

Chapter 8

Synthesis and Characterization of Thermoreversible Sucrose Hydrogels (Sucrogels)

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Sucrose-based monomers were synthesized for preparation of hydrogels with thermoreversible and degradable properties. New monomers synthesized were 6-(N-methacryloyl-6-aminocaproyl) sucrose (MACS), 6,6'-di(N-methacryloyl-6-amino caproyl) sucrose (DMACS), 6-(N-methacryloyl leucyl) sucrose (MLS), and 6-(N-methacryloyl-11-amino undecanoyl) sucrose (MAUS). They were prepared by Schotten-Bauman reaction and Mitsunobu reaction, and characterized by NMR spectroscopy, elemental analysis, and thin layer chromatography.

Modified sucrose monomers were copolymerized with other monomers such as poly(propylene glycol) methacrylate (PPGM) and poly(ethylene glycol) ethyl ether methacrylate (PEGEEM) to prepare sucrose hydrogels (sucrogels). DMACS, a bifunctional sucrose monomer, was used as a cross-linking agent. Prepared hydrogels showed inverse thermoreversible properties: they swelled at 5°C but shrank as the temperature increased up to 60°C. It took 2~3 days for the sucrogels to swell to equilibrium at 5°C. On the other hand, shrinking at 60°C requires only 2~4 h to complete. These sucrogels were degraded in both acidic (pH 2.0) and basic (pH 12.0) solutions. Degradation in acidic solution was quite slow but relatively fast in a basic environment. The sucrose monomers prepared in this study are useful in the synthesis of degradable, thermosensitive hydrogels for various applications including controlled drug delivery.

Introduction

Hydrogels with the abilities to respond to changes in environmental factors, such as pH (1,2), temperature (3,4), electric field (5,6), magnetic field (7), or specific molecules (8,9), are useful in various applications including drug delivery, biotechnology, and biosensors. Of the many environment-sensitive hydrogels, temperature-responsive hydrogels have been used quite frequently for controlled drug delivery and bioseparation (10,11). The most widely used thermosensitive hydrogels are based on acrylamide derivatives such as N-isopropyl acrylamide. In this study, we synthesized various sucrose-based monomers which can be used to prepare thermoreversible hydrogels by copolymerization with hydrophobic monomers. Sucrose was chosen in this study, since it has unique properties. Specifically, sucrose is degradable and absorbable in the body. The hydroxyl groups of sucrose not only serve as good reaction sites for chemical modifications, but also make the carbohydrate very water-soluble. The design of thermoreversible hydrogels was focused on balancing the hydrophilic and hydrophobic properties so that the synthesized hydrogels exhibited inverse thermosensitivity resulting from the presence of lower critical solution temperature (LCST).

Experimental

Materials. Methacryloyl chloride (90%), 6-amino caproic acid, 11-amino undecanoic acid, DL-leucine, anhydrous dimethylformamide, Hydrion buffers, triphenyl phosphine, diisopropyl azodicarboxylate, poly(propylene glycol) methacrylate (Mol. Wt. 350-389), poly(ethylene glycol) ethyl ether methacrylate (Mol. Wt. ~246), ammonium persulfate, N,N,N',N'-tetramethylethylenediamine (TEMED), and sucrose were purchased from Aldrich Chemical Co. (Milwaukee, WI). Methacryloyl chloride was purified with distillation at 150°C before use. Other organic solvents and chemicals used were reagent grade. Silica gel thin layer chromatography (TLC) plates (UNIPLATE) were obtained from Analtech, Inc (Newark, NJ). Charring agent for TLC (Sigma spray agent, sulfuric acid) was obtained from Sigma Chemical Co. (Milwaukee, WI).

Synthesis of Sucrose Monomers. Sucrose monomers were prepared by following the reactions in Fig. 1. Fig. 1-A shows modification of N-aminocarboxylic acids with methacryloyl chloride. N-methacryloyl-6-amino caproic acid and N-methacryloyl leucine were synthesized following the methods used by Kaczmar or Kulkarni (12,13). In a 250 ml round bottom flask, 0.1 mole of 6-aminocaproic acid or leucine was dissolved in 30 ml of deionized distilled water. In the case of leucine, 6 g of sodium hydroxide was added in advance. Then freshly distilled methacryloyl chloride and concentrated solution of sodium hydroxide (11.4 g of NaOH to 25 ml of deionized distilled water) were added dropwise to the mixture in an ice bath. During the addition of reagents, the temperature of reaction mixture was kept below 20°C and the pH at 8.5-9.5. After further reaction for 3 h, the solution was carefully acidified to pH 1-2 with 15% HCl solution and extracted with 150 ml of ethylacetate three times. The extract was dried with anhydrous magnesium sulfate, and crystallized with benzene and toluene. Final products were recrystallized with ethyl acetate. N-methacryloyl-11-aminoundecanoic acid (11-AUA) was prepared by the method outlined by Yeoh *et al.* (14). The purity of N-methacryloyl amino carboxylic acids was confirmed by TLC using a chloroform: methanol (10:1) mixture. The *rf* values in TLC and yields for N-methacryloyl-6-amino caproic acid, N-methacryloyl leucine, and N-methacryloyl-11-aminoundecanoic acid were 0.44 and 55%, 0.46 and 67%, and 0.54 and 48%, respectively.

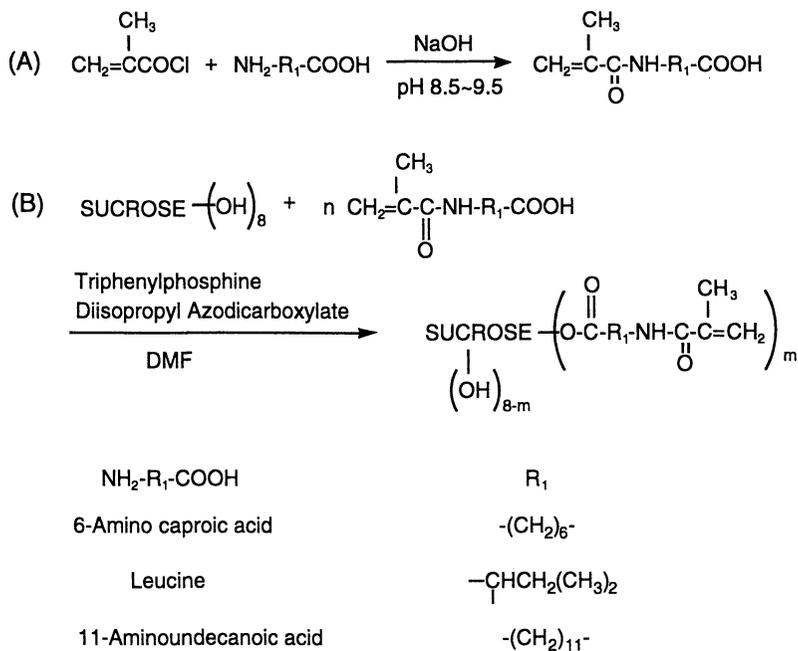


Figure 1. Synthetic reaction scheme of sucrose monomers. (A) Amino carboxylic acids were modified with methacryloyl chloride by Schotten-Bauman reaction at pH between 8.5~9.5. (B) Modified N-methacryloyl carboxylic acids were attached to sucrose by Mitsunobu reaction (B). m=1 or 2.

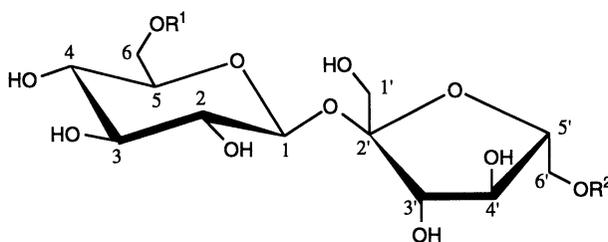
Sucrose was esterified with N-methacryloyl amino carboxylic acids by Mitsunobu reaction (Fig. 1-B). General synthetic procedure followed the method established by Abouhilale et al (15) with minor modifications. One equivalent of sucrose was reacted with N-methacryloyl amino carboxylic acid (1.5 eq. of N-methacryloyl caproic acid, and 1.0 eq. of N-methacryloyl leucine and N-methacryloyl-11-aminoundecanoic acid) in the presence of triphenylphosphine (1.7 eq. for N-methacryloyl-6-amino caproic acid, and 1.2 eq. for both N-methacryloyl leucine and N-methacryloyl-11-aminoundecanoic acid) and diisopropyl azodicarboxylate (same equivalent as triphenyl phosphine) using 200 ml of anhydrous dimethylformamide as solvent. The progress of the reaction was checked by TLC using chloroform:methanol (3:1) mixture. When the band of sucrose on TLC plate did not decrease further, the mixture was transferred to 1 L of hexane, and then chloroform was added to the mixture to precipitate sucrose monomers from the solvent mixture. The crude precipitates were purified further with gradient elution of chloroform-methanol eluents in the column chromatography. The chloroform:methanol ratios were 8:1, 6:1, and 4:1 for MACS, 10:1, 8:1, and 6:1 for DMACS and MLS, and 15:1, 12:1, and 10:1 for MAUS. Sucrose monomers were characterized by TLC using chloroform:methanol (3:1), ^1H - and ^{13}C -NMR with Bruker ARX 300 spectrometer in CD_3OD . Degree of substitution of DMACS was determined by quantitative ^{13}C -NMR. For quantitation by ^{13}C -NMR, chromium acetate, a NMR relaxation reagent for quantitative NMR analysis, was also dissolved in the sample to make its final concentration of 0.03 M. The quantitative ^{13}C -NMR analysis was performed at 75 MHz with a 3-second pulse delay time. The gate-decoupled pulse sequence was also employed to suppress the NOE effect.

The yields of modified sucrose ranged from 9% to 19%. The *rf* values in TLC were 0.26 for MACS, 0.49 for DMACS, 0.39 for MLS, and 0.42 for MAUS, respectively. Structures of monomers used for the hydrogel synthesis are shown in Fig. 2.

Elemental analysis. Calculation for $\text{C}_{22}\text{H}_{37}\text{O}_{13}\text{N}_1$ (MACS): C, 50.47; H, 7.12; N, 2.68. Found: C, 50.29; H, 7.45; N, 2.63. Calc. for $\text{C}_{32}\text{H}_{52}\text{O}_{15}\text{N}_2$ (DMACS): C, 54.54; H, 7.44; N, 3.97. Found: C, 54.27; H, 7.94; N, 3.45. Calc. for $\text{C}_{22}\text{H}_{37}\text{O}_{13}\text{N}_1$ (MLS): C, 50.47; H, 7.12; N, 2.68. Found: C, 48.54; H, 7.22; N, 2.42. Calc. for $\text{C}_{27}\text{H}_{47}\text{O}_{13}\text{N}_1$ (MAUS): C, 54.63; H, 7.98; N, 2.36. Found: C, 54.27; H, 8.35; N, 2.69.

Synthesis of Thermoreversible Hydrogels. Sucrose monomers (MACS, MLS, DMACS, and MAUS) were copolymerized with PPGM or PEGEEM to prepare thermoreversible hydrogels. Solutions of 0.5M MACS, 0.5M MLS, 0.5M PPGM, 0.5M PEGEEM, 0.25M DMACS and 0.25M MAUS were prepared with 50% methanol as solvent. Various sucrogels were obtained by changing molar ratio of the sucrose monomers to comonomers from 1:1 to 1:2. The final volume of monomer solution was 6 ml. Total amount of monomers was 3.0 mmole for hydrogels made of MACS or MLS and 2.0 mmole for hydrogels containing MAUS. DMACS was used as a crosslinking agent and the amount of DMACS ranged from 0.5 to 10.0 mole% of total monomers. Sixty microliter of 10% ammonium persulfate solution in 50% methanol and 60 μl of 10% tetramethylethylenediamine (TEMED) in 50% methanol were added to the monomer mixture as initiators. After mixing for 10 sec with a vortex mixer, the mixture was transferred into a mold to make films (7.5 cm x 7.5 cm x 0.3 cm). Polymerization was allowed for 10 h at room temperature. The prepared hydrogels were cut into discs with diameter of 1.5 cm for the investigation of swelling kinetics and 1.2 cm for degradation studies. Prepared hydrogel discs were washed once with ethanol and several times with cold deionized water. After the last washing, hydrogel discs were equilibrated for more than 1 day at 5°C.

SUCROSE MONOMERS



	R ¹	R ²
6-(N-methacryloyl-6-amino caproyl) sucrose (MACS)	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}(\text{CH}_2)_5\text{NHCOC} \\ \\ \text{CH}_3 \\ \parallel \\ \text{CH}_2 \end{array}$	H
6,6'-di (N-methacryloyl-6-amino caproyl) sucrose (DMACS)	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}(\text{CH}_2)_5\text{NHCOC} \\ \\ \text{CH}_3 \\ \parallel \\ \text{CH}_2 \end{array}$	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}(\text{CH}_2)_5\text{NHCOC} \\ \\ \text{CH}_3 \\ \parallel \\ \text{CH}_2 \end{array}$
6-(N-methacryloyl leucyl) sucrose (MLS)	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{CCHNHCOC} \\ \\ \text{CH}_2\text{CH}(\text{CH}_3)_2 \end{array}$	H
6-(N-methacryloyl-11-aminoundecanoyl) sucrose (MAUS)	$\begin{array}{c} \text{O} \\ \parallel \\ -\text{C}(\text{CH}_2)_{10}\text{NHCOC} \\ \\ \text{CH}_3 \\ \parallel \\ \text{CH}_2 \end{array}$	H

HYDROPHOBIC MONOMERS

Poly (propylene glycol) methacrylate (PPGM)	$\text{H}_2\text{C}=\text{C}(\text{CH}_3)\text{CO}_2\text{[CH}_2\text{CH}(\text{CH}_3)\text{O}]_n\text{H}$
Poly (ethylene glycol) ethylether methacrylate (PEGEEM)	$\text{H}_2\text{C}=\text{C}(\text{CH}_3)\text{CO}_2\text{[CH}_2\text{CH}_2\text{O}]_n\text{CH}_2\text{CH}_3$

Figure 2. Structures of monomers used in the preparation of thermo-reversible sucrogels.

Temperature Dependence of Swelling and Swelling Kinetics of Sucrogels. Swollen gels previously equilibrated at 5°C were placed in a 60°C water bath. Changes in the swelling ratio of hydrogels were measured by the gravimetric method. The swelling ratio of hydrogels was calculated by dividing the weight of a swollen gel by the weight of a dried gel.

The temperature-dependent swelling kinetics was examined by first swelling the hydrogel to an equilibrium at 60°C and then changing the temperature to 5°C. To investigate thermosensitive swelling of sucrogels, previously swollen hydrogels were put into the water bath with temperature changing from 5°C to 60°C.

Degradation of Thermoreversible Hydrogels. Thermoreversible hydrogels with molar composition of PPGM:MLS:DMAC=5:4:1 and PPGM:MACS:DMACS = 5.00:4.95:0.05 were placed into beakers containing 100 ml of acidic solution (Hydrion buffer, pH 2.0) or basic solution (Hydrion buffer, pH 12.0). Solutions were kept at room temperature during experiments. Degradation of hydrogels was followed by measuring the weights of hydrogels and dividing it by the weight of the fully swollen gel at timed intervals.

Results and Discussion

Synthesis of Sucrose Monomers. As shown in Fig. 1, sucrose monomers were prepared by first modifying N-aminocarboxylic acids with methacryloyl chloride by Schotten-Bauman reaction. The carbon length of N-aminocarboxylic acids determines the hydrophobicity of the substituents. One practical advantage of this approach is that various amino acids with different water solubility can be utilized for the preparation of hydrophobic sucrose monomers. N-methacryloyl amino carboxylic acids were then reacted with sucrose by Mitsunobu reaction. Since sucrose has 3 primary hydroxyl groups, sucrose derivatives with two polymerizable substituents or more could be used as a crosslinking agent in the synthesis of sucrose hydrogels.

¹³C-NMR spectrum of sucrose monomers showed that the most favorable site for esterification in sucrose was OH-6 (see Fig. 2). Reaction with 1:1 molar ratio mainly modified OH-6. This observation was consistent with the previous study by Abouhilale et al. who synthesized polyfluorinated 6-esters of sucrose by Mitsunobu reaction (15). All the carbon peaks and some proton peaks from sucrose were identified and assigned based on the results of Abouhilale et al. (15).

In the synthesis of DMACS, the molar ratio of sucrose:N-methacryl-6-amino caproic acid was 1:1.7. ¹³C-NMR spectrum of purified DMACS showed that two N-methacryloyl-6-aminocaproyl groups were attached to C-6 and C-6'. The C-5' peak (83.9 ppm) and the C-6' peak (64.1 ppm) of sucrose shifted to upfield by 3 ppm and downfield by 2.7 ppm, respectively. These shifts were consistent with the results obtained by Jansson et al. (16) in the modification of glucose. Their results showed that the introduction of an O-acetyl group in any position of a glycopyranoside caused deshielding of the substituted carbon by 0.7-3.5 ppm and shielding of the carbons next to those carbons (b carbons) by 1.2-2.8 ppm. Another proof for the disubstitution of sucrose was ¹³C-NMR spectrum of purified DMACS that showed two ester carbons peaks at 175.1 and 175.3 ppm.

Degree of substitution of DMACS was estimated by quantitative ^{13}C -NMR integration (Fig. 3). By mixing chromium acetate, a NMR relaxation reagent, ^{13}C -NMR peak could be integrated to provide quantitative information on the number of substituents. The integrated ^{13}C -NMR peaks of DMACS showed that the integration values of carbon peaks from substituents were about twice those of sucrose. Fig. 4 shows ^1H -NMR spectra of MACS and DMACS. An anomeric proton peak of sucrose appears at 5.3 ppm as doublet. In addition, two protons from $=\text{CH}_2$ of substituents show clear two resonance peaks at 5.3 and 5.6 ppm (Fig. 4-B). The integration ratio between proton peak of 5.6 ppm to that of 5.3 were 1/2 and 2/3 for monosubstituted MACS and disubstituted DMAC, respectively. These integration ratios also proved disubstitution of sucrose. Elemental analysis also showed that the observed elemental compositions were close to theoretical values.

More hydrophobic sucrose monomers can be prepared by using functionalized hydrophobic polymers, such as poly(propylene glycol) and dihydroxy polybutadiene. Poly(propylene glycol) (meth)acrylate can also be coupled with sucrose after reaction with succinic anhydride. Sucrose modified with hydrophobic polymer can experience thermal gelation even without crosslinking.

Temperature-Dependent Swelling Profiles. Sucrose monomers were copolymerized with commercially available monomers, such as PPGM and PEGEEM, to make thermoreversible hydrogels. The formation of hydrogels was tested by polymerization of monomer mixtures with different amounts of DMACS, a crosslinking agent used in this study. The mixture of MACS and PPGM formed a gel at a low concentration (0.5 mole%) even in the absence of DMACS. This may be due to interdigitation of long side groups of MACS and PPGM. As the polymerization continued, side chains of PPGM and MACS might entangle each other significantly to crosslink polymer backbone even without DMACS. MLS that had bulky leucyl side groups ($-\text{CH}_2\text{CH}(\text{CH}_3)_2$), however, needed a relatively large amount of DMACS to form a gel. This is probably because side groups were not linear and ineffective for entangling. At 5 mole% of DMACS, a very fragile hydrogel of poly(MLS-co-PPGM) was formed. In subsequent studies, MACS-containing sucrogels were crosslinked with 0.5 mole% of DMACS, while MLS-containing sucrogels were crosslinked with 10 mole% of DMACS for the formation of hydrogels with certain mechanical strength.

Sucrogels made of MACS and PPGM or DMACS and PPGM shrank as the temperature increased. As shown in Fig. 5, the volume decreased gradually as temperature increased until the temperature reached 35°C. The maximum of swelling ratio at 5°C was about 30, and the temperature-dependent volume change was slightly dependent on the amount of sucrose monomers used. As the amount of sucrose monomers in the gels increased from 33 mole% to 50 mole%, the maximum swelling ratio at 5°C decreased and the minimum swelling ratio at 35°C increased slightly without a clear change in the overall profile. This may be partially due to a slight loss of thermal sensitivity by the increase in hydrophilicity of sucrogels. When the concentration of DMACS was increased from 0.5 mole% to 5.0 mole%, swelling of sucrogels decreased while the overall thermosensitive swelling profiles remained very similar. Higher crosslinking density limited the swelling of hydrogels by forming tighter networks of polymer chains.

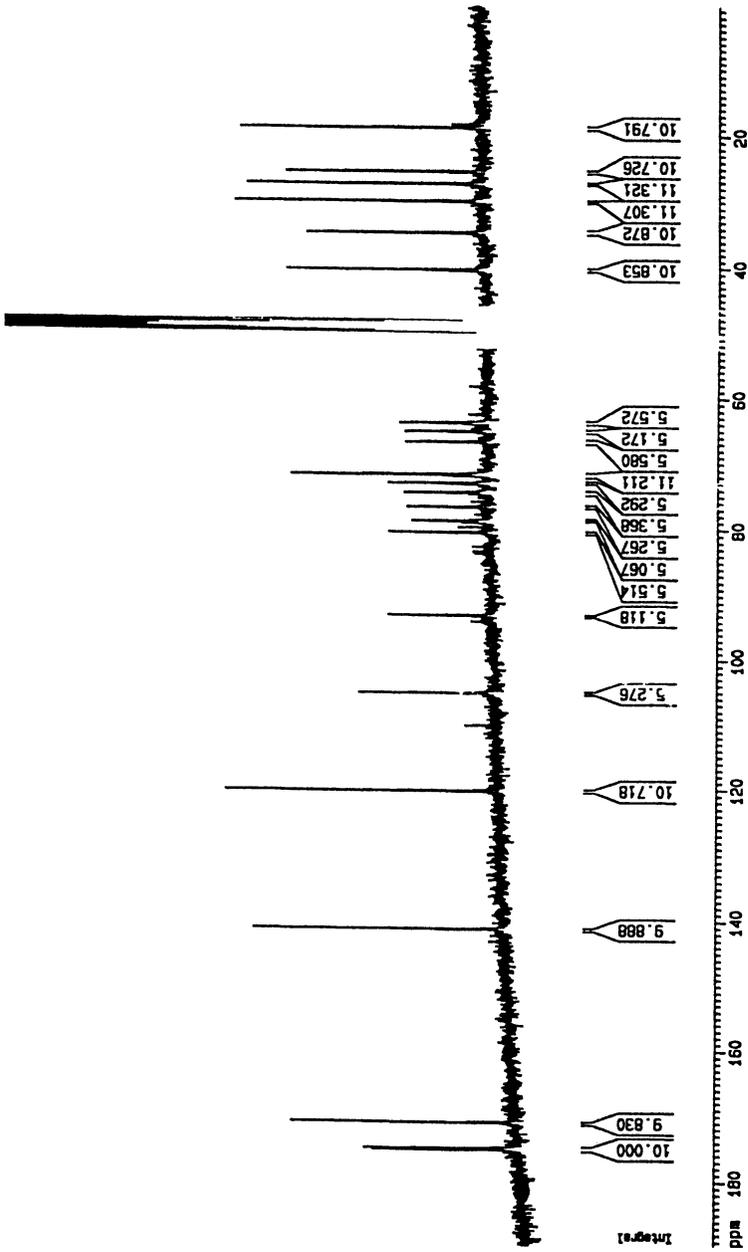


Figure 3. Degree of substitution of DMACS was determined using quantitative ^{13}C -NMR Spectroscopy. All peaks from DMACS were integrated (18.27, 25.43, 27.25, 29.88, 34.58, 40.30, 63.73, 65.05, 66.46, 71.65, 72.92, 74.36, 76.54, 78.67, 80.42, 92.98, 105.16, 120.23, 141.19, 170.98, 175.00 ppm) and sucrose peaks were found at 63.73, 65.05, 66.64, 71.65, 72.92, 74.36, 76.54, 78.67, 80.42, 92.98, 105.16 ppm. The sucrose peak at 71.65 resulted from the overlap of two carbons (C4 and C-5).

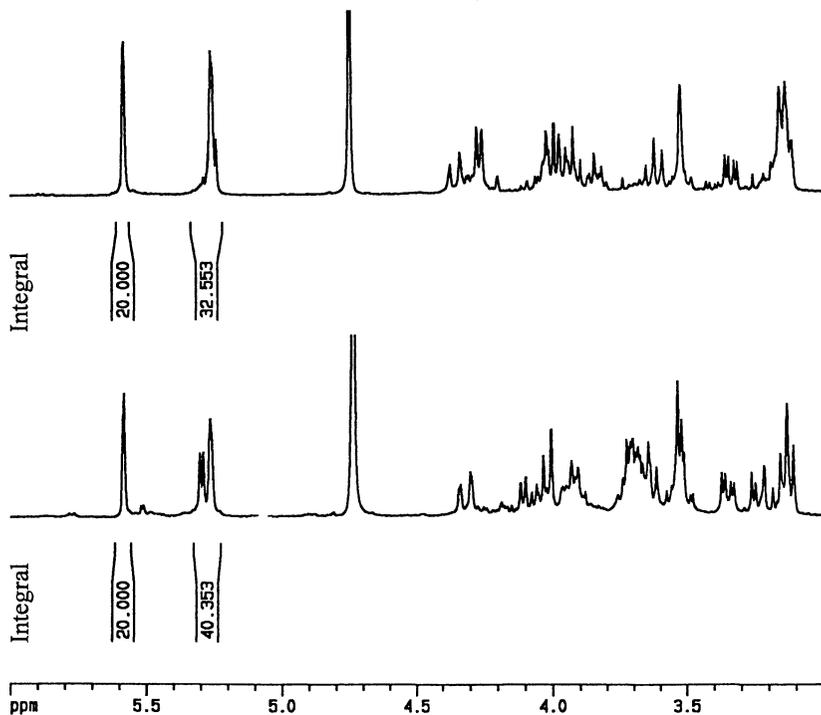


Figure 4. $^1\text{H-NMR}$ spectra of MACS and DMACS were recorded in CD_3OD . Integration ratios of proton peak at 5.6 ppm (one of $=\text{CH}_2$ protons) to proton peaks at 5.3 ppm (an anomeric proton peak of sucrose and the other $=\text{CH}_2$ proton) were $2/3$ (A) and $1/2$ (B) for DMACS and MACS, respectively.

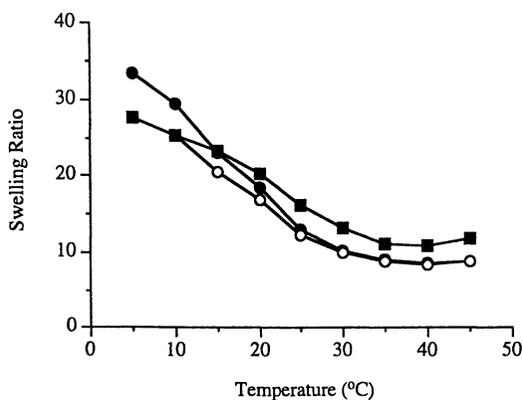


Figure 5. Thermosensitive volume change of sucrogels made of MACS and PPGM. The gels were cross linked with DMACS. The molar ratios of MACS:PPGM were $2:4$ (●), $2:3$ (○), and $2:2$ (■). $n=3$. The error bars are smaller than the size of symbols.

Thermoresponsive hydrogels were also prepared by copolymerization of MACS and PEGEEM in the presence of DMACS. The thermosensitive property of MACS-PEGEEM sucrogels was quite unique in that a linear decrease in volume change was observed in the temperature range of 5°C to 50°C (Fig. 6). On the other hand, hydrogels of PEGEEM showed a thermosensitive property only until the temperature increased to 20°C and no thermosensitive property was observed above 20°C. The linear temperature dependence of the swelling ratio may be more useful than sigmoid temperature dependence.

Another type of thermosensitive sucrogels were synthesized by copolymerization of MLS and PPGM (or PEGEEM) with 10 mole% of DMACS as a crosslinking agent. The molar ratio of MLS:PPGM was either 1:1 or 2:1. Hydrogels made of PPGM only were not temperature sensitive at all and the swelling ratio was quite low (around 5) in the temperature ranging from 5°C to 60°C (Fig. 7). The MLS-PPGM and MLS-PEGEEM sucrogels, however, showed inverse thermosensitive properties in the same temperature range. The MLS-PPGM and MLS-PEGEEM sucrogels showed different thermosensitive profiles. The MLS-PPGM sucrogels had a rather clear volume transition between 15°C and 30°C, while the MLS-PEGEEM sucrogels showed almost linear volume transition between 10°C and 60°C. When the concentration of sucrose monomers in the sucrogels increased from 50 mole% to 67 mole%, the maximum swelling ratio of the gels increased dramatically from 30 to 90. The MLS hydrogel showed the obvious change in swelling ratio while the MACS did not. This difference between the two types of sucrogels may be due to the difference in side chains of monomers. A relatively long linear side chain of MACS (Fig. 2) may entangle each other as polymerization continued and prevented swelling of sucrogels regardless of increase in the amount of sucrose monomer. On the other hand, a bulky compact side group of MLS could avoid chain entanglement and formed less crosslinked gels. However, the overall thermosensitive profile did not change with the increase in the amount of sucrose monomer as shown in Fig. 7.

Thermoreversible Properties of Sucrogels. Thermoreversible swelling and shrinking of sucrogels were investigated by repetitive temperature changes. When fully swollen sucrogels at 4°C were placed into water at 60°C, sucrogels underwent volume decrease quite fast (Fig. 8). Shrinking of sucrogels at 60°C was much faster than swelling at 5°C. Sucrogels made of different sucrose monomers and different hydrophobic monomers showed the same behavior. In general, the shrinkage to an equilibrium at 60°C required only 2–6 h, while equilibrium swelling at 5°C took 2–3 days. The slow swelling compared to shrinking of hydrogels is observed for almost all hydrogels. This is probably due to the fact that swelling requires relaxation of entangled polymer chains. Of the three sucrose monomers examined, the MAUS-PEGEEM sucrogels showed this lowest swelling ratio under the same condition. The may be due to more chain entanglement by longer side chain and more hydrophobicity of MAUS than other sucrose monomers.

Studies on the swelling kinetics and the thermoreversible properties showed that the most important parameter controlling the thermosensitivity was the type of sucrose monomers. It appears that the thermosensitive properties of sucrogels result from combination of hydrophobic side chains of comonomers and hydrophilic and bulky sucrose moiety of sucrose monomers. The thermosensitivity of these sucrogels can be controlled by adjusting various factors such as length and the bulkiness of side chains of the polymer backbone. Thus, various amino acids can be used in the preparation of sucrose monomers and these will provide sucrogels with different thermosensitive properties.

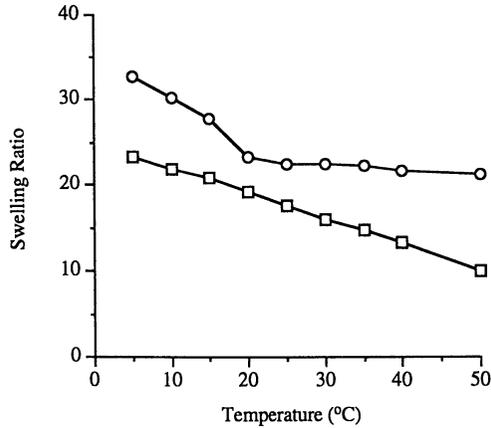


Figure 6. Thermosensitive changes in volume of hydrogels made of PEGEEM only (O) and MACS-PEGEEM copolymers (□). The molar ratio of MACS-PEGEEM was 1:1 and the sucrogels were formed using DMACS as a crosslinking agent. $n=3$. The error bars are smaller than the size of symbols.

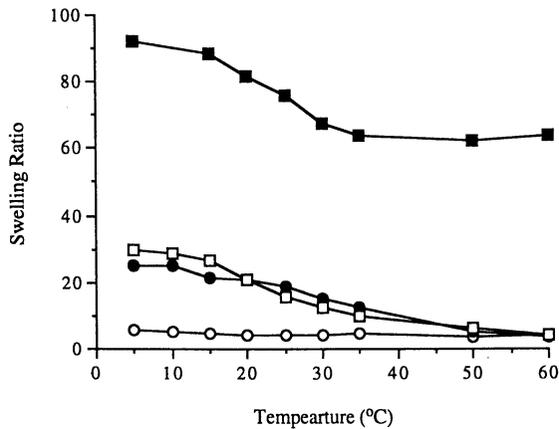


Figure 7. Thermosensitive changes in volume of hydrogels made of PPGM only (O), MLS-PPGM (□ and ■), and MLS-PEGEEM (●) copolymers. The molar ratios of MLS-PPGM were 1:1 (□) and 2:1 (■) and that of MLS-PEGEEM was 1:1. The sucrogels were formed using DMACS as a crosslinking agent. $n=3$. The error bars are smaller than the size of symbols.

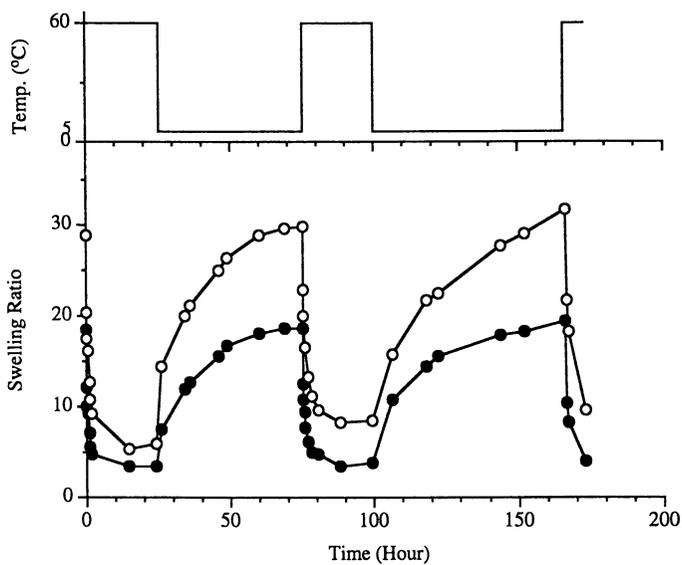


Figure 8. Temperature-dependent swelling and shrinking of sucrogels. Sucrogels were made of MACS-PPGM copolymer with the molar ratio of 2:3 and the concentration of DMAC was either 0.5 mole% (O) or 5.0 mole% (●). DMACS was used as a crosslinking agent.

Degradation of Thermoreversible Hydrogels. Degradation of MACS-PPGM sucrogels in acidic (pH 2) and basic (pH 12) solutions was examined. Sucrogels degraded much faster in the basic condition than in the acidic condition. Sucrogels degraded completely within 2 h in a pH 12 solution, while it took about 20 days for 80% degradation in a pH 2 solution (Fig. 9). The difference in degradation rates is most likely due to the intrinsic labile property of ester linkage by base and subsequent formation of anions. The electrostatic repulsion by the formed anions caused the swelling of the partially degraded hydrogel, which in turn made the base-catalyzed hydrolysis easier.

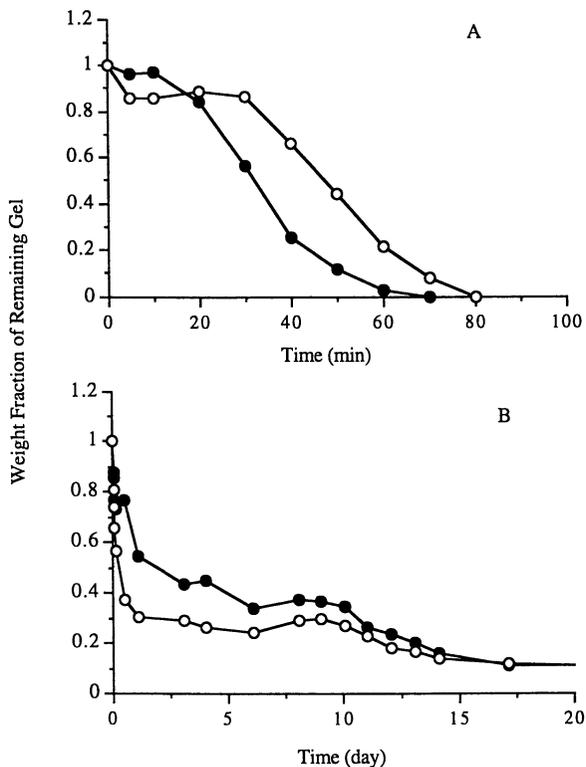


Figure 9. Degradation of sucrogel in basic solution (pH 12.0) (A) and in acidic solution (pH 2.0) (B). The sucrogels were made of MACS-PPGM (●) and MLS-PPGM (○) copolymers. The molar ratio of monomers was 1:1 and the sucrogels were formed using DMACS as crosslinking agent.

Conclusion

Four sucrose monomers were synthesized by regioselective modification of sucrose. These sucrose monomers were copolymerized with hydrophobic monomers to produce inverse thermoreversible sucrogels. Thermoreversible sucrogels exhibited reversible volume changes as the temperature was varied, and the thermoreversible process was reproducible. The thermosensitive sucrogels were degraded in both acidic and basic conditions. These degradable, thermoreversible sucrogels are expected to find various applications in diverse fields including controlled drug delivery and biotechnology.

Acknowledgments

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