Journal of Macromolecular Science, Part A
Publication details, including instructions for authors and subscription information:
http://www.informaworld.com/smpp/title~content=t713597274

A Novel IPN Hydrogel Based on Poly (*N*-Isopropylacrylamide) and β-Cyclodextrin Polymer

Yu-Yang Liu[a]; Xiao-Dong Fan[a]; Qiang Zhao[ab]
[a] Department of Chemical Engineering, Northwestern Polytechnic University, Xi'an, P.R. China [b] Department of Material Science and Engineering, Tianjin University, P.R. China

To cite this Article Liu, Yu-Yang , Fan, Xiao-Dong and Zhao, Qiang(2003) 'A Novel IPN Hydrogel Based on Poly (*N*-Isopropylacrylamide) and β-Cyclodextrin Polymer', Journal of Macromolecular Science, Part A, 40: 10, 1095 — 1105
To link to this Article: DOI: 10.1081/MA-120024466
URL: http://dx.doi.org/10.1081/MA-120024466

JOURNAL OF MACROMOLECULAR SCIENCE®
Part A—Pure and Applied Chemistry
Vol. A40, No. 10, pp. 1095–1105, 2003

A Novel IPN Hydrogel Based on Poly (*N*-Isopropylacrylamide) and β-Cyclodextrin Polymer

Yu-Yang Liu,* Xiao-Dong Fan, and Qiang Zhao#

Department of Chemical Engineering, Northwestern Polytechnic University, Xi'an, P.R. China

ABSTRACT

A novel interpenetrating polymeric network (IPN) was prepared based on poly (*N*-isopropylacrylamide) (PNIPA) and β-cyclodextrin (β-CD) polymer with two steps of polymerization techniques. A β-CD polymer (β-CD-EPI-PVA) was first synthesized by reaction of β-CD with epichlorohydrin (EPI) in diluent poly(vinyl alcohol) (PVA) aqueous solution, and the IPN was synthesized via dispersing NIPA monomer into the β-CD polymer, polymerized, and crossliked in situ. Infrared spectroscopy, element analysis, DSC, TGA, and swelling measurements were used to characterize the structures of β-CD-EPI-PVA polymer and related IPN hydrogel. The results indicated that equilibrium swelling ratio (ESR) of the β-CD-EPI-PVA network decreases gradually with the increase in temperature. The volume phase transition temperature (T_v) of IPN hydrogel is still sensitively kept at about 33°C.

Key Words: β-Cyclodextrin polymer; Poly(*N*-isopropylacrylamide); Hydrogel; Interpenetrating polymeric network.

---

*Correspondence: Yu-Yang Liu, Department of Chemical Engineering, Northwestern Polytechnic University, Xi'an, 710072, P.R. China; E-mail: yhyyliu@sohu.com.

#Current address: Department of Material Science and Engineering, Tianjin University, P.R. China.

DOI: 10.1081/MA-120024466
1060-1325 (Print); 1520-5738 (Online)

www.dekker.com

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

INTRODUCTION

Biomaterials have become a research focus in material science and engineering.[1,2] Among them, poly(*N*-isopropylacrylamide) (PNIPA) which exhibits a lower critic solution temperature (LCST),[2–11] and *β*-cylodextrin (*β*-CD) which can form so-called "host-gust" complex with many organic compounds,[10–14] are widely studied for pharmaceutical and medical applications. In order to combine the functions of the two materials, and develop a novel carrier for controlled drug-delivery, our research group recently suggested and studied novel hydrogels by copolymerization of NIPA with vinyl carboxylic *β*-CD, or vinyl carboxylic *β*-CD resin.[8,9] However, it should be noted that a hydrogel's properties not only depend on the functions of each component, but also are involved in their architecture forms in networks.[2–4] The concept has been demonstrated by many systems such as NIPA/MAA (methacrylic acid)[3] and NIPA/AA (acrylic acid)[4] systems. In these systems, in the presence of a small amount of AA or MAA, a random copolymer hydrogel exhibits an elevated T_v and drastically reduced volume change in response to external temperature under weak base solution compared with PNIPA hydrogel, whereas corresponding IPN hydrogel may maintain its T_v at about PNIPA's LCST.[2–4] This is because the hydrophilic component can markedly reduce dehydration of NIPA segments in copolymer. For an interpenetrating polymeric network (IPN) system, as there is no chemical bonding between two polymer networks, each polymer network can retain its individual property; however, due to physical entanglements, if one component swells or shrinks, the other component can be enforced to cooperate by attractive and repulsive interactions of the whole network. In addition, interpenetration of the two networks can also keep a much higher mechanical strength compared to the homopolymer network.[3]

The objective of this research is to synthesize and characterize a novel IPN hydrogel based on PNIPA and *β*-CD polymer. For this purpose, a polymer network consisting of a high *β*-CD content with a higher swelling ratio was first prepared in the presence of a small amount of poly(vinyl alcohol) (PVA). Then, a IPN was synthesized via dispersing NIPA monomer into a *β*-CD-based polymer network, polymerized, and crosslinked in situ. Finally, IR spectroscopy, thermal analysis, and swelling measurements were used to characterize the structure of the IPN hydrogel and related properties.

EXPERIMENTAL

Materials

NIPA was purchased from ACROS (more than 99% purity), UK. *β*-Cyclodextrin was from the Northwestern Geological Institute, China, and purified twice by recrystallization from water prior to use. Poly(vinyl alcohol) (polymerization degree, 1750 ± 50) was purchased from the Tianda Chemical Plant, Tanjin, China. All other reagents were analytic grade, made in China, and used as received without further purification

Preparation of β-Cyclodextrin Polymer

β-Cyclodextrin polymer (*β*-CD-EPI-PVA) containing a high *β*-CD content with a larger swelling ratio, was prepared by crosslinking *β*-CD with EPI in the presence of

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

a small amount of PVA. Particularly, based on feed composition shown in Table 1, β-CD was first dissolved in a PVA solution in a beaker, and then sodium hydroxide solution (40 wt.%) was added. After the mixture was kept at 50–60°C for 30 min, epichlorohydrin (EPI) was added dropwise under vigorous stirring. The stirring was stopped prior to gelation and the system was sealed and kept at the same temperature for 24 h. The hydrogel obtained was taken out from the beaker and cut into a desired size, and then immersed in distilled water for removing the unreacted reagents. The samples were kept in fresh distilled water, which was changed every 12 h, and lasted 6 days. Finally, samples were dried under ambient conditions for 2 days and in a vacuum oven at 80°C for 3 days. The β-CD content in β-CD-EPI-PVA was determined by a colorimetric method.[14,15]

Preparation of IPN Hydrogel Based on PNIPA and β-CD Polymer

In order to incorporate PNIPA component in β-CD polymer network, the β-CD-EPI-PVA was first swollen in a NIPA aqueous solution containing a crosslinker, *N*,*N*-methylene-*bis*(acrylamide)(BIS). The polymerization initiated with ammonium persulfate/sodium bisulfite redox system was kept at 10°C for 24 h. After polymerization, the IPN sample was cut into thin disks, and then immersed in distilled water for removing the unreacted monomer. The IPN samples were kept in fresh distilled water, which was changed every 12 h for 6 days. Finally, they were dried under ambient conditions for 2 days and in a vacuum oven at 80°C for 3 days. The composition of IPN was determined by element analysis.

For comparison, a pure PNIPA hydrogel was synthesized using BIS as crosslinking agent. The feed composition of NIPA and BIS of PNIPA was the same as that of IPN.

Instrument Analyses

Infrared spectroscopy measurements were preformed on a Specode 75 model, Germ, using KBr as the sample holder. Elemental analyses were carried out on a Vario ELIII Instrument, Germ. Differential scanning calorimetry (DSC) (model MDSC 2910, TA instrument) experiments were used to measure T_v of IPN hydrogel. The IPN sample was first swollen to an equilibrium state, and then heated from 10°C to 60°C with a rate of 3°C/min. The onset temperature of the thermogram was recorded as the T_v. Thermogravimetric analysis (TGA) was used via a USA. TA Hi-Res TGA 2950 instrument with a heating rate of 10°C/min in a nitrogen atmosphere to study the thermal stability of polymers.

Table 1. Feed compositions of β-CD-EPI-PVA and IPN hydrogels.

β-CD/EPI (mole/mole)	NaOH/EPI (mole/mole)	β-CD/PVA (wt.%/wt.%)	NIPA/BIS (mole/mole)
1/12	1.2/1	22/1	100/1.6

Measurement of Swelling Ratio

The swelling behavior of the hydrogel was tested in distilled water. Within a desired time interval, samples were carefully removed from the solution, wiped with a filter paper to remove the free water from the surface of the sample, and then weighed. The swelling ratio (SR, g/g) was calculated using the equation as follows:

$$\mathrm{SR} = \frac{w_1 - w_0}{w_0}$$

where w_0 and w_1 are weights of dry and wet sample, respectively. When a hydrogel achieved its swelling equilibrium under a fixed condition, its SR refers to the equilibrium swelling ratio (ESR).

Dynamic Swelling Measurement

To understand the swelling behaviors of hydrogel with the change of time, the dried gels were immersed in distilled water at different temperatures. The swelling degree was obtained by weighing the initial and swollen samples at various time intervals. The following equation is used to calculate the diffusion coefficient D[7,16–18]:

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

where W_t and W_∞ represent the water uptake at time t and infinite time, respectively. L is the initial thickness of the dried sample.

RESULTS AND DISCUSSION

Characterization of Hydrogel

Figure 1(a–c) shows IR spectra of β-CD-EPI-PVA and PNIPA and IPN polymer, respectively. In Fig. 1(a) and (c), A strong band around 1040 cm^{-1} can be assigned as a stretching vibration of C—OH. In Fig. 1(b) and (c), a C=O stretching vibration and a N—H deformation vibration occur around 1650 and 1540 cm^{-1}, respectively. In Fig. 1(c), a strong and wide band at 3300–3520 cm^{-1} is a combination of absorption of amide and hydroxyl groups from both β-CD-EPI-PVA and NIPA components. Also, the results in Fig. 1 indicate that there is no chemical bonding formed between β-CD-EPI-PVA and PNIPA networks. This is because the IR spectrum of the IPN is a simple superposition of those of β-CD-EPI-PVA polymer and PNIPA, and no new bands can be observed. The above evidence confirms that a new IPN hydrogel is synthesized successfully.

Figure 2 presents TGA for IPN, β-CD-EPI-PVA, and PNIPA polymer. As can be seen, the thermal stability of IPN increases slightly compared to β-CD-EPI-PVA, but it is lower than that of the PNIPA polymer. Their decomposition temperatures are 330.7°C, 323.2°C, and 396.1°C, respectively.

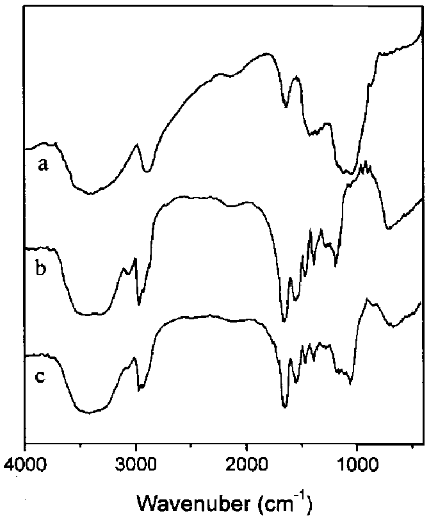

Figure 1. IR spectra of β-CD-EPI-PVA (a), PNIPA (b), and IPN (c).

Swelling Behavior of β-CD-EPI-PVA Hydrogel

β-Cyclodextrin-based polymer prepared from β-CD and EPI has been extensively investigated,[19,20] but this polymer possesses a lower ESR.[20] In order to make the NIPA monomer easily diffuse into a β-CD polymer network, polymerized, and crossliked in situ forming an IPN hydrogel, a polymer network containing a high content of β-CD with a higher swelling ratio was first prepared by crosslinking EPI with β-CD in the presence of

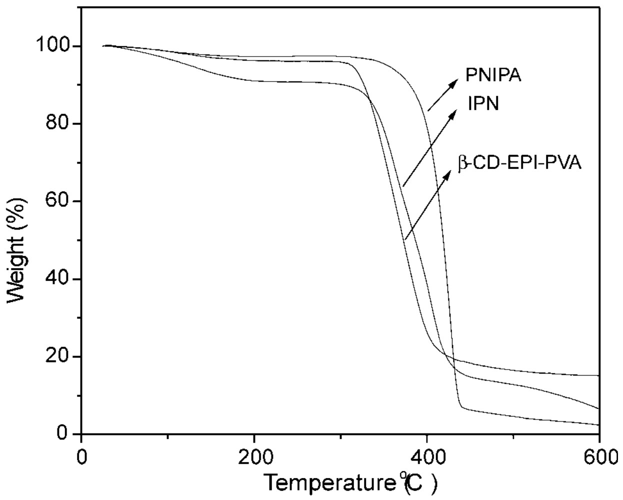

Figure 2. Thermogravimetric thermograms for IPN (PNIPA content, 57.6 wt. %), PNIPA, and β-CD-EPI-PVA (β-CD content, 76.1 wt. %).

a small amount of PVA. Figure 3 shows swelling ratios of the β-CD polymer obtained as a function of time at 25°C, 40°C, and 60°C, respectively. The results indicate that the swelling rate of β-CD polymer increases with the temperature increasing prior to achieving its equilibrium state. This is attributed to the fact that polymer segmental mobility increases with the increase in external temperature, consequently, leads to the increase in the rate of water diffusing and in its SR value with the temperature increasing.[18] On the other hand, it can be clearly seen from Fig. 3 that although the β-CD-EPI-PVA network exhibits a higher SR at equilibrium swelling state in the investigated temperature range, its corresponding SR values decrease slightly with the temperature increase.

To further investigate water diffusion behavior in the β-CD-EPI-PVA polymer, the coefficient D is calculated from the slope in the plot of $\log(W_t/W_\infty)$ against $t^{1/2}$ at different temperatures based on Eq. (1). The results are listed in Table 2. Obviously, D increases with the increase in environmental temperature. To elucidate the diffusion mechanism, the swelling curve was fitted to the following exponential Eq. (2):[16,18]

$$\frac{W_t}{W_\infty} = kt^n \tag{2}$$

where k is a characteristic constant of the hydrogel and n is a characteristic exponent for the mode of the water diffusion process. The values of n are shown in Table 2, and they are calculated from the slopes of the plot of $\log(W_t/W_\infty)$ against $\log(t)$ at a different temperature from Fig. 4. If $n = 0.5$, the diffusion process presents a limited rate and follows Fickian kinetics. If n varies between 0.5 and 1, its water-uptake process is a non-Fickian type.[7,16–18] Obviously, the feature of the water diffusing within the hydrogel of β-CD-EPI-PVA is related to their swelling temperature.

Swelling Behavior of IPN Hydrogel

Figure 5 presents ESR curves of IPN, PNIPA, and β-CD-EPI-PVA polymers as a temperature function. It is clear that the ESR of β-CD-EPI-PVA polymer decreases with

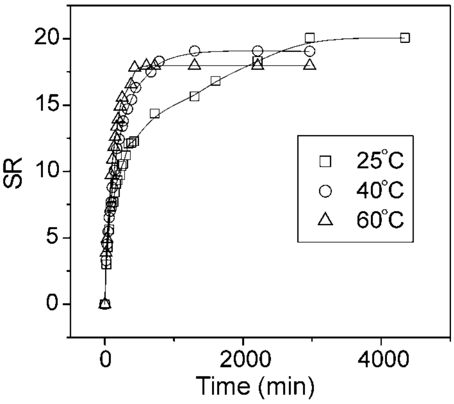

Figure 3. Swelling curves of β-CD-EPI-PVA (β-CD content, 76.1 wt. %) hydrogel at different temperatures.

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016

Table 2. Analysis of dynamic swelling experiment.

T(°C)	$D \times 10^{13}$(m^2 s^{-1})	n	k
25	3.09	0.40	−1.26
40	10.9	0.50	−1.37
60	30.3	0.56	−1.34

the increase in external temperature. Obviously, this observation is different from other non-thermosensitive hydrogels made of hydrophilic materials such as poly(acrylic acid-co-methyl methacrylate)[18] and polyacrylamide-polyvinylpyrrolidone-gelatin[21] hydrogels. For these systems, usually their ESRs slightly increases with the increase in temperature due to the elevated temperature being conductive to polymer networks' expansion. But for β-CD-EPI-PVA polymer, the phenomenon observed may be attributed to the unique structure of β-CD-EPI-PVA polymer due to the presence of β-CD. It is well known that a cone-shaped β-CD molecule possesses a hydrophilic outside and a hydrophobic cavity.[12–14] Thus, locally hydrophobic regions in β-CD-EPI-PVA polymer may cause the polymer to have a lower ESR following the increase in temperature due to hydrophobilicity of these cavities. But due to the hydrophobic cavity, β-CD are surrounded by its hydrophilic groups outside and do not exhibit mobility, they cannot show drastically hydrophobic interactions between these groups with temperature rising as the PNIPA hydrogel shown in Fig. 5(b). Poly(*N*-isopropylacrylamide) hydrogel exhibits a volume phase transition at its LCST (about 34°C), which is slightly above the coil-globule transition temperature of a linear PNIPA.[22] For the IPN system, in Fig. 5(c), the variation of its ESR with temperature is similar to that of PNIPA. This may be attributed to the fact that the β-CD-EPI-PVA component exists as a swollen state, and does not have volume transition temperature. Therefore, thermo-sensitivity of the IPN may be dependent on the PNIPA component only. Interestingly, below PNIPAs LCST, the IPN hydrogel exhibits a good swollen state, and the results may be from the contribution of both PNIPA and

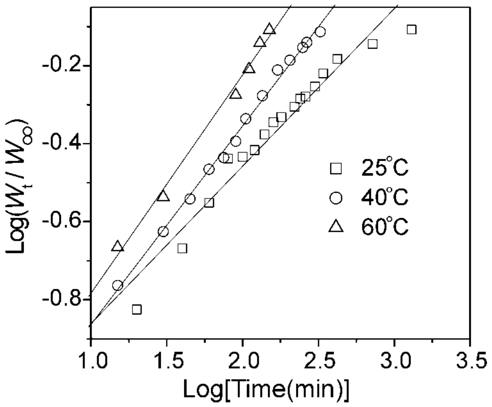

Figure 4. A representative plot for evaluating n values according to Eq. (2) (β-CD content in β-CD-EPI-PVA, 76.1 wt. %).

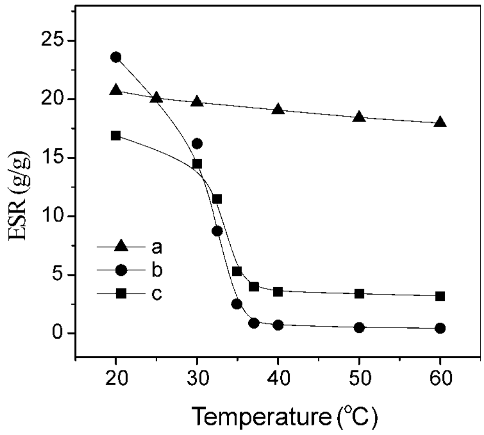

Figure 5. Equilibrium swelling ratio as a function of temperature for β-CD-EPI-PVA (a), PNIPA (b), and the IPN (c) (PNIPA content, 57.6 wt.%).

β-CD-EPI-PVA components. However, in this temperature region, the IPN presents the lowest ESR value among three hydrogels. Analyzing these data, a higher crosslinking density of the IPN via the interpenetration of PNIPA and β-CD-EPI-PVA networks may play an important role for these results. On the other hand, in the temperature region above PNIPAs LCST, as the PNIPA network dehydrates and shrinks to form a compact structure, the IPN also exists as a deswelling state. But in this temperature range, the IPNs ESR value lies in between the values of β-CD-EPI-PVA and PNIPA samples. This may be from the β-CD-EPI-PVA network which can effectively prevent the PNIPA component from organizing a more compact structure. Also, the deswelling process of the IPN can be further confirmed via an evident endotherm on DSC curve in Fig. 6, which is the result of

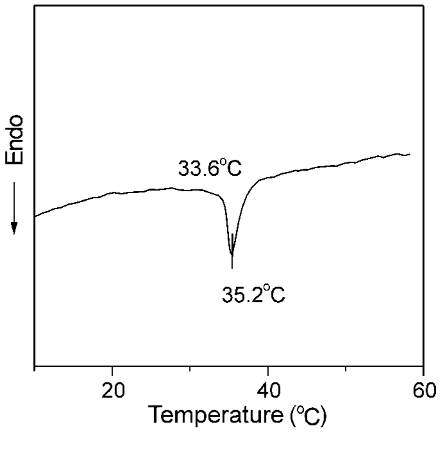

Figure 6. Differential scanning calorimetry thermogram of the IPN sample swollen in distilled water (PNIPA content in the IPN sample, 57.6 wt.%).

dissociation of water clusters through the IPN as the temperature reaches PNIPA' LCST.[3,6,23,24] The result demonstrates that there is no significant deviation between IPNs T_V and pure PNIPAs LCST, and the IPN synthesized can retain a good thermo-sensitivity as that of pure PNIPA. It is also indicated that the IPN synthesized is a polymer network in which each component can keep its own property independently.

Interpenetrating Polymeric Network Hydrogel in Response to Changes in Temperature

Figure 7 shows oscillatory swelling behavior of the IPN sample as a function of time and temperature. The results indicate that the IPN can respond well to an alternating temperature between 25°C to 40°C, respectively. The reversible changes between the swollen at and shrunken states of IPN hydrogel are attributed to thermal sensitivity of PNIPA, which can exhibit transition of hydration and dehydration at LCST. This clearly demonstrates that the IPN can response to a change in temperature by attractive and repulsive polymer–polymer interactions, as well as polymer–water interactions.[2] Also, as can be seen in Fig. 7, the shrinking rate of IPN sample is faster than its swelling rate. This may suggest that the swelling process of the hydrogel is still a rate-related diffusing process.[25]

CONCLUSION

A β-CD-EPI-PVA polymer containing a high content of β-CD with a higher SR can be prepared by crosslinking EPI with β-CD. The swelling behavior of this polymer indicates that its ESR decreases slightly with the increase in temperature in distilled water. This may be attributed to a weak interaction between water and the hydrophobic cavity of β-CD. Based on the β-CD-EPI-PVA polymer, an IPN hydrogel can be prepared by

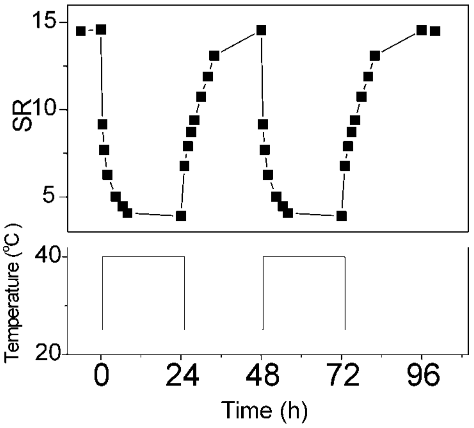

Figure 7. Oscilatory swelling behavior of the IPN hydrogel as a function of time and temperature (PNIPA content in the IPN sample, 57.6 wt. %).

incorporating a PNIPA network. Infrared spectra, element analysis, DSC, TGA, and measurement were used to character the structure of the IPN sample. The swelling measurements indicated that the IPN synthesized possesses a good thermal sensitivity, and its volume phase transition still remains around 33°C.

ACKNOWLEDGMENT

This work was supported by the Doctorate Foundation of Northwestern Polytechnic University, China.

REFERENCES

1. Kwon, I.C.; Bae, Y.H.; Kim, S.W. Electrically erodible polymer gel for controlled release of drugs. Nature **1991**, *354* (28), 291–293.
2. Akoi, T.; Kawashiko, M.; Katono, H.; Sanui, K.; Ogata, N.; Okano, T.; Sakurai, Y. Temperature-responsive interpenetrating polymer networks constructed with poly (acrylic acid) and poly(*N*,*N*-dimethyacrylamide). Macromolecules **1994**, *27* (4), 947–952.
3. Zhang, J.; Peppas, N.A. Synthesis and characterization of pH- and temperature-sensitive poly(methacrylic acid)/poly(*n*-isopropylacylamide) interpenetrating polymeric networks. Macromolecules **2000**, *33* (1), 102–107.
4. Kokufuta, E.; Wang, B.; Yoshida, R.; Khokhlov, A.R.; Hirata, M. Volume phase transition of polyelectrolyte gels with different charge distributions. Macromolecules **1998**, *31* (20), 6878–6884.
5. Ju, H.K.; Kim, S.Y.; Lee, Y.M. pH/temperature-responsive behaviors of semi-IPN and comb-type graft hydrogels composed of alginate and poly(*N*-isopropylacrylamide). Polymer **2001**, *42*, 6851–6857.
6. Shibayama, M.; Mizutani, S.Y.; Nomura, S.J. Thermal properties of copolymer gels containing *N*-isopropylacrylamide. Macromolecules **1996**, *29*, 2019–2024.
7. Lee, W.F.; Shieh, C.H. pH-thermoreversible hydrogel. II. Synthesis and swelling behaviors of *N*-isopropylacrylamide-co-acrilic acid-co-sodium acrylate hydrogels. J. Appl. Polym. Sci. **1999**, *73*, 1955–1967.
8. Liu, Y.Y.; Fan, X.D. Synthesis and characterization of pH- and temperature-sensitive hydrogel of *N*-isopropylacrylamide/cyclodextrin based copolymer. Polymer **2002**, *43* (18), 4997–5003.
9. Liu, Y.Y.; Fan, X.D. Preparation and characterization of a novel responsive hydrogel using a *β*-Cyclodextrin based macromonomer. J. Appl. Polym. Sci. **2003**, *89* (2), 361–367.
10. Nozaki, T.; Maceda, Y.; Ito, K.; Kitano, H. Cyclodextrin modified with polymer chains which are responsive to external stimuli. Macromolecules **1995**, *28* (2), 522–524.
11. Nozaki, T.; Maeda, Y.; Kitano, H. Cyclodextrin gels which have a temperature responsiveness. J. Polym. Sci. A: Polym. Chem. **1997**, *35*, 1535–1541.

12. Sreenivasan, K. On the restriction of the release of water-soluble component from polyvinyl alcohol film by blending β-cycliodextrin. J. Appl. Polym. Sci. **1997**, *65*, 1829–1832.
13. Baille, W.E.; Huang, W.Q.; Nichifor, M.; Zhu, X.X. Functionalized β-cyclodextrin polymers for the sorption of bile salts. J. Macromol. Sci.-Pure & Appl. Chem. **2000**, *A* (7), 677–690.
14. He, B.L.; Zhao, X.B. Studies on synthesis of novel polymers carrying β-cyclodextrin. Science in China (Ser. B) **1992**, *12*, 1240–1247.
15. Dubois, M.; Gilles, K.A.; Hamilton, J.K.; Pebers, P.A.; Smith, F. Colorimetric method for determination of sugars and related substances. Anal. Chem. **1956**, *28* (3), 350–356.
16. Franson, N.M.; Peppas, N.A. Influence of copolymer composition on non-Fickian water transport through glassy copolymers. J. Appl. Polym. Sci. **1983**, *28*, 1299–1310.
17. Korsmeyer, R.W. Solute and penetrant diffusion in swellable polymer. II. Verification of theoretical models. J. Polym. Sci.: Polym. Phys. Ed. **1986**, *24*, 409–434.
18. Bajpai, A.K.; Shrivastava, M. Dynamic swelling behavior of polyacrylamide based three component hydrogels. J. Macromol. Sci.-Pure & Appl. Chem. **2000**, *A37* (9), 1069–1088.
19. Renard, E.; Deratani, A.; Volet, G.; Sebilie, B. Preparation and characterization of water soluble high molecular weight β-Cyclodextrin-epichlorohydrin polymer. Euro. Polym. J. **1997**, *33* (1), 49–57.
20. Liu, Y.Y.; Fan, X.D.; Cao, Z. State of water in β-cycliodextrin/epichlorohydrin hydrogel and swelling behavior of the crosslinked polymer. J. Functional Polymer **2001**, *14* (2), 169–173.
21. Katime, I.; Apodaca, E.D. Acrylic acid/methyl methacrylate hydrogels. II. Effect of composition on mechanical and thermodynamic properties. J. Macromol. Sci.-Pure & Appl. Chem. **2000**, *A37* (4), 307–321.
22. Gündogan, N.; Okay, O. Reentrant phase transition of poly(*N*-isopropylacrylamide) gel in polymer solutions: thermodynamic analysis. J. Appl. Polym. Sci. **2002**, *85*, 801–813.
23. Fan, X.D.; Uludag, H. Synthesis and characterization of thermo-reversible and protein-conjugation functional copolymers of poly(*N*-isopropylacrylamide-co-*N*-acryloxysucci-nimide). Polymer Preprints **1999**, *41* (1), 361–362.
24. Chen, G.H.; Hoffman, A.S. Graft copolymers that exhibit temperature-induced phase transitions over a wide range of pH. Nature **1995**, *373* (5), 49–52.
25. Yoshida, R.; Uchida, K.; Kaneko, Y.; Sakai, K.; Kikuchi, A.; Sakural, Y.; Okano, T. Comb-type grafted hydrogels with rapid de-swelling response to temperature changes. Nature **1995**, *374* (16), 240–242.

Received October, 2002
Revised April, 2003

Marcel Dekker, Inc.
270 Madison Avenue, New York, New York 10016