Selective permeation across a blend film of cellulose acetate and polymer or copolymer of c-(N^{ε}-AcrLys-Sar)

Akihisa Mori and Yukio Imanishi
Department of Polymer Chemistry, Kyoto University, Yoshida Honmachi, Sakyo-ku, Kyoto, Japan 606
(Received 25 June 1984; revised 24 October 1984)

A blend film of cellulose acetate and the homopolymer (PCP) or the copolymer with styrene[P(CP–ST)] or 4-vinylpyridine[P(CP–VP)] of cyclo(N^{ε}-acryloyl-L-lysylsarcosyl) [c-(N^{ε}-AcrLys–Sar)], which is a vinyl compound carrying a cyclic dipeptide in the side chain, was prepared and investigated as a selectively permeable film for ions and polar substances. For the permeation of alkali metal chlorides, the solubility coefficient S increased in proportion to the content of PCP in the blend film, whereas the diffusion constant D_s increased up to 20 wt% of PCP content and levelled off beyond it. D_s of Rb^+ was greatest for any blend film regardless of the composition. It was considered that the hydrophilic PCP forms water channels in the blend film and metal salts diffuse by coordination with cyclic dipeptide ligand groups which are arrayed along the water channels. In this process, the cooperative interaction of the ligand groups with a metal ion along the flexible polymer chain should work most efficiently with Rb^+, leading to the Rb^+ selectivity in the permeation. A similar ion selectivity was observed with the blend film of P(CP–ST). For the blend film of P(CP–VP), S increased in proportion to the content of P(CP–VP), where D_s was a minimum at 20 wt% of P(CP–VP) content. The ion selectivity was not observed with either S or D_s. For the permeation of alkali metal salts across the blend film of PCP, D_s and the ion selectivities were compared for chlorides and thiocyanates, and no remarkable difference was observed. D_s for the permeation of alkaline earth metal salts across various blend films were smaller than those for alkali metal salts. A blend film containing 20 wt% of PCP was found to permeate L-phenylalanine about three times as fast as D-phenylalanine. The optical resolution of racemic phenylalanine by the permeation across the blend film was possible. With increasing content of PCP in the blend film, the urea permeability increased but the oxygen permeability decreased.

(Keywords: blend film; cellulose acetate; poly[c-N^{ε}-AcrLys–Sar)]; styrene/c-(N^{ε}-AcrLys–Sar) copolymer; 4-vinylpyridine/c-(N^{ε}-AcrLys–Sar) copolymer; metal ion salt permeation; optical resolution; urea permeation; oxygen permeation)

INTRODUCTION

Polymers have been widely used as film materials and the development of polymeric materials for selectively permeable films for use in such processes as blood purification, desalination and oxygenation is strongly desired. Cellulose triacetate has been most popular as a permeation film. Recently, an approach toward highly functional polymeric films was started by providing the film with chemical or biological function[1].

We have synthesized cyclo-N^{ε}-acryloyl-L-lysyl-sarcosyl [c-(N^{ε}-AcrLys–Sar)], which is a vinyl compound carrying a highly dipolar cyclic dipeptide in the side chain, and its homopolymer and various copolymers by radical polymerization[2]. We have found that these polymers are soluble in water and a wide range of organic solvents, and that the polymers have strong ion–dipole or dipole–dipole interactions with ionic or polar substances in solution. It was also found that a highly efficient and selective complexation with metal ions was possible by the intramolecular cooperation of side chain groups along the flexible polymer chain[2].

On the basis of these experimental results, we attempted to use polymers and copolymers of c-(N^{ε}-AcrLys–Sar) as selectively permeable film materials for ionic or polar substances. From the polymers and copolymers of c-(N^{ε}-AcrLys–Sar) only, a film strong enough for practical use was not prepared, so that blend films with cellulose triacetate were prepared. The permeabilities of the blend films toward metal ion salts, α-amino acid, urea and oxygen were investigated.

EXPERIMENTAL

Preparation of homopolymer and copolymers of c-N^{ε}-AcrLys–Sar)

The synthesis and the radical polymerization or copolymerization of c-(N^{ε}-AcrLys–Sar) have been described in the previous paper[2]. Copolymers of c-(N^{ε}-AcrLys–Sar) and styrene and 4-vinylpyridine were prepared. In *Scheme 1* the chemical structure of poly[c-(N^{ε}-AcrLys–Sar)] (PCP) is shown.

Preparation of blend film with cellulose triacetate

PCP or the copolymers of c-(N^{ε}-AcrLys–Sar) were mixed in various ratios with cellulose triacetate (Wako Pure Chem. Ind., Ltd.) and the mixture (0.1 g) was dissolved in dimethylformamide ($HCONMe_2$) (2 ml). The solution was spread on a clean glass plate, and a film
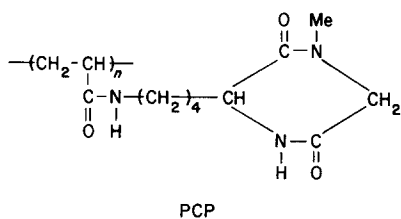
was cast by the evaporation of the solvent under the illumination of an infra-red lamp. The blend film appears to be homogeneous and transparent. The composition of a blend film of PCP will be represented by PCP(X), in which the numerical X represents the weight % of PCP contained in the blend film. A blend film which is strong enough for practical use was prepared, when the content of cellulose triacetate is more than 20 wt%, in other words, X is smaller than 80. In cases of blend films with styrene copolymer [P(CP–ST)] or 4-vinylpyridine copolymer [P(CP–VP)], the composition of the blend film is represented in the same way.

The blend film (8 cm × 6 cm, 20 μm thick) was immersed in distilled water at 30°C for 48 h. After attached water was wiped off with soft paper, the weight in the wet state (W_l) was determined. Next, the wet film was placed over P_2O_5 in a vacuum desiccator. After the film reached a constant weight, the weight in the dry state (W_0) was determined. The water content of the film (H, wt%) was calculated according to equation (1). H values were determined for various blend films and are listed in *Table 1*.

$$H = \frac{W_l - W_0}{W_l} \times 100 \qquad (1)$$

Determination of diffusion constant of metal ions

Permeation of alkali and an alkaline earth ion chloride or thiocyanate across the blend film was measured[3] and the diffusion constant D_s and the solubility coefficient S were determined. The apparatus used for measurement is shown in *Figure 1*. One quarter of a film was subjected to the measurement in order to minimize the experimental error due to the casting conditions. A blend film (5 cm × 5 cm, 20 μm thick) was immersed in 1 M aqueous alkali metal chloride solution at 30°C for 2 days. After removal of the attached solution and dipping into distilled water for a few seconds, the blend film was placed in the

conductivity cell containing distilled water (100 ml), the electrical conductivity ($1/R_0$) of which was predetermined, and the increase of electric conductivity due to elution of the metal chloride was measured with a Wayne Kerr B-224 universal bridge at 30°C. Finally $1/R_\infty$ was determined at final equilibrium.

D_s was calculated using equation (2), in which $1/R_t$ represents the conductivity at t seconds after the start of the measurement and l the film thickness (cm).
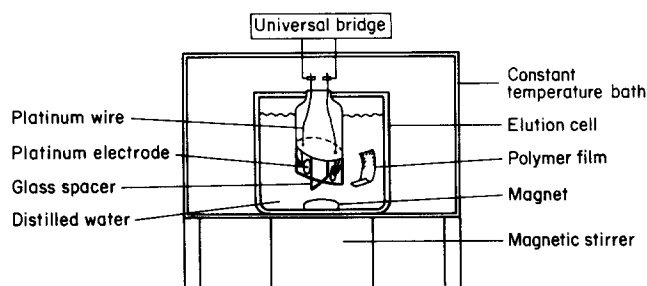
$$\frac{1/R_\infty - 1/R_t}{1/R_\infty - 1/R_0} = 1 - \left(\frac{16D_s}{\pi}\right)^{1/2} t^{1/2}/l \qquad (2)$$

Figure 2 shows an example of the determination of D_s of NaCl across PCP(0) film, which is a pure cellulose acetate film not containing PCP. From the slope of the linear part, D_s was calculated to be 4.41×10^{-10} cm^2 s^{-1} according to equation (1). Lonsdale *et al.*[4] have reported $D_s = 9.4 \times 10^{-10}$ cm^2 s^{-1} for NaCl across cellulose acetate film under slightly different conditions. The agreement of both values shows the validity of the present method for the determination of D_s. The reliability of D_s determination is $\pm 6\%$.

Moles of metal chloride contained in the blend film were calculated from $1/R_\infty - 1/R_0$ using a calibration curve. The solubility of metal salts into blend film, S (mol/mg), was thus determined. The reliability of S determination is $\pm 1\%$.

Permeation of phenylalanine[5]

Enantiomer-selective permeation of D- or L-phenyl- was as that for the permeation of phenylalanine. At capacity was divided into two halves by a blend film with surface area 6 cm^2. One of the chambers was filled with 1 g/100 ml aqueous phenylalanine solution, and the other

Scheme 1 Structure of poly[c-(N^ε-AcrLys–Sar)] (PCP)

Figure 1 Conductometric elution cell

Table 1 Water content H % of various blend films at 30°C

Film designation	CP (X)[a]					PCP (X)						
X (wt%)	0	10	20	30	40	5	10	20	30	40	50	60
H (wt%)	4.87	6.53	7.58	9.43	10.6	5.90	6.97	9.28	11.7	13.8	15.6	18.8

Film designation	P(CP–VP) (X)					P(CP–ST) (X)						
X (wt%)	10	20	30	40	50	20						
H (wt%)	5.54	10.6	15.6	18.4	20.5	9.18						

[a] Cellulose acetate film containing cyclo(L-Lys–Sar) (CP) in X wt%

with distilled water. The concentration of phenylalanine in the latter chamber was determined by JASCO J-20 spectropolarimeter at 25°C.

Permeation of urea[5]

The permeability of urea was determined in the same way as that for the permeation of phenalalanine. At suitable time intervals, 1 ml of the solution in the distilled water chamber was taken out, and any permeated urea was converted to a Schiff base of *p*-dimethylamino-benzaldehyde and its concentration was determined on the basis of the optical density at 440 nm. The permeation constant *P* was calculated according to equation (3). C_0 and C_t represent the initial concentration

$$\ln\frac{C_0}{C_0 - 2C_t} = \frac{2PA}{\delta V}t \tag{3}$$

of feed solution and the concentration of urea transported at time *t* (min), respectively. *A* is the film area (cm^2), δ is film thickness (cm), and *V* is cell volume (cm^3). The reliability of *P* determination is ±5%.

Permeation of oxygen[6,7]

The oxygen permeabilities of blend films were determined in the dry state. A blend film was placed between a Pyrex glass plate and an ethyl cellulose film containing a dyestuff, erythrocin, which absorbs light of a certain wavelength and excites oxygen, and dimethylanthracene which quenches excited singlet oxygen, and irradiated with a 546 nm light from the side of the Pyrex glass. The oxygen permeability $P(\text{cm}^3 \cdot \text{cm} \times 10^{10}/\text{cm}^2 \cdot \text{s} \cdot \text{cmHg})$ was
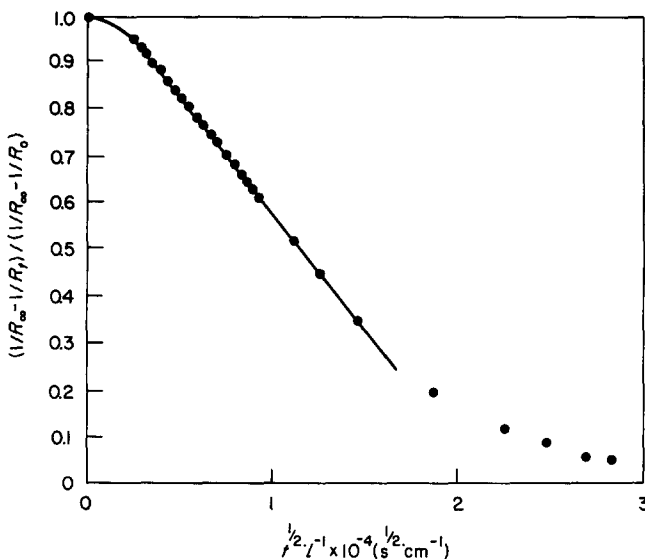

Figure 2 Desorption of NaCl from cellulose acetate film PCP(0) (H, %=4.87) at 30°C

calculated by measuring the decrease in the optical density of dimethylanthracene at 359 nm. This method worked satisfactorily, because it reproduced reported values of *P* for commercial polymers which had been determined by other methods[8].

RESULTS AND DISCUSSION

Determination of diffusion constant of metal ions

Table 2 lists the water contents *H* and the diffusion constants D_s of NaCl for a variety of blend films containing different ratios of PCP. The blend of relatively hydrophilic PCP with relatively hydrophobic cellulose acetate increased *H* and D_s. The effect of PCP on D_s is opposite to the experimental results reported by Shchori and Jagur-Grodzinski[3] that D_s of NaCl across hydrophilic poly(*N*-vinylpyrrolidone) film decreased by blending a ligand polymer poly(crown ether). The disagreement may be explained by the fact that in the present blend film PCP molecules take up water to make the ion diffusion easy or the increase of PCP content perturbs the structure of the blend film.

In the case of a film consisting of one kind of polymer, solute dissolves out into solution according to the Fick's law and D_s is independent of the film thickness. However, when a film consists of two kinds of polymers, one component affects the mobility of the other component so that the elution behaviour of solute apparently obeys the Fick's law, but D_s depends on the film thickness[9]. For the blend films of cellulose acetate with PCP used in the present investigation, the logarithmic plot of D_s and the film thickness was linear. The slope of the straight line increased with increasing content of PCP. In other words, the dependence of D_s on the film thickness became more important for blend films containing more PCP. The diffusion constants for blend films with various compositions were corrected for the film thickness and those for blend films with 20 μm thickness were determined for different kinds of metal salts and are shown in *Figure 3*. In *Figure 3* it can be seen that D_s stopped increasing when the PCP content increased beyond 20 wt%, and that Rb$^+$ possessed the largest D_s amongst the metal ions in any blend films with different compositions.

Figure 4 shows the solubility *S* of metal salts into blend films. Clearly, *S* is larger for blend films containing more PCP. Therefore, it is concluded that the PCP component in the blend film does not affect D_s but affects *S*.

For ion permeation through a blend film, it is speculated that a water channel could be formed along an array of highly dipolar cyclic dipeptide ligand groups and ions could diffuse through the channels with coordination to the ligand, as shown in *Figure 5*. Therefore, in blend films with 5–20 wt% PCP content, with the formation of water channels, that is, D_s increases with increasing PCP content. Further increase of PCP content should streng-

Table 2 Diffusion coefficient NaCl across the blend films

Film	PCP (0)	PCP (10)	PCP (20)	PCP (30)
$D_s \times 10^{10 a}$ (cm^2 s^{-1})	3.83	5.91	20.1	25.8
H %[b]	4.87	6.97	9.28	11.7

[a] After two days for equilibration with 1 M NaCl at 30°C
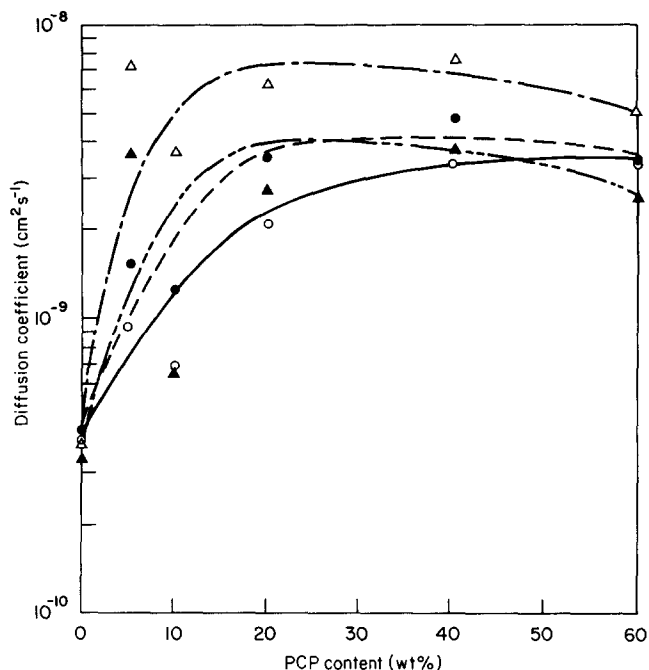[b] Calculated according to equation (1)

Figure 3 Dependence of D_s of alkali metal chlorides on the composition of blend film. (◯), NaCl; (●), KCl; (△), RbCl; (▲), CsCl
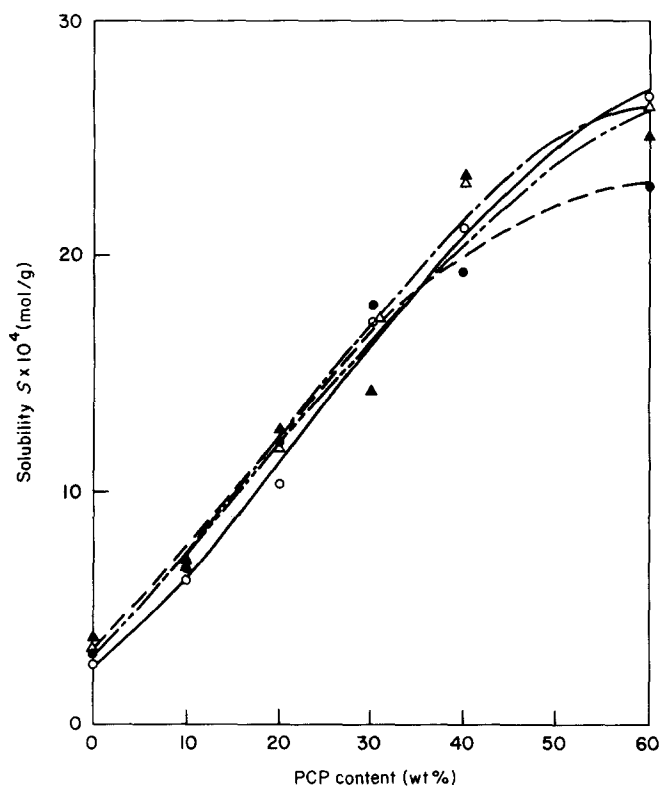

Figure 4 Dependence of S of alkali metal chlorides on the composition of blend film. (◯), NaCl; (●), KCl; (△), RbCl; (▲), CsCl

then the interaction of ion with ligand groups, which compensates the increase in D_s by the formation of water channels. In homogeneous solution, ion specificity was not observed for the interaction of PCP with alkali metal ions[2]. However, in the ion permeation across the blend film, a weak selectivity for Rb$^+$ was observed. In the film the mobility of ligand groups should be less than in solution. This situation would be favourable for the

interaction of ligand groups with Rb$^+$, leading to the Rb$^+$ specificity during the diffusion process.

D_s and S were determined for metal salts permeating across cellulose acetate film containing cyclo(L-Lys–Sar) (CP). The relationship between D_s and CP is shown in *Figure 6*. D_s increased with increasing content of CP until 10–20 wt%. Further increase in CP content did not affect D_s. This behaviour is similar to that observed with blend films of PCP. However, for different metal ions D_s increased in the order, Na$^+$ < K$^+$ < Rb$^+$ < Cs$^+$, which is an increasing order of ionic radius. The different behaviours of ion selectivity indicates that the selective interaction of cyclic dipeptide ligand groups in PCP with ions along a flexible polymer chain in the blend film of PCP does not take place in the blend film in which cyclic dipeptide molecules are only randomly dispersed.

The relationship between S and the CP content is shown in *Figure 7*. S did not increase with increasing CP content, which contrasts with the fact that in the blend film of PCP S increased almost linearly with increasing PCP content.
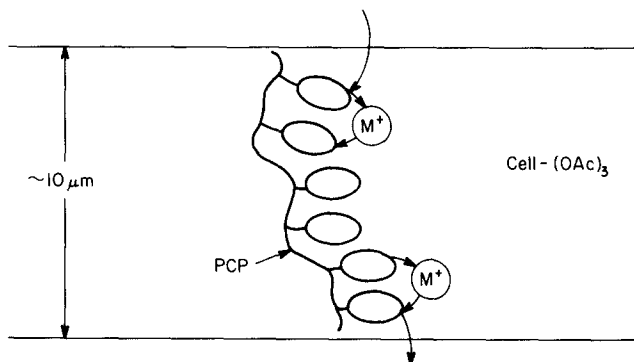

Figure 5 Proposed mechanism for the diffusion of metal ions across the blend film containing ligand polymer PCP
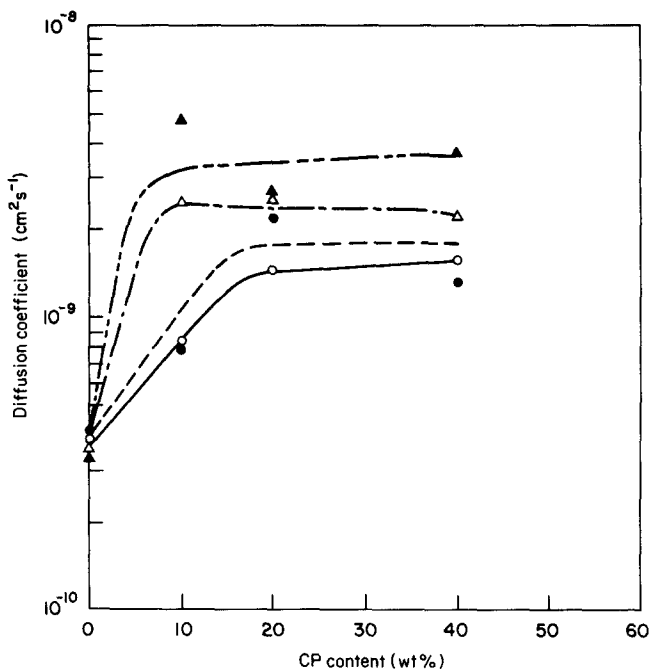

Figure 6 Dependence of D_s of alkali metal chlorides on the composition of blend film containing cyclic dipeptide. (☐), NaCl; (●), KCl; (△), RbCl; (▲), CsCl

A copolymer of c-(N^ε-AcrLys–Sar) with styrene (the molar ratio 1:1) [P(CP–ST), 0.02 g] was mixed with cellulose acetate (0.08 g). For this blend film P(CP–ST) (20) D_s values of different metal salts were determined and are shown in *Table 3*. The ratio of D_s for Cs$^+$ against D_s for Na$^+$ is about six, and therefore the ion selectivity was increased by the introduction of styrene units as spacers into the ligand polymer. The addition of glycerin lowered the polarity of the medium but the ratio of D_s Cs$^+$/Na$^+$ was about six. For the complexation with metal salts in a homogeneous solution, P(CP–ST) showed a high ion selectivity[2]. The relatively low ion selectivity in the blend film of P(CP–ST) (20) should therefore represent the standardization of the ion diffusion in the solid state according to the mechanism illustrated in *Figure 5*.

Copolymers of c-(N^ε-AcrLys–Sar) with 4-vinylpyridine [P(CP–VP)] were mixed with cellulose acetate. For these blend films, D_s values of different metal salts were determined and are shown in *Figure 8*. For the complexation with metal salts in a homogeneous solution, P(CP–VP) was found to be highly efficient operating by the intramolecular cooperation between adjacent CP and

VP units[2]. With regard to the blend film, D_s decreased with increasing P(CP–VP) content until 20 wt%. A strong cooperative coordination of CP and VP units may have a bearing on this phenomenon.

However, the solubility S of metal salts in blend films increased simply with increasing P(CP–VP) content as shown in *Figure 9*. The experimental finding that D_s increased for blend films with more than 20 wt% P(CP–VP) content may be related to the formation of water channels formed by the P(CP–VP) component in the blend film. Neither D_s nor S showed a metal ion specificity for the blend films of P(CP–VP).

The permeation of alkaline earth metal salts across blend films containing cyclic dipeptide ligand groups was investigated, and D_s values are shown in *Table 4*. Values are lower than those for alkali metal salts. A larger solvation energy for alkaline earth metal ions may explain the slower diffusion across the film than alkali metal ions. The experimental findings that D_s for PCP is larger than for CP and that D_s for P(CP–VP) blend film is smaller than those for PCP and P(CP–ST) blend films are the same for alkali and alkaline earth metal salts.

D_s values for alkali metal thiocyanates are shown and compared with those for alkali metal chlorides in *Table 5*. D_s values of PCP(5) blend film for chlorides are nearly the same as those for thiocyanates. But D_s values of PCP(0) and PCP(10) blend films for thiocyanates are larger than
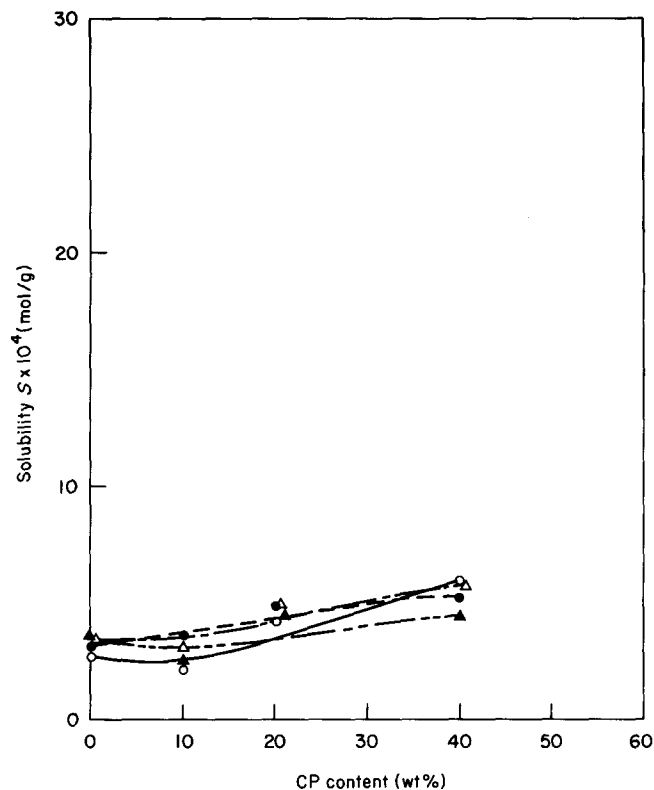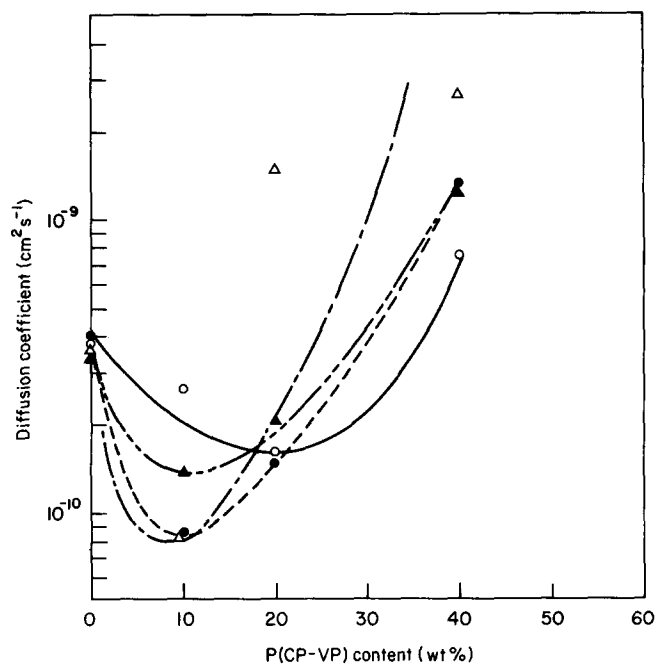

Figure 7 Dependence of S of alkali metal chlorides on the composition of blend film containing cyclic dipeptide. ($\bigcirc$), NaCl; ($\bullet$), KCl; ($\triangle$), RbCl; ($\blacktriangle$), CsCl

Figure 8 Dependence of D_s of alkali metal chlorides on the composition of blend film containing P(CP–VP) copolymer. ($\bigcirc$), NaCl; ($\bullet$), KCl; ($\triangle$), RbCl; ($\blacktriangle$), CsCl

Table 3 Diffusion coefficient of alkali metal chlorides across P(CP–ST) (20) film[a] in different media

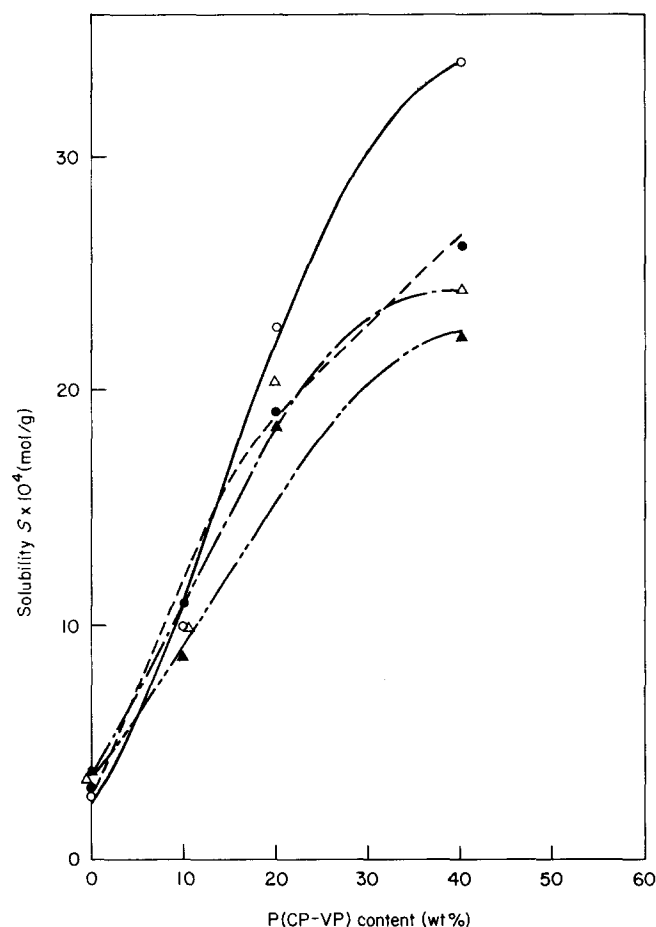|	Diffusion coefficient, $D_s \times 10^{10}$ (cm^2 s^{-1})			
Medium	NaCl	KCl	RbCl	CsCl
H$_2$O	12.6	24.9	39.5	74.7
H$_2$O + Glycerin (5:3 v/v)	1.56	2.98	1.08	9.28

[a] H = 9.18%

those for chlorides. The selectivity ratio of $D_s K^+/Na^+$ was not much affected by the nature of anion, but that for chloride was a little larger than that for thiocyanate.

Permeation of phenylalanine

In *Figure 10*, the experimental results on the permeation of L- and D-phenylalanine across PCP(20) film are shown. It was found that the L-enantiomer permeates faster by about 3 times than that for the D-enantiomer. The enantiomer-selective permeation should have resulted from a favourable permeation of one of the enantiomorphic α-amino acid salts accompanying the interaction with asymmetric ligand groups which are due to L-lysyl residues involved in PCP component.

A similar experiment was performed with racemic phenylalanine for possible optical resolution. The time-resolved L-enantiomer excess in the permeated phenyl-

Table 5 Diffusion coefficient of NaSCN, KSCN across PCP (*X*) film

Film	Diffusion coefficient, $D_s \times 10^{10}$ (cm² s⁻¹)		H (%)
	NaSCN	KSCN	
PCP (0)	1.99	5.47	4.87
PCP (5)	9.83	14.0	5.90
PCP (10)	28.7	49.3	6.97

Figure 10 Concentration change with time of phenylalanine permeated across blend film containing ligand polymer PCP(20)(H, %=9.28), (◯), D-Phe; (●), L-Phe

Figure 9 Dependence of *S* of alkali metal chlorides on the composition of blend film containing P(CP–VP) copolymer. (◯) NaCl; (●), KCl; (△), RbCl; (▲), CsCl
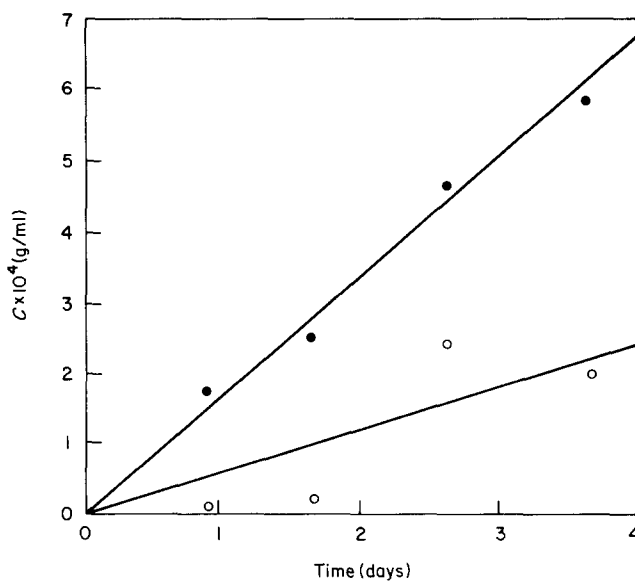

Figure 11 Enantiomer excess of phenylalanine permeated across blend film containing ligand polymer PCP(20)(H, % =9.28)

Table 4 Diffusion coefficient of alkaline earth metal chlorides for blend films containing cyclic dipeptides

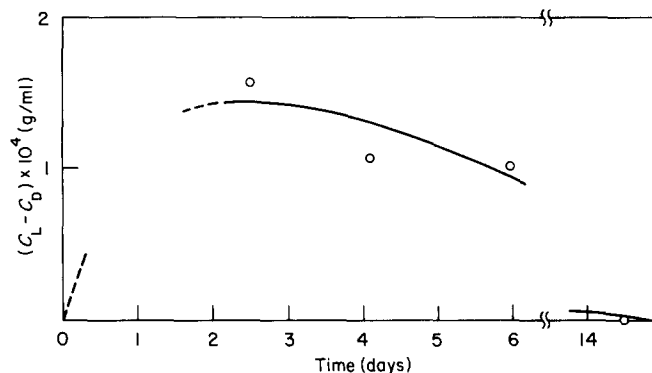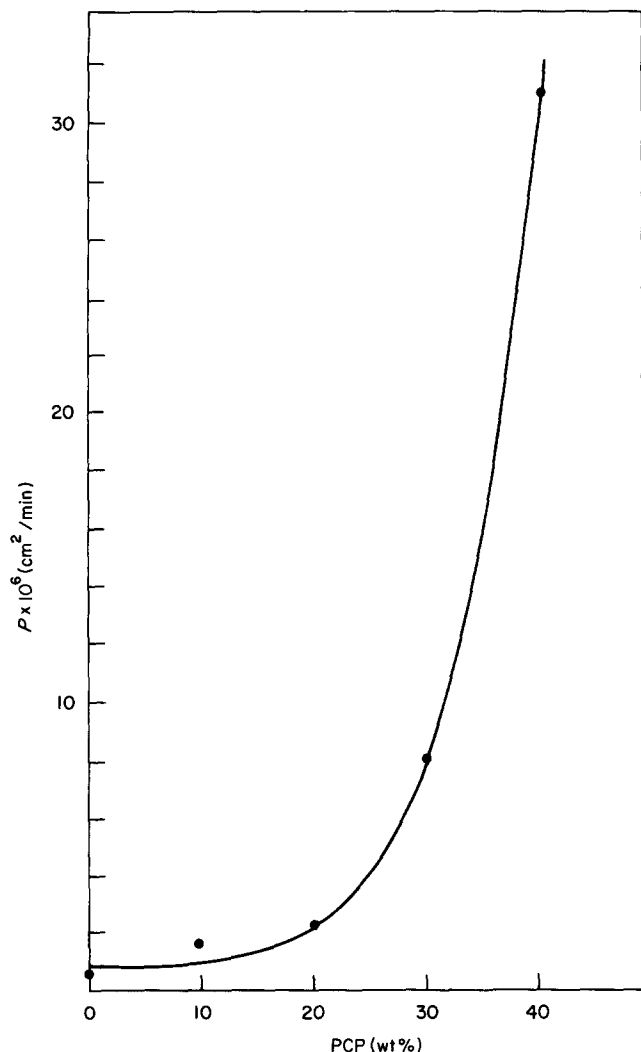| Film	$D_s \times 10^{10}$ (cm² s⁻¹)[a]		H (%)
	BaCl₂	CaCl₂	
Cellulose acetate	3.83	5.17	4.87
CP 20 wt%	23.7	19.4	7.58
PCP (20)	23.9	28.2	9.28
P(CP–ST) (20)	11.3	13.4	9.18
P(CP–VP) (20)	9.28	8.17	10.6

[a] After two days for equilibration with 1 M aqueous solution at 30°C

Figure 12 Dependence of urea permeability on the composition of blend film containing ligand polymer PCP

Figure 13 Dependence of oxygen permeability on the composition of blend film containing PCP

Permeation of oxygen

The relationship between the oxygen permeability and the PCP content in the blend film is shown in *Figure 13*. The oxygen permeability decreased drastically with increasing PCP content. It has been advocated for the permeation of gases through blend films[10] that the low compatibility of the component polymers increases the segmental motion to enhance the gas permeation. For the blend film of PCP with cellulose acetate, the compatibility of both polymers was considered to be low, whereas the experimental findings in *Figure 13* indicate that the compatibility is high and the blend film becomes more dense by the increase of PCP content.

alanine is shown in *Figure 11*, and the highest enantiomer excess was observed at 2–3 days after the initiation of permeation.

Permeation of urea

The relationship between the urea permeability and the PCP content in the blend film is shown in *Figure 12*. The urea permeability increased drastically with increasing PCP content. The increase of PCP content increases the water content of the blend film, and enhances the permeation of polar urea molecules.
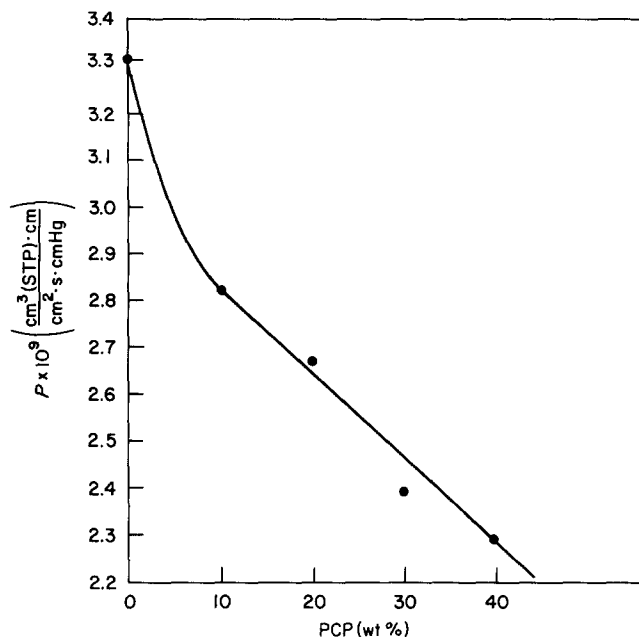
REFERENCES

1   Imanishi, Y. *Membrane* 1983, **8**, 75
2   Mori, A. and Imanishi, Y. *Polymer* 1984, **25**, 1837
3   Shchori, E. and Jagur-Grodzinski, J. *J. Appl. Polym. Sci.* 1976, **20**, 773
4   Lonsdale, H. K., Merten, U. and Riley, R. L. *J. Appl. Polym. Sci.* 1965, **9**, 1341
5   Brown, H. H. *Anal. Chem.* 1959, **31**, 1844
6   Holland, R. V., Rooney, M. L. and Santangelo, R. A. *Angew. Makromol. Chem.* 1980, **88**, 209
7   Petrak, K. and Pitts, E. *J. Appl. Polym. Sci.* 1980, **25**, 879
8   Kumaki, T., Sisido, M. and Imanishi, Y. *J. Biomed. Mater. Res.* submitted
9   Odani, H., Uchikura, M., Taira, K. and Kurata, M. *J. Macromol. Sci.-Phys.* 1980, **B17**, 337
10 Rånby, B. G. *J. Polym. Sci., Polym. Symp. Edn.* 1975, **51**, 89