

Preparation of Poly(vinyl alcohol)-*graft-N*-isopropylacrylamide Copolymer Membranes with Triphenylmethane Leucocyanide and Permeation of Solutes Through the Membranes

SEIJI KURIHARA, YOSHIKO UENO, TAKAMASA NONAKA

Department of Applied Chemistry and Biochemistry, Faculty of Engineering, Kumamoto University, Kurokami 2-39-1, Kumamoto 860, Japan

Received 18 February 1997; accepted 1 June 1997

ABSTRACT: Thermo- and photosensitive hydrogel membranes were prepared by graft copolymerization of an *N*-isopropylacrylamide (NIPAAm) and triphenylmethane leucocyanide (LeCN) monomer onto poly(vinyl alcohol) (PVA). The yield of the graft copolymerization as well as the content of the poly(NIPAAm) segments grafted onto PVA was depressed by copolymerization of the LeCN monomer. The change in the permeation rate of poly(ethylene glycol)s through the hydrogel membranes was induced photochemically by dissociation of LeCN moieties in the membranes. © 1998 John Wiley & Sons, Inc. *J Appl Polym Sci* **67**: 1931–1937, 1998

Key words: thermosensitive membrane; *N*-isopropylacrylamide; photosensitive membrane; triphenylmethane leucocyanide; permeation

INTRODUCTION

Poly(*N*-isopropylacrylamide) [poly(NIPAAm)] hydrogels are well known to show a reversible volume-phase transition from a swollen state to a shrunken state around 33°C, due to a lower critical solution temperature (LCST) of poly(NIPAAm) segments. Many studies have focused on the thermosensitive swelling behavior of poly(NIPAAm) hydrogels in such fields as drug delivery,^{1,2} regulation of activity of enzymes and cells,^{3,4} and chromatography.⁵ In addition, several studies on the phase transition of the hydrogels have been described in relation not only to temperature dependence, but also to solvent composition, pH, ionic composition, and electric-field dependencies.⁶ Irie et al. reported the synthesis of photoresponsive gels by incorporating photosensi-

tive triphenylmethane leuco derivatives into polyacrylamide gels and poly(NIPAAm) gels.^{7,8} For some applications, it would be desirable if such a phase transition could be controlled by the irradiation of light, because light can be used instantly. However, there are few studies on the photochemical switching of the permeation of solutes through membranes consisting of poly(NIPAAm) segments, because of the difficulty of making strong membranes which consist of poly(NIPAAm) segments containing photochromic molecules such as triphenylmethane leuco derivatives, spiropyranes, and azobenzenes. To control, photochemically, the permeation of solutes through membranes, we prepared glass-fiber membranes grafted with poly(NIPAAm containing triphenylmethane leucocyanide) and investigated the photochemical switching of the permeation of solutes.⁹ Earlier, we reported the preparation and permeation behavior of poly(vinyl alcohol)-*graft-NIPAAm* copolymer membranes (PGN membranes). The PGN membranes were found to

Correspondence to: T. Nonaka.

Journal of Applied Polymer Science, Vol. 67, 1931–1937 (1998)
© 1998 John Wiley & Sons, Inc. CCC 0021-8995/98/111931-07

show flexible and strong mechanical properties and thermal switching of the permeation of solutes.^{10–12} To prepare flexible and strong hydrogel membranes showing thermal and photochemical switching of the permeation of solutes, we attempted to introduce triphenylmethane leucocyanide (LeCN) moieties into the PGN copolymer membranes. In this article, we describe the preparation of hydrogel membranes by copolymerization of NIPAAm and the LeCN monomer onto PVA and investigate the thermal and photochemical changes of permeation of solutes through the hydrogel membranes.

EXPERIMENTAL

Materials

N-Isopropylacrylamide (NIPAAm) was kindly provided by the Kohjin Co. and was purified by recrystallization with hexane and benzene. PVA (degree of polymerization, 1700; degree of saponification, 98%) was kindly supplied by the Nippon Gosei Co. Bis[4-(dimethylamino)phenyl](4-vinylphenyl)methyl leucocyanide (LeCN monomer) was synthesized according to the method described previously.⁷ Other chemicals were of reagent grade.

Graft Copolymerization

First, PVA was dissolved in 20 mL of dimethyl sulfoxide (DMSO), and then, NIPAAm, the LeCN monomer, and potassium peroxydisulfate (KPS, initiator) were dissolved in the DMSO solution. After nitrogen was introduced into the DMSO solution for 1 h in a glass tube, polymerization was carried out at 40°C for 24 h with shaking. After polymerization, the mixture in the glass tube was poured into a large excess of acetone. The copolymer obtained was washed several times with acetone to remove the polymers of NIPAAm and LeCN, unreacted monomers, the initiator, and DMSO. The compositions of copolymers were estimated from the nitrogen contents determined by elemental analysis. The molecular weights of non-grafted polymers of NIPAAm and LeCN, which were obtained from the acetone washing solutions after polymerization, were determined by gel permeation chromatography (Jasco 880-PU, Shodex KF-80M + KF-80M column, tetrahydrofuran eluent).

Preparation of Hydrogel Copolymer Membranes

The copolymers were dried *in vacuo* and were dissolved in DMSO. Hydrogel membranes were prepared by pouring 4 mL of 5% (wt/vol) copolymer DMSO solutions into a flat laboratory dish (4.8-cm diameter), and the solvent was allowed to evaporate at 50°C for 96 h. The membranes were removed from the dish in water.

Swelling Ratio

The hydrogel membranes were immersed in water at various temperatures. After immersion for 24 h, the membranes were wiped with a filter paper to remove water on the surface of the membranes. The swelling ratios of the membranes at various temperatures were determined by measuring the weights of the dried and swollen membranes.

Phase-Transition Temperature

The phase-transition temperature of the hydrogel membranes was measured by differential scanning calorimetry (Seiko DSC100). The membranes were immersed in water at room temperature for 2 days. The membranes were picked up from the water, followed by wiping off water on the surface of the membranes with a filter paper, and sealed in an aluminum capsule. DSC thermograms were measured at a heating rate of 1°C/min. The maximum endothermic point was taken as the phase-transition temperature.

Permeation of Poly(ethylene glycol)s

Permeation experiments were carried out at various temperatures with magnetic stirring, using a diaphragm cell consisting of two detachable parts (22 mL each). Each membrane was immersed in water at each temperature prior to use for the permeation experiments. The swollen membrane was set in the middle of the two parts of the cell, which were clamped together and sealed tightly with silicone rubber packing. The effective membrane area in the cell was 3.14 cm². Poly(ethylene glycol)s were used as solutes for permeation experiments: diethylene glycol (DEG) and poly(ethylene glycol)s with average molecular weights of 300 (PEG300) and 1000 (PEG1000). The left (L) side was an aqueous solution containing each solute, and the right (R) side was deionized water. The initial concentration of each solute on the L side was 0.5% (wt/vol). The concentration of each

Table I Preparation of PGN and PGN–LeCN Membranes

	Feed (g)				LCST (°C)	ΔH (mJ/mg)	Content of NIPAAm (%)	Content of Leuco (%)	Yield (%)
	PVA	NIPAAm	Leuco	KPS					
PGN–P5K3	0.5	5.00	0	0.03	32.3	2.4	77	0	41
PGN–LeCN									
(No. 1)	0.5	4.95	0.05	0.03	32.9	1.2	65	0.78	20
(No. 2)	0.5	4.95	0.05	0.06	33.3	1.8	67	0.91	33
(No. 3)	0.5	4.95	0.05	0.09	33.2	1.9	73	0.82	36
(No. 4)	0.5	4.95	0.05	0.12	33.4	1.4	71	0.90	31
(No. 5)	0.6	5.94	0.06	0.09	32.6	1.2	77	0.82	40
(No. 6)	0.7	6.93	0.07	0.09	32.8	1.6	78	0.78	41
(No. 7)	0.7	6.86	0.14	0.09	32.7	0.1	60	0.99	17
(No. 8)	0.7	6.79	0.21	0.09	32.7	0.1	44	0.84	13

Polymerization was carried out for 24 h at 40°C in 20 mL of DMSO.

solute permeated on the R side was measured on a Shodex refractometer SE-11.

To reveal an effect of the photodissociation of LeCN moieties on the permeation of solutes, the amount of each solute permeated on the R side was measured when the membrane surface of the L side was exposed to ultraviolet (UV) light with a 75-W high-pressure mercury lamp.

RESULTS AND DISCUSSION

Synthesis of Copolymers

The graft copolymerization of NIPAAm and the LeCN monomer onto PVA was carried out by varying the content of the monomers and the ratio of the LeCN monomer to NIPAAm, PVA content, and KPS content in 20 mL of DMSO. The weight ratio of the monomer mixtures of NIPAAm and the LeCN monomer to PVA was kept constant at 10. Some of the results are given in Table I. The graft copolymers of NIPAAm on PVA without and with LeCN are abbreviated as PGN and PGN–LeCN, respectively. The yields of the PGN–LeCN copolymers were lower than that of the PGN copolymer, namely, the copolymerization of the LeCN monomer depressed the polymerization yield. Steric hindrance of the triphenylmethane moiety of the LeCN monomer is considered to be one of factors depressing the polymerization yield. The yield increased with increasing content of KPS up to 0.09 g, while the yield decreased by using 0.12 g of KPS. Formation of linear polymers of NIPAAm and LeCN, as well as an oxidation reaction of PVA, may be brought about with an

excess of KPS, lowering the polymerization yield.¹³ In addition, the yield also increased with increasing content of the monomer mixtures of NIPAAm, LeCN, and PVA. However, gelation was induced with the total contents of the mixtures more than 7.7 g in 20 mL of DMSO.

The aim of this study was to prepare hydrogel membranes showing a photochemical switching of the permeation of the solutes. Therefore, it is of particular interest to increase the amount of LeCN moieties introduced in the PGN–LeCN copolymers. However, the polymerization yield was considerably depressed by increasing the LeCN monomer contents, whereas no increase in the amount of the LeCN moieties introduced was obtained. The depression of the yield may also be attributed to the steric hindrance of the triphenylmethanemioety of the LeCN monomer. The copolymerization of the LeCN moieties was found to lower the enthalpy change on the phase transition, although the phase-transition temperature was almost constant around 33°C. The enthalpy change of the PGN membrane was 2.4 mJ/mg, whereas those of the PGN–LeCN membranes (Nos. 1–6) were in the range of 1.2 to 1.9 mJ/mg. On the other hand, the PGN–LeCN membranes (Nos. 7 and 8), which were prepared by the copolymerization of the LeCN monomer higher than 20 wt % relative to PVA, showed the enthalpy change to be smaller than 0.1 mJ/mg. The result can be interpreted in terms of the decrease in the amount of poly(NIPAAm) segments grafted due to the steric hindrance of the LeCN monomer.

The weight-average molecular weights of non-grafted linear polymers, extracted with acetone

Table II Weight-Averaged Molecular Weight of Extracted Linear Polymers with Acetone

	\overline{M}_w
PGN	70,000
PGN–LeCN	
(No. 1)	18,500
(No. 4)	15,300
(No. 6)	32,300

after graft copolymerization, are given in Table II. It can be clearly seen that the copolymerization of the LeCN monomer resulted in not only a decrease in the yield, but also a decrease in the weight-average molecular weight of the linear polymers. In addition, the comparison of the results of PGN–LeCN (No. 1) and PGN–LeCN (No. 6) indicates that the increase in the concentration of the monomer mixture in the DMSO copolymerization solution increases the yield as well as the molecular weight of the nongrafted linear copolymers. It can be assumed that the conditions of the formation of the grafted poly(NIPAAm–LeCN) segments on PVA are almost similar to those of the formation of the nongrafted linear polymers. Consequently, the molecular weight of the grafted polymer segments on PVA can be estimated with the molecular weights of the nongrafted linear polymers extracted with acetone. The length of the grafted poly(NIPAAm–LeCN) segments decreased with increasing KPS concentration and increased with increasing monomer mixture concentration.

Figure 1 shows changes in the swelling ratios of the PGN and PGN–LeCN membranes as a function of temperature. The swelling ratios of the membranes decreased gradually with increasing temperature and became almost the same as those of the dry state above 35°C. The changes in the swelling ratios were reversible, namely, the membranes showed a reversible volume-phase transition from the swollen state to the shrunken state around 33°C. Below 30°C, the swelling ratios of the PGN–LeCN membranes were strongly depressed compared to those of the PGN membrane. Irie and Kunwathakun stated that a higher content of LeCN moieties in the gels resulted in the contraction of the gels, because of the higher hydrophobicity of LeCN moieties.⁷ The depression of the swelling ratios below 30°C is related to the hydrophobicity of LeCN moieties. On the other hand, the swelling ratios of the PGN–LeCN membranes were higher than those of the PGN mem-

brane at temperatures higher than 35°C, according to the amounts of LeCN fed in the graft polymerization. The shrinkage of poly(NIPAAm) segments grafted due to the volume-phase transition resulted in a decrease in the swelling ratio. The amounts of poly(NIPAAm) segments grafted decreased with an increasing content of the LeCN monomer fed in the polymerization. The temperature dependence of the swelling ratio of the PGN–LeCN membranes is closely related to the amounts of the poly(NIPAAm) segments grafted, as well as to the hydrophobic interaction between LeCN moieties.

Effects of Photodissociation of LeCN

Figure 2 shows the absorption spectra of the PGN–LeCN membrane (No. 6) in water before and after UV irradiation, respectively, with a 75-W high-pressure mercury lamp. An increase in absorbance at 550 nm was observed by UV irradiation, indicating photodissociation of the LeCN moieties.

To clarify the effects of the dissociation of LeCN moieties on the properties of the membranes, the swelling behavior of the PGN–LeCN membranes was examined in the dark and under UV irradiation at various temperatures. Figure 3 shows the

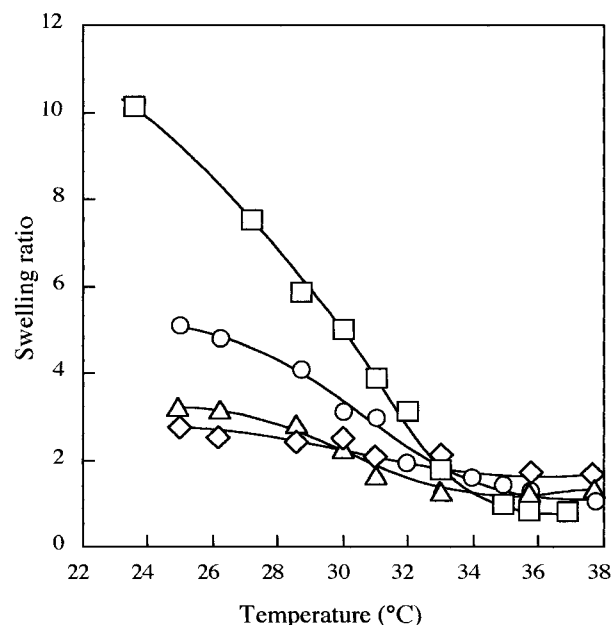


Figure 1 Temperature dependence of swelling ratio of the PGN and PGN–LeCN membranes: (□) PGN; (○) PGN–LeCN (No. 6); (△) PGN–LeCN (No. 7); (◇) PGN–LeCN (No. 8).

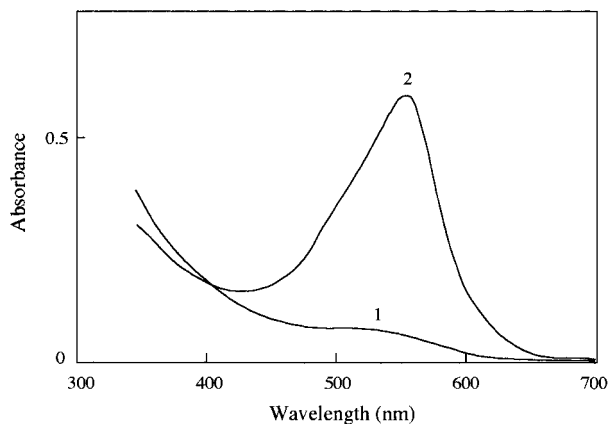


Figure 2 Absorption spectra of the PGN-LeCN membrane (No. 6) in water (1) before and (2) after UV irradiation.

transmittance at 700 nm of the PGN-LeCN membrane (No. 6) at various temperatures. The transmittance decreased with increasing temperature, in the dark, above 30°C, corresponding to the phase transition of poly(NIPAAm) segments to the shrunken state. The UV irradiation caused an increase in the transmittance above 30°C, although no change was observed below 30°C. The increase in the transmittance by UV irradiation indicates the increase in the swelling ratio of the

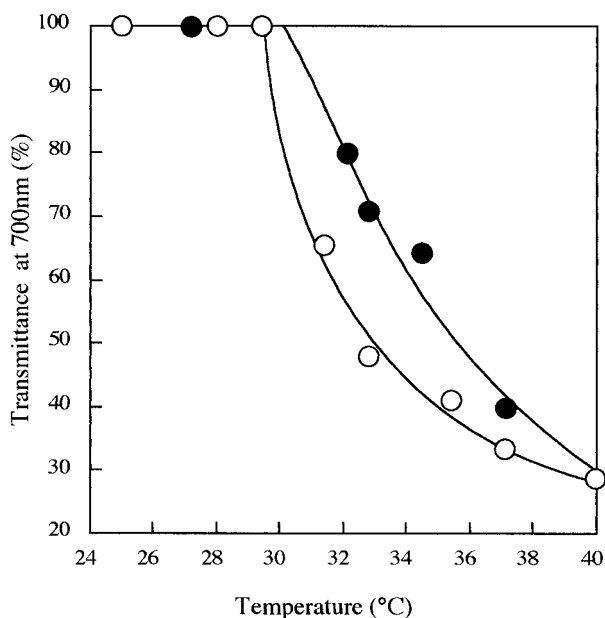


Figure 3 Changes in transmittance at 700 nm of the PGN-LeCN membrane (No. 6) as a function of temperature: (○) in the dark; (●) under UV irradiation.

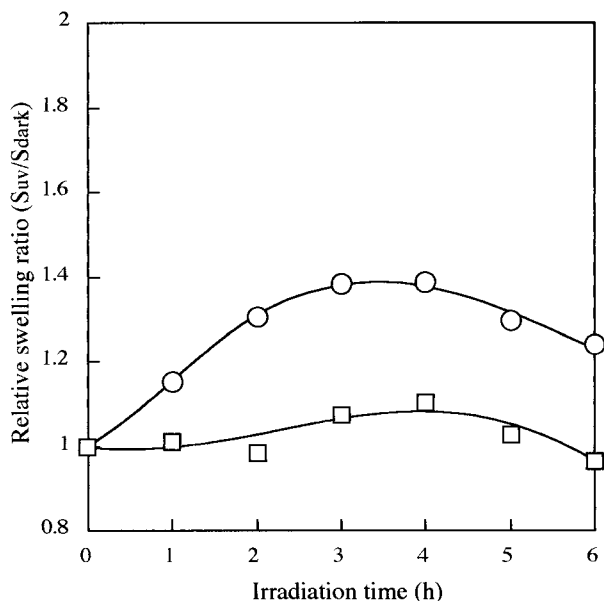


Figure 4 Changes in the swelling ratio of the PGN-LeCN membranes by UV irradiation at 32°C. S_{uv} and S_{dark} represent the swelling ratios under UV irradiation and in the dark, respectively: (□) PGN-LeCN membrane (No. 3); (○) PGN-LeCN membrane (No. 6).

membrane. Figure 4 shows the changes in the swelling ratio of the PGN-LeCN membranes (Nos. 4 and 6) by UV irradiation. The UV irradiation caused a significant increase in the swelling ratio of the PGN-LeCN membrane (No. 6) at 32°C. However, the prolonged UV irradiation decreased the swelling ratio again. The decrease in the swelling ratio by prolonged UV irradiation may be related to slow relaxation of the polymer segments. The PGN-LeCN membrane (No. 6) showed the largest change in the swelling ratio on the phase transition among the PGN-LeCN membranes studied in the dark. The magnitude of change in the swelling ratio by varying temperature or UV irradiation may be related to both the amount and the length of poly(NIPAAm-LeCN) segments grafted. The photodissociation of the LeCN moieties in the membranes produced fixed triphenylmethane cations and free cyanide anions in the membranes. Consequently, the increase in the osmotic pressure differential due to the formation of charges in the membranes brought about the photochemical change in the swelling ratio. In the case of the PGN-LeCN membranes, however, the photochemical change in the swelling ratio was much smaller compared to those of the hydrogels.^{7,8} The smaller photochemical change in the swelling ratio of the PGN-LeCN membranes may

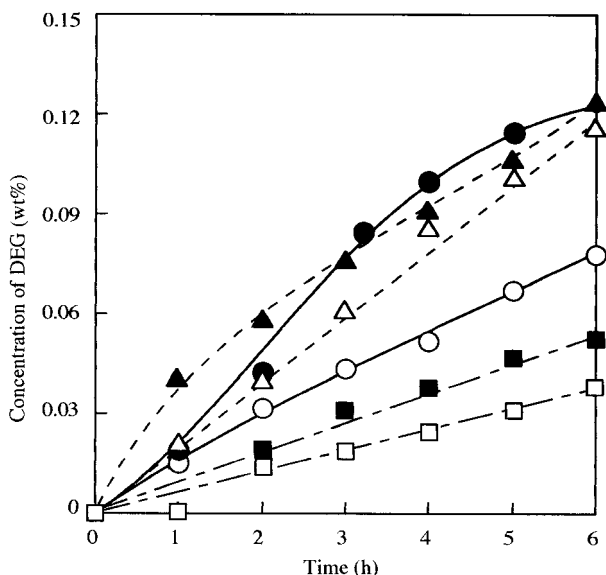


Figure 5 Time plots of the amounts of DEG permeated through the PGN–LeCN membrane (No. 6) in the dark (open symbols) and under UV irradiation (solid symbols) at (Δ , \blacktriangle) 25°C, (\circ , \bullet) 32°C, and (\square , \blacksquare) 35°C.

be attributed to PVA as a graft polymerization substrate, improving the mechanical strength of the membranes. We reported the graft polymerization of NIPAAm onto PVA (PGN copolymers) and the preparation of membranes from the PGN copolymers.¹⁰ The membranes prepared by using PVA with lower degrees of polymerization were not suitable as membranes for permeation experiments, because of their high swelling and softness. The molecular weight of PVA influenced strongly the properties of the membranes containing PVA. Actually, the PGN–LeCN membranes containing PVA with a degree of polymerization of 2600 showed little change in the swelling ratio photochemically by UV irradiation.

Figure 5 shows the permeation of diethylene glycol (DEG) through the PGN–LeCN membrane (No. 6) with or without UV irradiation at 25, 32, and 35°C, respectively. The amount of DEG permeated in the dark increased monotonously with time and decreased with increasing temperature due to the shrinkage of the membrane. The UV irradiation was found to enhance the permeation rate of DEG through the membrane. In particular, the permeation rate at 32°C was increased considerably more than were the others. As mentioned above, the photochemical dissociation of LeCN moieties in the membranes produced fixed cations and free anions in the membranes. The increase in the osmotic pressure differential caused an in-

crease in the swelling ratio. The photochemical increase in the swelling ratio at 32°C is larger than that at 35°C, as can be seen in Figure 3. The result indicates that the photochemical change in the permeation rate of DEG is closely related to the increase in the swelling ratio, indicating an increase in the micropore size of the membranes. A larger osmotic pressure differential may be required to increase the micropore size of the membrane at 35°C, because the membrane is in the shrunken state at 35°C. Therefore, the change in the permeation rate at 35°C is smaller than that at 32°C. On the other hand, the UV irradiation at 25°C caused only a slight increase in the permeation rate. No significant increase in the swelling ratio was induced by UV irradiation at 25°C, because the membrane is well swollen even in the dark. The introduction of LeCN moieties in the membrane enhances the hydrophobicity, resulting in the decrease in the swelling ratio as shown in Figure 1, whereas the charges produced by the photodissociation of the LeCN moieties increase the hydrophilicity in the membrane systems. The increase in the permeation rate at 25°C may be related to the increase in the hydrophilicity of the membranes. The change in the hydrophilicity as well as the generation of the osmotic pressure differential may be an important factor in controlling the permeation rate through the photoresponsive membranes.

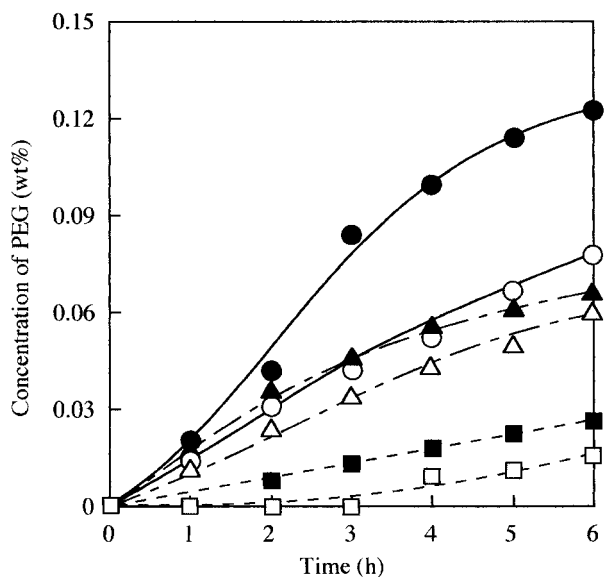


Figure 6 Time plots of the amounts of poly(ethylene glycol)s permeated through the PGN–LeCN membrane (No. 6) in the dark (open symbols) and under UV irradiation (solid symbols) at 32°C: (\circ , \bullet) DEG; (Δ , \blacktriangle) PEG300; (\square , \blacksquare) PEG1000.

The permeation behavior of three poly(ethylene glycol)s with different molecular weights through the PGN–LeCN membrane (No. 6) at 32°C is shown in Figure 6. The permeation rates decreased with an increase in the molecular size in the order of DEG < PEG300 < PEG1000 in the dark. In addition, the effect of UV irradiation on the permeation of solutes depends on the molecular size, namely, the change in the micropore size by UV irradiation is not large compared with the molecular size of the solutes used in this study.

CONCLUSION

PGN–LeCN membranes, showing thermal and photochemical change in the permeation of solutes, were prepared by the graft copolymerization of NIPAAm and the LeCN monomer onto PVA in DMSO using KPS as an initiator. The yield of the graft polymerization was found to depend on the contents of the monomer, LeCN, and KPS in the DMSO solution. The hydrogel PGN–LeCN membranes showed a reversible volume-phase transition around 33°C, namely, the membranes are in the swollen and shrunken states below and above this temperature in the dark, respectively. In the dark, the permeation rate of poly(ethylene glycol)s through the membranes decreased monotonously with increasing temperature due to the shrinkage of the membrane. The significant in-

crease in the permeation rates was induced by UV irradiation of the PGN–LeCN membrane (No. 6) at 32°C. On the other hand, a small change in the permeation rates was observed by UV irradiation at 25 and 35°C.

REFERENCES

1. L. C. Dong and A. S. Hoffman, *J. Control. Release*, **13**, 21 (1990).
2. T. Okano, Y. H. Bae, and S. W. Kim, *J. Control. Release*, **9**, 271 (1989).
3. T. G. Park and A. S. Hoffman, *J. Biomed. Res.*, **24**, 21 (1990).
4. T. G. Park and A. S. Hoffman, *Biotech. Bioeng.*, **35**, 152 (1990).
5. M. Gewehr, K. Nakamura, N. Ise, and H. Kitano, *Makromol. Chem.*, **193**, 249 (1992).
6. T. G. Park and A. S. Hoffman, *Macromolecules*, **26**, 5045 (1993).
7. M. Irie and D. Kunwatchakun, *Macromolecules*, **19**, 2476 (1986).
8. A. Mamada, T. Tanaka, D. Kunwatchakun, and M. Irie, *Macromolecules*, **23**, 1517 (1990).
9. S. Kurihara, K. Yoshimura, T. Ogata, and T. Nonaka, *J. Appl. Polym. Sci.*, **57**, 887 (1995).
10. T. Nonaka, T. Ogata, and S. Kurihara, *J. Appl. Polym. Sci.*, **52**, 951 (1994).
11. T. Ogata, T. Nonaka, and S. Kurihara, *J. Membr. Sci.*, **103**, 159 (1995).
12. S. Kurihara, S. Sakamaki, S. Mogi, T. Ogata, and T. Nonaka, *Polymer*, **37**, 1123 (1996).
13. Y. Ikada, Y. Nishizaki, and I. Sakurada, *J. Polym. Sci. Polym. Chem.*, **12**, 1829 (1974).