

# Preparation of Poly(vinyl alcohol)-*graft-N*-isopropylacrylamide Copolymer Membranes and Permeation of Solutes through the Membranes

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## SYNOPSIS

Thermosensitive copolymers were prepared by graft copolymerization of *N*-isopropylacrylamide onto poly(vinyl alcohol) in dimethyl sulfoxide (DMSO) using potassium peroxydisulfate as an initiator. The phase transition temperature was measured by differential scanning calorimetry. The copolymers exhibited almost the same transition temperature (about 33°C) as that of poly(*N*-isopropylacrylamide) regardless of the composition of the copolymers. The copolymer membranes were obtained by evaporating solvent from the DMSO solution of the graft copolymers and were insolubilized by annealing the membranes at 120°C for 10 h. Permeation of the lithium ion and Methylene Blue through the membranes was investigated at various temperatures. The permeation of solutes was greatly affected by temperature, i.e., the permeation of the solutes could be controlled at temperatures below and above 33°C. © 1994 John Wiley & Sons, Inc.

## INTRODUCTION

It is known that poly(*N*-isopropylacrylamide)-[poly(NIPAAm)] hydrogel is a thermally reversible hydrogel and exhibits a lower critical solution temperature (LCST) around 33°C in aqueous solutions, i.e., the poly(NIPAAm) hydrogels swell and shrink at temperatures below and above 33°C, respectively. Poly(NIPAAm) hydrogels have recently been of increasing interest in the fields of controlled drug delivery,<sup>1,2</sup> immobilization of enzymes<sup>3</sup> and cells,<sup>4</sup> and dewatering of protein solutions.<sup>5</sup> However, it is very difficult to make thin membranes from such hydrogels. So far, only a few studies on the separation of solutes in aqueous solution controlled by temperature through poly(NIPAAm) hydrogel membranes have been performed.<sup>6,7</sup> We could make membranes thin and strong enough from poly(vinyl alcohol)-*graft-NIPAAm* (PVA-*g*-NIPAAm) copolymers to use as separation membranes. The LCSTs of the copolymers are almost the same as that of

poly(NIPAAm) hydrogel regardless of the composition of PVA-*g*-NIPAAm copolymers and the molecular weight of PVA. Of course, the LCST of the copolymers can be changed by introduction of hydrophilic or hydrophobic groups into the PVA-*g*-NIPAAm copolymers. This article is concerned with the synthesis and characterization of the PVA-*g*-NIPAAm copolymer membranes and the temperature-dependent permeation of several solutes in aqueous solution.

## EXPERIMENTAL

### Materials

NIPAAm was kindly provided by Kohjin Co. and purified by recrystallization using hexane and benzene. PVAs with different degrees of polymerization (D.P.) and of saponification (D.S.) were kindly supplied by Nippon Gosei Co. PVAs used in this study included NH-26 (D.P. = 2600, D.S. > 99%), AH-26 (D.P. = 2600, D.S. = 98%), NH-22 (D.P. = 2200, D.S. > 99%), NH-20 (D.P. = 2000, D.S. > 99%), and AH-17 (D.P. = 1700, D.S. = 98%). PVA was dried at 40°C for 24 h prior to use. Potassium per-

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oxodisulfate (KPS) was purified by the usual method. Other chemical compounds were of reagent grade.

### Synthesis of PVA-*g*-NIPAAm Copolymers

PVA-*g*-NIPAAm copolymers were prepared as follows: PVA was dissolved in dimethyl sulfoxide (DMSO) and then NIPAAm and KPS (initiator) were dissolved into the solution in a glass tube. After nitrogen was introduced into the mixture solution for about 1 h, the glass tube was sealed. The polymerization was carried out at 40°C for 20 h with shaking. After polymerization, the mixture in the glass tube was poured into a large excess of acetone. The copolymers obtained were washed several times with acetone to eliminate poly(NIPAAm), monomer, initiator, and DMSO. The composition of PVA-*g*-NIPAAm copolymers was estimated from the nitrogen content determined by elemental analysis.

### Preparation of Membranes

The dried PVA-*g*-NIPAAm copolymer was dissolved in DMSO. The membranes were made by pouring 4 cm<sup>3</sup> of 5% (wt/vol) PVA-*g*-NIPAAm copolymer DMSO solution into a flat laboratory dish (4.8 cm diameter), and the solvent was allowed to evaporate at 50°C for 96 h. To restrain the swelling of the membranes, the membranes obtained were followed by annealing above 100°C for the desired time. The membranes prepared were removed from the dish in water. The thickness of the dried membranes was about 35 μm.

### Swelling Ratio of the Membranes

Hydrophilic polymer gels usually swell in water. In particular, thermosensitive polymer gels containing poly(NIPAAm) exhibit different swelling degrees at different temperatures. The swelling ratio of the wet membranes at various temperatures was measured as follows:

$$\text{Swelling ratio} = \frac{a' \times b' \times c'}{a \times b \times c} \quad (1)$$

where  $a$ ,  $b$ , and  $c$  represent the lengths of two sides and the thickness of dry rectangular membranes and  $a'$ ,  $b'$ , and  $c'$  represent those of the swollen membranes in water. The length of the two sides and the thickness of rectangular membrane in the dry state could be measured easily with a ruler or micrometer.  $a'$  and  $b'$  could also be measured with a ruler. How-

ever, it was very difficult to measure  $c'$  exactly with a micrometer, because the membranes swell considerably and became soft in water. It is assumed that the membranes swell almost uniformly in all directions. Therefore, the swelling ratio of the membranes could be rewritten as follows:

$$\text{Swelling ratio} = \left( \frac{a' \times b'}{a \times b} \right)^{3/2} \quad (2)$$

i.e., the swelling ratio was estimated by measuring the length of two sides of rectangular membranes both in dry and swollen states.

### Phase Transition Temperature

The phase transition temperature of poly(NIPAAm) and PVA-*g*-NIPAAm copolymers was examined using differential scanning calorimetry (DSC) (SEIKO Denshi Co., DSC/100). The membranes were first immersed in water at room temperature for at least 2 days. The membranes were picked up from water, followed by wiping off water on the surface of the membranes with filter paper, and sealed in an aluminum capsule. The DSC thermograms were measured at a heating rate of 1°C/min. The maximum endothermic point was taken as the phase transition temperature.

### Annealing the Membranes

The PVA-*g*-NIPAAm copolymer membranes were too swellable and soft to use for permeation experiments, because both PVA and poly(NIPAAm) are water-soluble polymers. It is known that PVA becomes insoluble in water by annealing above 100°C<sup>8</sup> or by the freeze-thaw method. In this study, the membranes were heated at various temperatures from 50 to 140°C to give enough strength for permeation experiments.

### Permeation of Solute Through the Membranes

Permeation experiments were carried out at various temperatures with magnetic stirring, using a diaphragm glass cell consisting of two detachable parts (22 cm<sup>3</sup> each). The membrane was set in the middle of the two parts of the cell, which were clamped and sealed tightly with silicon rubber packing. The effective membrane area in the cell was 3.14 cm<sup>2</sup>. The left (L) side was the solution containing a solute and the right (R) side was deionized water. The concentration of lithium ion (Li<sup>+</sup>) was measured by a flame emission spectrophotometer (Shimadzu,

AA-640-13S). The concentration of Methylene Blue was determined by an UV spectrophotometer (Shimadzu, UV350).

The permeation rate was defined as

$$\text{permeation rate} = \frac{C_t \times v}{t \times S} \text{ (mmol h}^{-1} \text{ cm}^{-2}\text{)} \quad (3)$$

where  $C_t$  is the concentration of solutes in the  $R$  side ( $\text{mmol dm}^{-3}$ );  $v$ , the volume of solution in the  $R$  side ( $\text{dm}^3$ );  $t$ , the transport time (h); and  $S$ , the effective membrane area ( $\text{cm}^2$ ).

## RESULTS AND DISCUSSION

### Synthesis of PVA-*g*-NIPAAm

It is known that vinyl monomers can be grafted onto PVA by using KPS in aqueous and DMSO media.<sup>9</sup> Poly(NIPAAm) exhibits an LCST around 33°C in aqueous solutions, i.e., poly(NIPAAm) is soluble below and insoluble above 33°C. In this study, DMSO was used as a medium for homogeneous graft copolymerization to prevent precipitation of the copolymers during the polymerization. First, the graft copolymerization of NIPAAm onto PVA was carried out in 20 cm<sup>3</sup> of DMSO by using various amounts of KPS at 40°C for 20 h. The total amounts of NIPAAm and PVA were 5.5 g and the weight ratio of NIPAAm to PVA was varied from 5/1 to 15/1. Some of the results are shown in Table I. The yield of PVA-*g*-NIPAAm copolymers increased with increasing amounts of KPS up to 10 mg as well as increasing weight ratio of PVA to NIPAAm, whereas the yield of PVA-*g*-NIPAAm copolymer with 15 mg of KPS decreased. In addition, the yield increased with increasing both the degree of polymerization and saponification of PVA, although the results are not shown in Table I. The composition of the PVA-*g*-NIPAAm copolymers was calculated from the nitrogen content determined by elemental analysis. The weight fraction of NIPAAm in the copolymers prepared was ca. 0.6–0.8 and were slightly increased with increasing ratio of NIPAAm to PVA. However, the phase transition of all the copolymer gels was found to take place around 33°C regardless of the composition of the copolymer gels. The PVA-*g*-NIPAAm gel was transparent below 33°C and became opaque above 33°C.

All the copolymers obtained under the above conditions exhibited high thermosensitivity. However, the PVA-*g*-NIPAAm copolymers that were prepared by adding less than a weight ratio of 3 of NIPAAm to PVA had lower thermosensitivity. This

**Table I** Yields and NIPAAm Content of PVA-*g*-NIPAAm Copolymers Obtained Under Various Conditions

Polymerization <sup>a</sup> Conditions			
PVA <sup>b</sup> : NIPAAm <sup>c</sup>	Initiator (KPS) (mg)	Yield (g)	NIPAAm Content in Copolymer (Weight Fraction)
1 : 5	1	2.5	0.63
	5	3.4	0.78
	10	4.4	0.78
	15	3.8	0.83
1 : 10	1	1.5	0.71
	5	2.0	0.75
	10	2.5	0.81
	15	2.5	0.81
1 : 15	1	1.4	0.70
	5	1.4	0.78
	10	2.1	0.83
	15	1.8	0.84

<sup>a</sup> Polymerization was carried in 20 cm<sup>3</sup> of DMSO at 40°C for 20 h.

<sup>b</sup> NH-26; D.P. = 2600, D.S. > 99%.

<sup>c</sup> Total amount of PVA and NIPAAm were 5.5 g.

is probably due to the higher PVA content in the copolymers. In these graft copolymerizations, water- and organic-insoluble copolymers were obtained when a large excess of KPS or a high-concentration solution of PVA was used. This is attributed to cross-linking of PVA by coupling of radicals that were formed on PVA chains.

The IR spectrum and <sup>1</sup>H-NMR spectrum of the PVA-*g*-NIPAAm copolymer membrane are shown in Figures 1 and 2, respectively. In the IR spectrum (Fig. 1),<sup>10</sup> the absorption bands at 3200–3600 cm<sup>-1</sup> due to the —OH group ( $\nu_{\text{OH}}$ ), at 1650 cm<sup>-1</sup> due to amide I and 1550 cm<sup>-1</sup> due to amide II, and at 1370 cm<sup>-1</sup> due to —CH(CH<sub>3</sub>)<sub>2</sub> were observed. In the <sup>1</sup>H-NMR spectrum (Fig. 2),<sup>10</sup> peaks at 4.4 ppm due to —OH, at 3.8 ppm due to —CH in PVA, at 1.3 ppm due to —CH<sub>2</sub>— in PVA, at -7.2 ppm due to —NH—, and at 1.1 ppm due to —CH<sub>3</sub> in NIPAAm were observed. From these results, the graft copolymerization of NIPAAm onto PVA was confirmed.

### Annealing of PVA-*g*-NIPAAm and the Swelling Ratio

The membranes were prepared by evaporation of DMSO from the copolymer DMSO solution (5%)

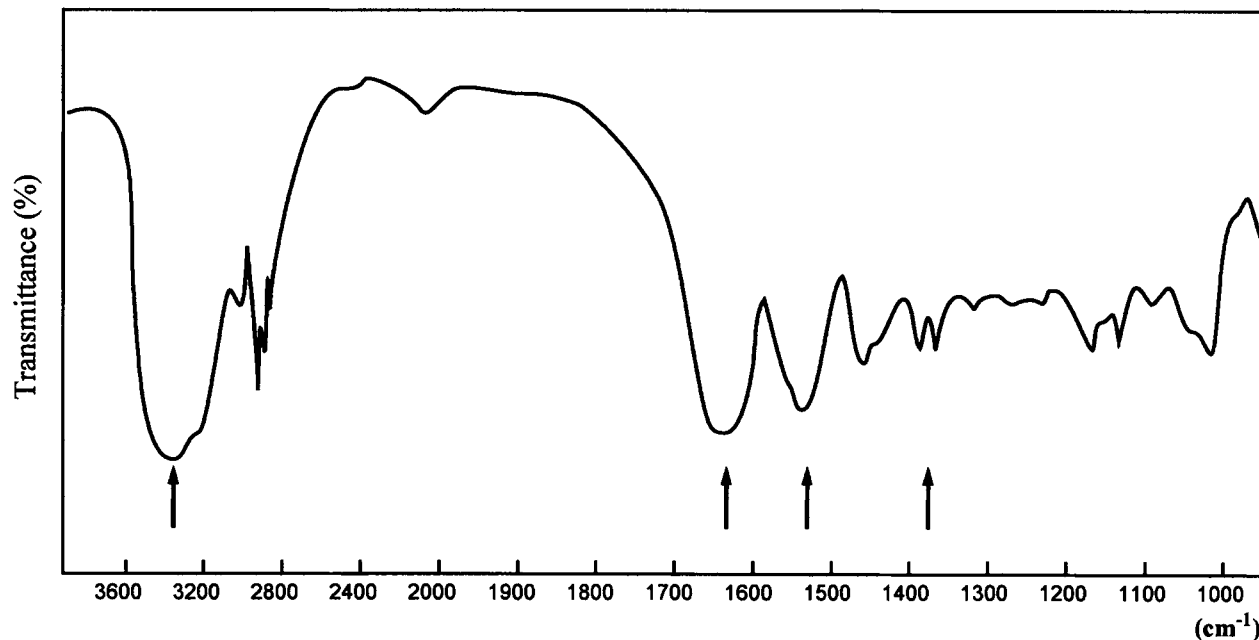


Figure 1 IR spectrum of PVA-*g*-NIPAAm copolymer.

at 50°C for 96 h. The membranes obtained swelled considerably in water at room temperature and were very soft. They were not suitable as membranes for permeation experiments. To obtain a strong enough membrane for permeation experiments, PVA (NH-26; D.P. = 2600, D.S. > 99%) was used for graft copolymerization and the membranes were annealed at various temperatures (50–140°C).

The swelling ratio of the PVA-*g*-NIPAAm membranes annealed at various temperatures for 24 h

was measured while changing temperature. The results are shown in Figure 3 and compared with the result for the membrane without annealing. It is clearly seen that below 30°C the swelling ratio of the annealed membranes was strongly depressed compared to that of the membrane without annealing. In addition, reversible thermosensitivity was observed for all the membranes. The swelling ratio of all the membranes decreased considerably above 30°C and became almost the same as that of the dry

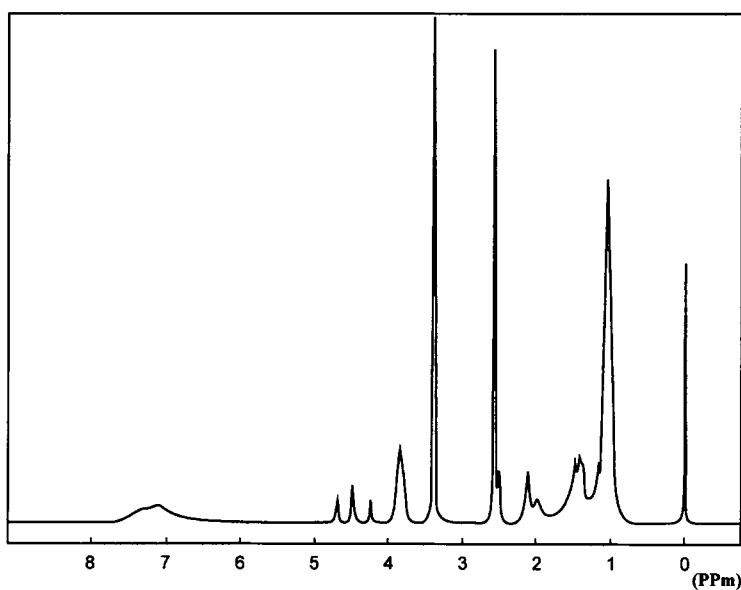
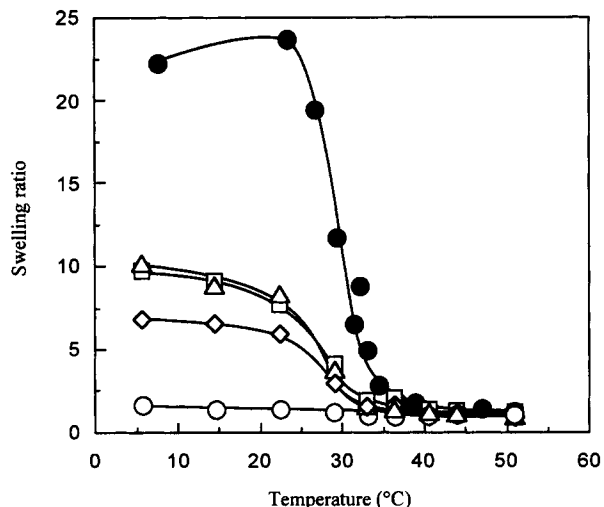
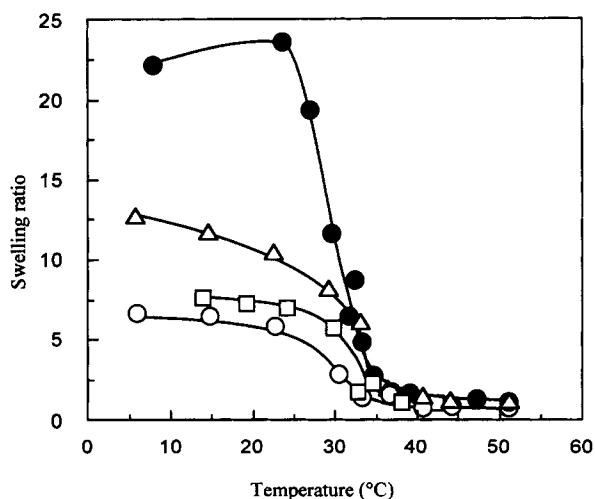


Figure 2 <sup>1</sup>H-NMR spectrum of PVA-*g*-NIPAAm copolymer. Solvent: *d*-DMSO.



**Figure 3** Swelling ratio of membranes annealed at various temperatures for 24 h: ( $\Delta$ ) 80°C; ( $\square$ ) 100°C; ( $\diamond$ ) 120°C; ( $\circ$ ) 140°C; ( $\bullet$ ) without annealing.

state. However, the membranes became brownish and fragile when the membranes were annealed at 140°C. The swelling ratios of membranes annealed at 120°C for times between 6 and 24 h were measured. The results are shown in Figure 4 with the result of membrane without annealing. The swelling ratio of the membranes decreased with increasing annealing time and the membranes became fragile by annealing at 120°C for 24 h. The membrane annealed at 120°C for 10 h was found to show high thermosensitivity and had adequate strength. Consequently, the membrane annealed at 120°C for 10 h was used for the following permeation experi-



**Figure 4** Swelling ratio of membranes annealed at 120°C for various times: ( $\Delta$ ) 6 h; ( $\square$ ) 10 h; ( $\circ$ ) 24 h; ( $\bullet$ ) without annealing.

ments. It has been reported that the annealing of PVA above 100°C results in high crystallization of PVA, providing its low swellability.<sup>8</sup> It is considered that the high crystallization of PVA is brought about by annealing even the PVA-*g*-NIPAAm containing more than 50 wt % NIPAAm.

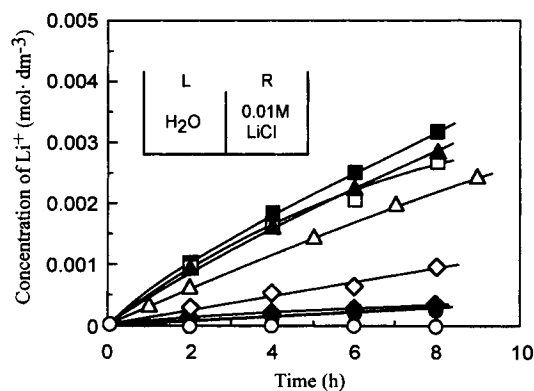
### Phase Transition Temperature

A clear endothermic point was observed in the DSC thermogram of the PVA-*g*-NIPAAm copolymer. The maximum endothermic point was taken as the phase transition temperature. All the phase transition temperatures of PVA-*g*-NIPAAm membranes obtained were almost the same (31–32°C). This result means that the phase transition behavior of the PVA-*g*-NIPAAm copolymers is almost independent of the compositions and molecular weight of poly(NIPAAm) grafted and degree of polymerization of PVA.

### Permeation of Solutes Through the PVA-*g*-NIPAAm Membranes

#### Permeation of $\text{Li}^+$

As mentioned before, the swelling ratio was significantly affected by temperature. This implies that the size of micropores in the swollen hydromicrogel, consisting of the PVA-*g*-NIPAAm copolymers, could be controlled by changing temperature. The permeation of solutes through the membranes could be expected to be controlled by changing the temperature of the solution. The permeation of  $\text{Li}^+$  with small hydrated ion radius (3.8 Å) through the PVA-*g*-NIPAAm membranes annealed at 120°C for 10 h was studied over the temperature range 20–50°C.



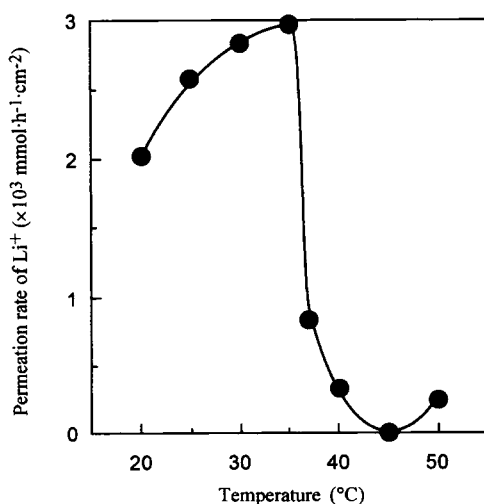
**Figure 5** Changes in concentration of  $\text{Li}^+$  on the left side of the membrane at various temperatures: ( $\Delta$ ) 20°C; ( $\blacktriangle$ ) 25°C; ( $\square$ ) 30°C; ( $\blacksquare$ ) 35°C; ( $\diamond$ ) 37°C; ( $\blacklozenge$ ) 40°C; ( $\circ$ ) 45°C; ( $\bullet$ ) 50°C.

The changes in concentration of  $\text{Li}^+$  with time on the left side are shown in Figure 5. It can be seen that the slope below  $35^\circ\text{C}$  increased with increasing temperature up to  $35^\circ\text{C}$  and suddenly decreased above  $37^\circ\text{C}$ . The temperature dependence of the permeation rate of  $\text{Li}^+$  based on eq. (3) is shown in Figure 6. The maximum permeation rate was obtained at  $35^\circ\text{C}$ , although the swelling ratio was depressed considerably at  $35^\circ\text{C}$ , as shown in Figure 3. This discrepancy between the highest permeation rate and the highest swelling ratio is probably due to the fact that the motion of  $\text{Li}^+$  in water increases with increasing temperature. The slight increase at  $50^\circ\text{C}$  is interpreted in terms of the increasing motion of both  $\text{Li}^+$  and polymer segments in the membranes at higher temperature.

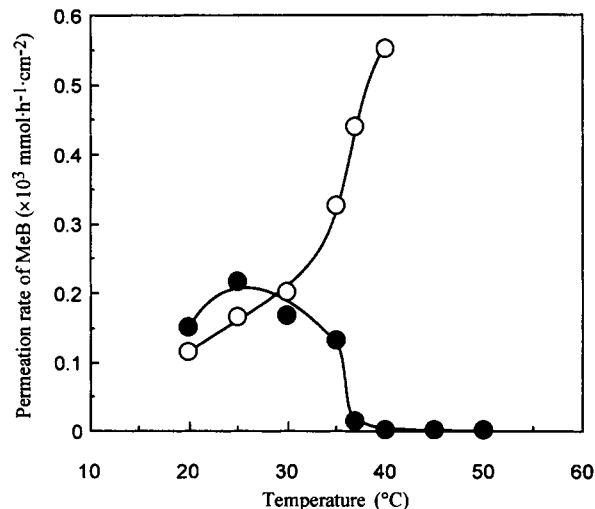
### Permeation of Methylene Blue

The temperature dependence of permeation of Methylene Blue (MeB) with its larger hydrated molecular size was studied. Figure 7 shows the permeation rate of MeB through the PVA-*g*-NIPAAm membrane at various temperatures. It is clear that the permeation rate of MeB was lower than  $\text{Li}^+$  (Fig. 6) and the maximum permeation rate was observed at  $25^\circ\text{C}$ , which was shifted to a lower temperature compared to that of  $\text{Li}^+$  (about  $35^\circ\text{C}$ ).

As shown in Figure 7, the permeation rate of MeB through the PVA membrane increased with increasing temperature. This implies that the depression of permeation rates of both  $\text{Li}^+$  and MeB at higher temperature results from the phase transition of the PVA-*g*-NIPAAm membrane. The micropore size of membranes depends on the temperature as



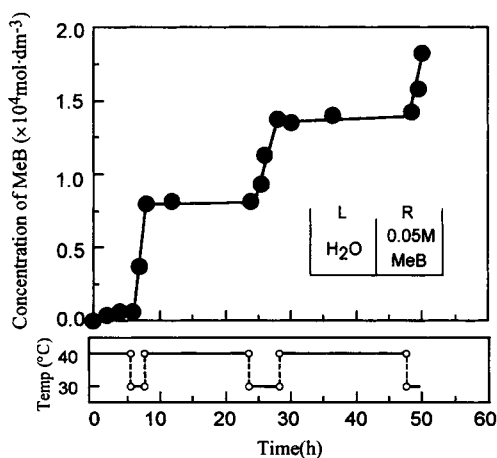
**Figure 6** Permeation rate of  $\text{Li}^+$  from  $\text{LiCl}$  solution at various temperatures.



**Figure 7** Permeation rate of MeB at various temperatures: (●) PVA-*g*-NIPAAm membrane; (○) PVA membrane.

described above: The micropore size decreases slowly over a temperature range around  $25\text{--}35^\circ\text{C}$  based on the results of the swelling ratio as shown in Figure 3. The difference in temperature of the maximum permeation rate between  $\text{Li}^+$  and MeB can be explained in terms of change in micropore size on the phase transition and hydrated size of solutes. Therefore, the depression of the permeation rate of MeB having larger hydrated molecular size took place at a lower temperature compared to the case of  $\text{Li}^+$  through the PVA-*g*-NIPAAm membrane.

Since we found that the permeation of MeB did not occur at  $40^\circ\text{C}$ , the permeation of MeB through the PVA-*g*-NIPAAm membrane was investigated by



**Figure 8** Changes in concentration of MeB on the left side of the membrane with stepwise changing of the temperature between  $30$  and  $40^\circ\text{C}$ .

alternating temperature at 30 and 40°C (Fig. 8). It can be seen that a discontinuous change in concentration of MeB was brought about by stepwise changing of the temperature; the concentration of MeB at 40°C changed hardly at all, but at 30°C, it increased steeply. The result demonstrates the possibility of controlled release of solutes such as a drug through the PVA-*g*-NIPAAm membrane by changing temperature.

## CONCLUSION

Thermosensitive copolymers were prepared by graft copolymerization of NIPAAm of PVA using KPS as an initiator in DMSO. Annealing of copolymer membranes at 120°C for 10 h provided enough strength for them to be used for permeation experiments. The permeation of solutes such as alkali metal ions and MeB were greatly affected by temperature. The permeation of MeB through the PVA-*g*-NIPAAm membranes was continuously controlled by changing the temperature between 30 and 40°C.

This work was partially supported by a Grant-in-Aid for Scientific Research for the Ministry of Education, Science and Culture.

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Received July 12, 1993

Accepted October 12, 1993