D.I.H. are grateful to Hanyang University for providing a Fellowship under auspices of the Brain Korea 21 Program. Also, this study was supported by a grant from the International Mobile Telecommunications 2000 R&D Project, Ministry of Information and Communication, Republic of Korea.

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