Permeation of Isomers of Mandelic Acid Through Isotropic and Cholesteric Fluid Polypeptide Membranes

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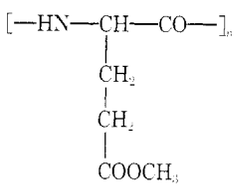
ABSTRACT: Permeation of mandelic acid through liquid membranes composed of a solution of poly(γ-methyl D-glutamate) in tetrachloroethane was studied. A significant change in the dependence of the diffusion coefficient was observed when the liquid membrane underwent a lyotropic phase transition from biphasic to cholesteric. Measurement of the permeation characteristics was performed using an automatic permeation cell constructed specifically for liquid membranes. The time lag and the cell average diffusion coefficient of mandelic acid were measured in the concentration range from 4.0 to 25% polypeptide by volume. The lyotropic phase transitions of the polypeptide solutions were followed by viscometry and light microscopy. The solutions were isotropic below 9% polymer and cholesteric above 14% by volume. Between these two volume fractions the isotropic and the anisotropic phases existed concurrently. The logarithmic plot of the diffusion coefficients against the volume fraction of the polymer appeared to consist of two straight lines, one below 13% and another above 15% volume fraction. This change has been related to morphological rearrangement of the membrane structure upon formation of a continuous liquid crystalline phase. The permeation coefficients of D-, L-, and DL-mandelic acid through cholesteric phases of these polypeptide solutions were found to be identical with each other, eliminating the possibility of resolution of the racemic acid by diffusion through these asymmetrical membranes.

In a previous paper[2] it was shown that the permeation properties of polypeptide membranes were dependent on the nature of the lyotropic liquid crystalline solutions from which the membranes were prepared. It seemed therefore natural to investigate the permeation properties of membranes composed of polypeptide solutions in the concentration ranges where the solution exhibited cholesteric liquid crystalline behavior.

Further incentive for this investigation was provided by the suggestion that liquid crystalline structures are present in various biological systems[3] including membranes. Formation of cholesteric structure in solutions of numerous helical macromolecules, including polypeptides, DNA,[4a] and RNA,[4] has been known for sometime, and the many unique properties of such solutions have been reported. However, the transport properties of small molecules through such solutions have not been investigated.

Another point of interest was the possibility of separation of optical isomers by diffusion of racemates through cholesteric membranes. Since the observed high optical activity of cholesteric systems is a consequence of high asymmetry of the system, it might be speculated that this asymmetry could also result in preferential permeability of the membrane to the diffusion of appropriate optical isomers.

In this paper we report on the permeation of mandelic acid through solutions of poly(γ-methyl D-glutamate),



PMDG, in an α-helical solvent, tetrachloroethane. The emphasis has been placed mainly on two objectives. First an attempt was made to evaluate the effect on the diffusion coefficient of mandelic acid of the changes in the volume fraction of the polymer and accompanying phase changes. The second objective was to study the effect of the configuration of the mandelic acid, D or L, on its diffusion coefficient through the cholesteric liquid crystalline PMDG membranes. The choice of mandelic acid for use in this study was made basically on three grounds: the availability of the isomer, the relative ease and accuracy of the spectroscopic determination of its concentration (due to the presence of an aromatic group), and the high optical activity of the pure D or L acid.

The diffusion of low molecular substances through polymer solutions has been studied by others using optical[5] and spin–echo[6] techniques. In this paper we have described an automatic permeation apparatus for liquid membranes. The advantages of this procedure over the optical method are that it could be easily assembled and that complicated calculations are not required for evaluation of the diffusion coefficient. Unlike the spin–echo technique, the diffusion of low molecular weight substrates other than solvent could be studied using this apparatus.

Experimental Section

(a) Materials. Solvents used in this experiment were tetrachloroethane from Fisher Scientific Co., boiling range 145–150°; chloroform, reagent grade, from Matheson Coleman and Bell; and ethanol, Gold Shield USP. They were used without further purification. L-(+)-Mandelic acid, Lot No. B2A, and D-(−)-mandelic acid, Lot No. 711-1, were obtained from Eastman Kodak Co. DL-Mandelic acid, mp 119–121°, was from Aldrich Chemical Co. Poly(γ-methyl D-glutamate), PMDG, was obtained from Ajinomoto Co., Inc., Tokyo 2690, in the form of a resin solution which was purified by precipitation from ethanol. The intrinsic viscosity of the purified PMDG solution in dichloroacetic acid was 1.33 dl/g at 25°. Element analysis of C, H, and O of the purified polymer agrees with calculated values.

(b) Permeation and Diffusion Through a Liquid Membrane. (1) Description of Apparatus. A schematic diagram of the permeation setup is shown in Figure 1. The liquid crystal membrane separates a concentrated aqueous mandelic acid solution (in side I) from water (in side II). The concentrated half-cell (side I) is connected to a large reservoir (*ca.* 300 ml) of the aqueous mandelic acid solution of 0.50 *M* concentration. A centrifugal pump (pump I) constantly circulates the mandelic acid solution at the rate of 1.0 l./min or higher between side I and the large reservoir. In this way suitable agitation with a minimum amount of vibration is provided for the high-concentration side. This agitation is necessary to minimize a boundary layer formation. At the same time, because of the large volume of the reservoir, the concentration change of the mandelic acid solution due to diffusion is negligible. For example, in a typical experiment the concentration of the mandelic acid changes from 0.508 *M* in the beginning to 0.502 *M* at the end of the experiment. The dilute side of the half-cell (side II) is connected to another centrifugal pump (pump II) which constantly circulates a constant volume of water at a rate of 1.0 l./hr through a quartz optical cell back into side II. The 1.0-cm optical cell is placed in a Cary 14 spectrophotometer to monitor the increase in concentration of the mandelic acid in side II. The perme-

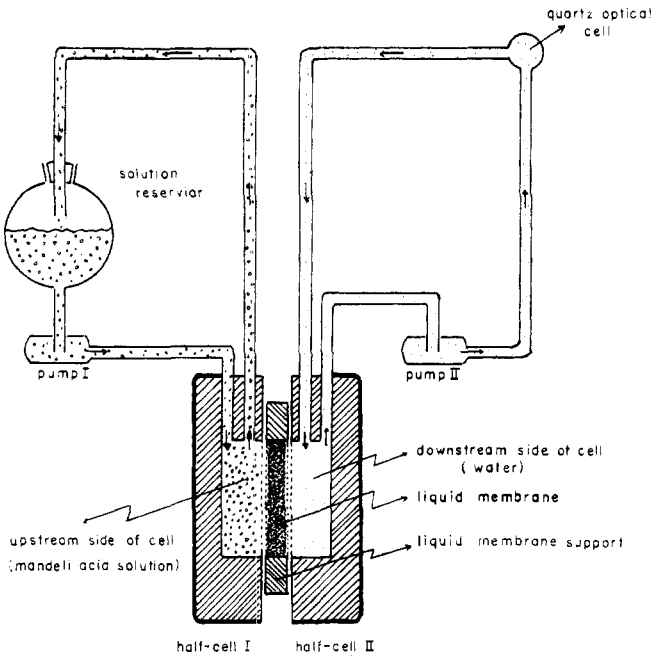


Figure 1. Schematic diagram of the permeation setup.

ation cell is placed in a constant temperature bath set at 22.0°. A schematic description of the cell follows.

The entire body of the cell is made of stainless steel. The cell consists mainly of three parts as shown in Figure 2A: two half-cells (I and II) and a membrane support (III). A half-cell is made by milling out a cylindrical cavity of 5.5-cm diameter and 0.7-dm depth in the center of a rectangular solid piece of stainless steel, 12.2 cm × 7.5 cm × 0.9 cm (Figures 2A and 2B). The membrane support consists of a spacer, two sheets of filter paper, two circular pieces of wire gauze, and two rigid back-up plates (see Figure 2C).

An experiment is performed by the following procedure. One side of the membrane support is first assembled in the order shown (Figure 2C) after wetting the filter papers with water. A slight excess of the liquid membrane (the polymer solution) is poured into the cavity and immediately the other side is screwed into place. The excess liquid is allowed to flow out through the small opening at the top of the spacer. In this way the cavity is completely filled, leaving no voids. The assembled membrane support (Figure 2D) is then clamped between the two half-cells with two ring seals (Figure 2A). The downstream side of the apparatus (side II of Figure 1) is filled with a saturated solution of tetrachloroethane in distilled water. The saturated solution is used so that the composition of the liquid membrane will not change extensively due to the slight solubility of tetrachloroethane in water (approximately 1 g/350 ml at 25°).

After placing the optical cell in the spectrophotometer, pump II is started and allowed to circulate the water through side II of the system. The spectrophotometer is set at 2578 Å, the wavelength of an absorption maximum for mandelic acid (ϵ = 208 mol/(l. cm)), and the absorbance as a function of time is recorded. The absorption, at this wavelength, due to water or tetrachloroethane is less than 0.05 when a cell of 1.00 cm thickness is used. The system is assumed to have reached equilibrium when there is no further change in the recorded base line. At this point the mandelic acid solution is introduced into side I and the time is recorded ($t = t_0 = 0$). The permeation of the acid through the membrane is then monitored automatically by observing the increase in the absorbance with time. This in turn is related to the increase in concentration of mandelic acid through the Beer–Lambert law.

(2) Calculation of P and D. The permeability P is determined from the flux J, the difference in the concentrations of the diffusant, ΔC (although the concentration of the mandelic acid solutions at the upstream and the downstream sides of the cell changed by as much as 1.0 and 0.5%, respectively, during a permeation run, the change in the difference in concentration, ΔC, was less than 2% total; therefore ΔC was taken to be constant and equal to the original value), at the upstream and downstream sides of the membrane, and the thickness of the membrane l.[7]

$$J = -P(\Delta C/l) \tag{1}$$

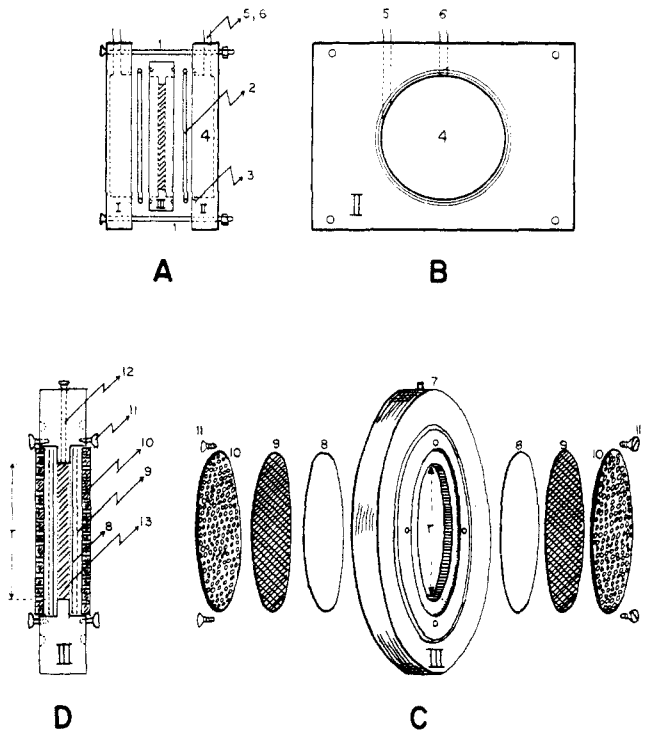


Figure 2. Schematic diagram of the permeation cell: (1) screw for tightening half-cells together; (2) o-ring gasket; (3) groove for placing o-ring; (4) half-cell cavity; (5) inlet; (6) outlet; (7) spacer; (8) filter paper; (9) wire gauze; (10) rigid back-up plate, perforated; (11) screw; (12) opening; (13) polypeptide solution.

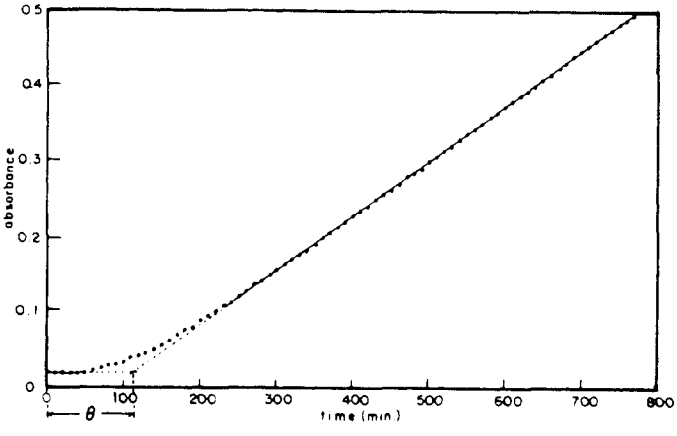


Figure 3. A typical permeation run.

The average diffusion coefficient can be obtained utilizing the equation

$$P = S\bar{D} \tag{2}$$

where S is the partition coefficient and $\bar{D}$ is the average diffusion coefficient. This treatment is valid provided that the concentration of the diffusant in the membrane, C^{memb}, is governed by a relationship of the type

$$C^{memb} = SC^{soln} \tag{3}$$

where C^{soln} is the concentration of the diffusant in contact with the membrane at the upstream side of the cell (side I).

The diffusion coefficient can also be obtained from the time lag, θ, using

$$D = l^2/6\theta \tag{4}$$

where θ is the time at which the extrapolation of the linear portion of the steady state absorbance–time graph intercepts the extrapolation of the initial linear region as shown in Figure 3. In this graph $t = 0$ is the time at which the diffusant is first introduced. How-

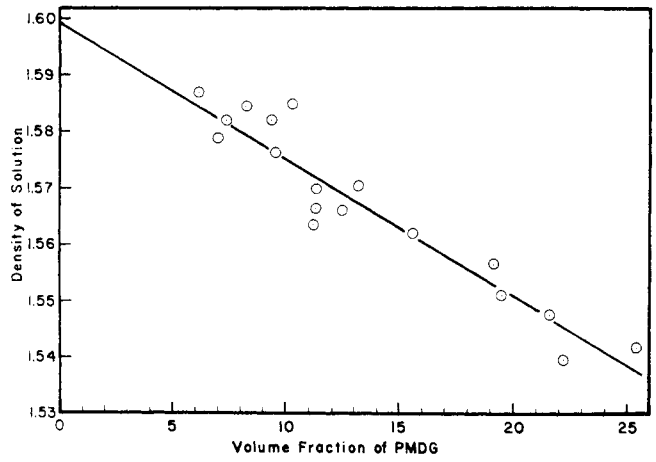


Figure 4. The dependence of the density of solutions of PMDG in tetrachloroethane on the volume fraction of PMDG. Density in g/cm^3.

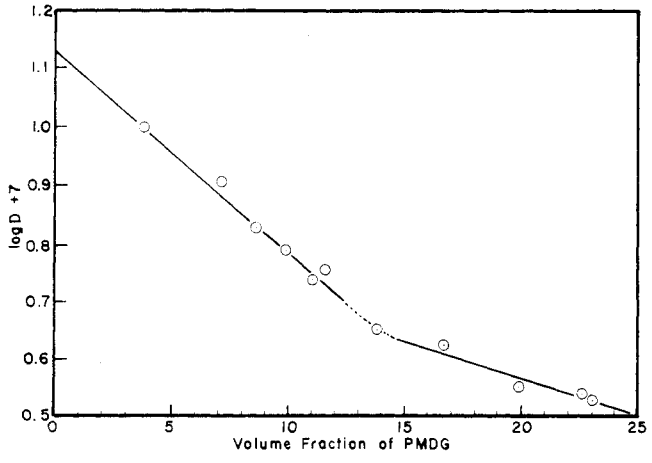


Figure 5. The dependence of the time lag diffusion coefficient of mandelic acid on the volume fraction of PMDG in the liquid membrane (D is in cm^2/sec).

ever, as will be discussed later, the value of the time lag diffusion coefficient should be used qualitatively due to many complicating factors.

(c) Measurement of the Composition of the PMDG Solutions. Since the concentration of the polypeptide solutions changed due to the evaporation of the solvent tetrachlorethane it was necessary to measure the concentration independently before using the solution. A given quantity of the PMDG solution, between 1 and 2 g, was placed on thin aluminum foil and then quickly weighed. The solvent was evaporated in a vacuum oven at 50° and the weight of the dry PMDG was obtained by weighing the dry polymer. The volume fraction of the polymer was calculated by assuming linear additivity of the volumes of the solvent and the polymer. A plot of the density of the polypeptide solution against the volume fraction of PMDG is linear (see Figure 4), indicating that the above assumption concerning the additivity of volumes is correct. The density of PMDG was found to be 1.30 g/cm^3 as discussed later.

(d) Measurement of the Solubility Coefficient. An accurately measured volume (2.00 ml ± 0.01) of 0.500 M aqueous solution of mandelic acid was pipetted into a 5 ml glass ampoule. A given quantity of a solution of PMDG in tetrachlorethane (between 1.5 and 2.5 g) was transferred into the ampoule which was then sealed. The ampoule was agitated by inverting it with a motor at the rate of 1 rpm. This agitation was necessary to ensure reproducibility of the experiment. After a period of 48 hr the ampoule was broken and the concentration of the mandelic acid in the aqueous phase was measured. The measurement of the concentration was done spectroscopically by a determination of the absorbance of the diluted mandelic acid solution at 2578 Å.

(e) Density of the PMDG Solutions in Tetrachloroethane. The densities of the polypeptide solutions and solid PMDG films were measured by displacing water from a 5-ml pycnometer at 25°

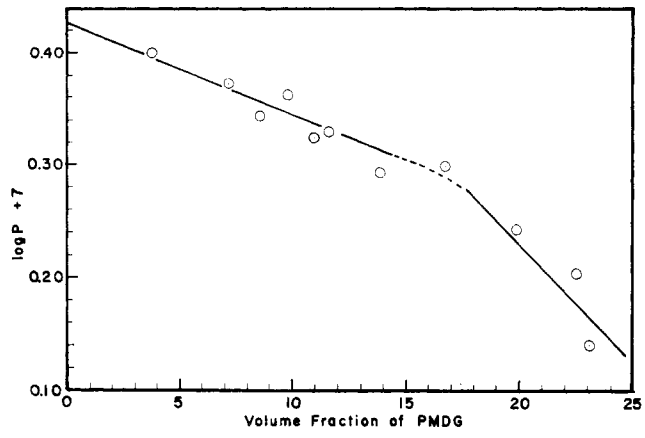


Figure 6. The dependence of the permeation coefficient of mandelic acid on the volume fraction of PMDG in the liquid membrane (P is in cm^2/sec).

as described elsewhere.[8] No correction was made for the buoyancy of air. The density of PMDG solutions in tetrachloroethane is plotted in Figure 4.

(f) Viscosity. Since the viscosities of the polypeptide solutions were between 20 and 400 P, they were measured by the falling-ball method described in ref 8. The polypeptide solutions were poured into a graduated cylinder of 1.0-cm diameter and the rate of fall of a steel ball of 0.25-cm diameter was measured as it flowed through the solutions. The viscosities were calculated using eq 5, where g =

$$\eta = \frac{2gr^2(\Psi - \Psi_0)}{9v}\left[1 - 2.104\left(\frac{r}{R}\right) + 2.09\left(\frac{r}{R}\right)^3\right] \quad (5)$$

acceleration of gravity, r = radius of the ball, Ψ = density of the ball, Ψ_0 = density of the fluid, R = radius of the cylinder, and v is the rate of fall.

Since the polypeptide solutions exhibited a thixotropic behavior, their viscosities were measured under two different conditions. The first measurement was taken immediately after stirring the solution with a glass rod for 1 hr at approximately 2 rpm. The second measurement was taken after the same solution was allowed to stand for 24 hr.

(g) Optical Studies. The polymer solution was placed between a microscope slide and a cover slip with a 0.2-mm spacer. The samples were stored for 2 days in a desiccator before observation. Photomicrographs of the polypeptide solutions were taken on a Zeiss optical microscope with the polarizer and the analyzer crossed. The magnification of the microscope was 120 ×.

Results and Discussion

Figure 5 shows the dependence of the diffusion coefficient of DL-mandelic acid on the concentration of PMDG in the liquid membrane. The abscissa is the concentration of the polypeptide expressed in volume fraction of the PMDG in tetrachloroethane and the ordinate is the diffusion coefficient obtained from the time lag method (see Experimental Section). The logarithmic plot of the steady state permeation coefficient of DL-mandelic acid *vs.* the volume fraction of PMDG in the liquid membrane is shown in Figure 6.

Figure 7 is a linear plot of the partition coefficient of DL-mandelic acid between water and PMDG solutions in tetrachloroethane *vs.* the volume fraction of PMDG in the polymer solutions. As the concentration of the polypeptide increases in the polymer solution, the solubility coefficient of mandelic acid is also enhanced. This is indicative of favorable interactions between the acid and the polypeptide. The intercept of this graph with the y axis gives the partition coefficient of mandelic acid between pure tetrachloroethane and water.

Figure 8 shows the dependence of the average diffusion coefficient, $\bar{D}$, on the volume fraction of the polypeptide in the liquid membrane. The time lag diffusion coefficients

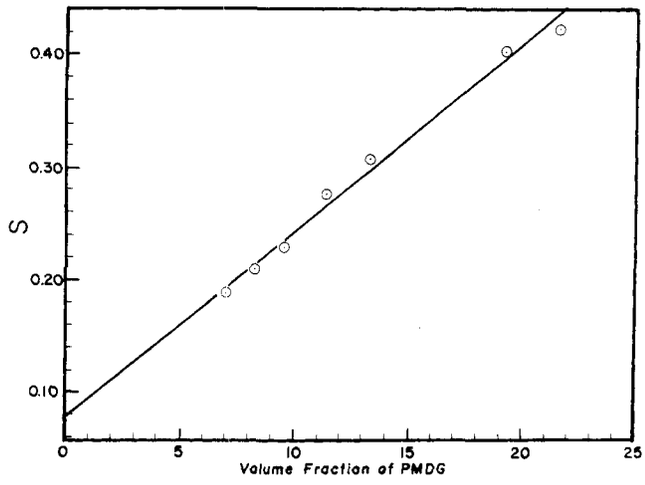


Figure 7. The dependence of the partition coefficient of mandelic acid on the volume fraction of PMDG.

have been included in this figure for comparison. Values of $\bar{D}$ are obtained using eq 2 and the data in Figures 6 and 7.

The value of the time lag diffusion coefficient at any volume fraction of PMDG is different from the value of the average diffusion coefficient calculated *via* the steady state permeation. The major source of this discrepancy could be attributed to formation of boundary layers, which introduce complication in the system. Another reason for making the above choice was the observation of the dependence of the time lag diffusion coefficients on the thickness of the membranes. The permeation experiments were performed on the liquid membrane using two different spacers. In this way the thickness of the membrane could be varied from 0.2 to 0.1 cm. This variation of the thickness caused consistently large changes in value of the time lag diffusion coefficient as calculated from eq 4, whereas the value of the average diffusion coefficient remained the same for both membrane thicknesses.

We note in Figure 8 that the logarithm of the diffusion coefficient of DL-mandelic acid decreases linearly with the increase in the volume fraction of PMDG in the liquid membrane at low volume fraction. This is true for both the time lag diffusion coefficient and the average diffusion coefficient. At approximately 13 to 14% volume fraction PMDG the slopes change, and at higher volume fractions the plots seem to become linear again. The changes in the diffusion properties of the liquid membrane at a specific concentration of the polypeptide reflect changes in the structure of the liquid polypeptide membrane. It is therefore essential to study the morphological changes of the liquid membrane as a function of the polypeptide concentration. Attempts will be made to correlate these structural changes to the permeation properties.

Structure of the Liquid Membrane. The structural changes of the liquid membrane were investigated by studying the viscosity of the polypeptide solutions. The viscosity studies were supplemented by direct optical observation of the solution.

Figure 9 shows the plot of the viscosity of the solution *vs.* the volume fraction of the PMDG. Since it was found that the PMDG solutions were thixotropic, the viscosity measurements were performed under two different conditions. The broken line in Figure 9 represents the viscosity of the polypeptide solution immediately after application of a disturbance. The disturbance was brought about by stirring the polypeptide solution for an hour prior to measuring its viscosity (see the Experimental Section for details). The solid line represents the viscosity of the PMDG solution

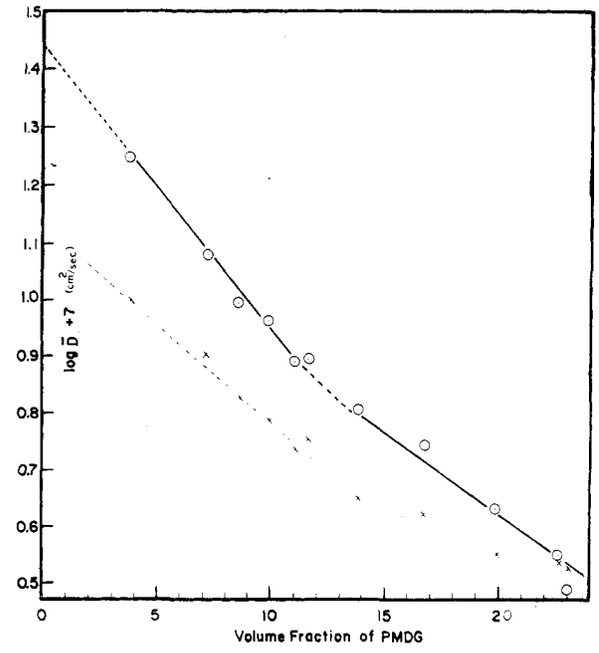


Figure 8. The dependence of the average diffusion coefficient of mandelic acid on the volume fraction of PMDG in the liquid membrane. The time lag coefficients are also plotted for comparison: O, average diffusion coefficients; ×, time lag diffusion coefficients.

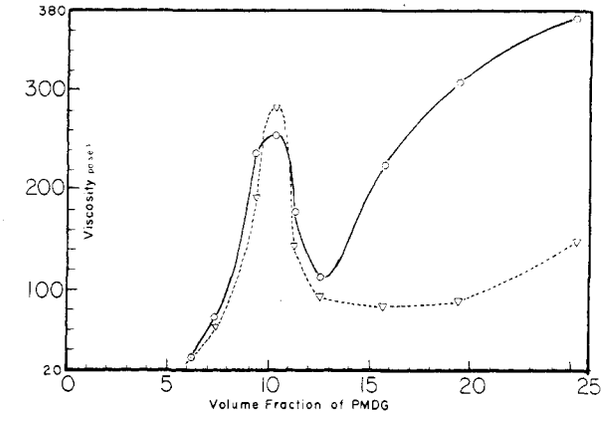


Figure 9. The dependence of the viscosity of the PMDG solutions on the volume fraction of PMDG. The broken line represents the viscosity of the solution taken immediately after stirring the solutions. The solid line represents the viscosity of the same solutions after allowing the solutions to rest for 24 hr.

after the polymer solution was allowed to stand for a period of 24 hr. It was found that the viscosity of the solution did not change appreciably after this 24-hr period. Although the absolute value of the viscosity depends on the condition of measurement, the general dependence of the viscosity on the volume fraction of PMDG for the disturbed and undisturbed solutions is the same. The viscosity of the polypeptide solution increases with increasing concentration of the PMDG in tetrachloroethane. At approximately 10% PMDG the viscosity of the solution reaches a maximum. Thereafter, with the increase in volume fraction of PMDG there is a decrease in viscosity which reaches a minimum in the 12 to 13% PMDG region (a plateau for the stirred solution). At higher volume fractions, the viscosity again increases with increasing concentration of the polymer, just as expected.

A similar behavior has been observed for thermotropic liquid crystals[9] and colloidal segregating mixtures.[10] The sudden maximum in the viscosity occurs at the onset of the anisotropic to isotropic transition. Lawrence[9] has suggested

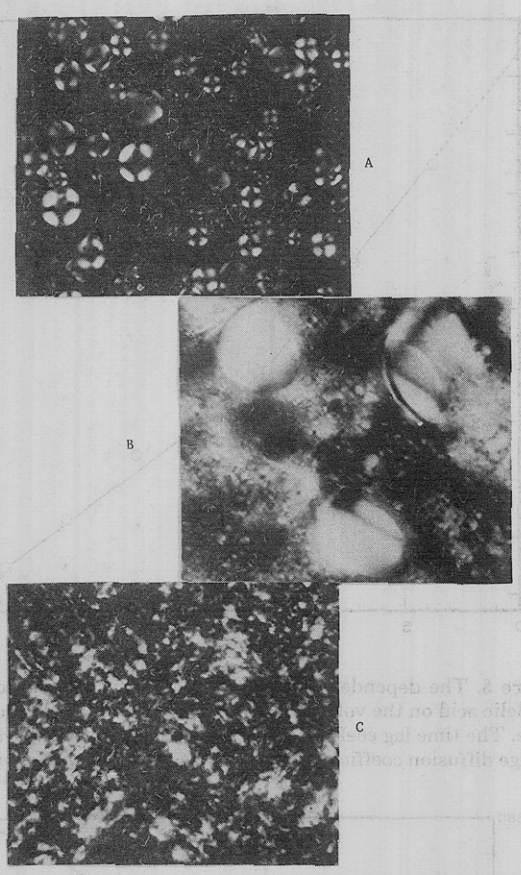


Figure 10. Photographs of solutions of PMDG in tetrachloroethane observed under a polarizing microscope. The polarizer and the analyzer are crossed. The volume fractions of the polypeptide in the solutions are: A, 9.9%; B, 11.3%; C, 19.9%.

that this rise in viscosity could be due to formation of swarms or aggregates.

Figure 10 shows the photographs of PMDG solutions of various compositions in tetrachloroethane observed under a polarizing microscope with the polarizer and the analyzer crossed. Below 8.5% volume fraction PMDG, the entire solution is isotropic. Formation of spherulites is observed around 9% PMDG, and by 10% PMDG the entire field of the microscope is covered by spherulites of various sizes (see Figure 10A). The increase in the viscosity of the polypeptide solution at this concentration is probably due to the presence of these anisotropic spherical particles which are suspended in the isotropic polypeptide solution. As the concentration of the PMDG in the polypeptide solution is increased, the spherulites begin to coalesce as observed in Figure 10B, and concurrently the viscosity of the solution decreases. Between 12 and 14% volume fraction PMDG, the biphasic system is replaced by a continuous monophasic liquid crystalline phase. Figure 10C shows the microphotograph of the PMDG solution at 19.9% volume fraction PMDG. Above 14% PMDG, the solution has a texture of cholesteric liquid crystal. The thixotropic behavior of the PMDG solution above 14% volume fraction PMDG could be due to the formation of this structure. The mechanical deformation of the polypeptide solution could destroy the structures which exist in the lyotropic cholesteric phase,[11] thereby changing the macroscopic properties of the solution.

A question of theoretical importance is whether there is any relationship between the macroscopic viscosity of the liquid membrane and the permeability of the membrane. A question of practical importance (which also relies on the viscosity of the liquid membrane) is whether any portion of the transport of the mandelic acid occurred through the convectional mixing of the polypeptide solution during the permeation experiments. The latter question will be examined first.

In order to minimize the transport of mandelic acid due to a possible convectional mixing of the liquid membrane in our permeation setup, a Teflon disk of 2-cm thickness and 3.8-cm diameter was made. Holes of 1 mm in diameter were drilled in the disk. This perforated disk was then inserted in the liquid membrane compartment of the permeation cell inside the spacer cavity (see Figure 2C). The polypeptide solution was poured into the holes of the perforated plate and the remaining space of the liquid membrane holder. After assembly as described previously a normal permeation experiment was performed. The effect of the disk was to restrict the exposed area of the liquid membrane to the total area of the holes since the diffusion of the mandelic acid through the liquid membrane could only occur through the holes. The function of the holes was to reduce the possible convectional mixing of the liquid membrane by confining the fluid to the small holes. The permeation and the diffusion coefficient obtained from such an arrangement, after accounting for the reduction of the surface area, were identical with a case with no disk in between. This indicated that the transport due to convectional mixing was negligible, at least for the case of liquid membranes with viscosity higher than 10 P.

Returning to the question of the dependence of diffusion coefficient on viscosity, it is well known that the intrinsic viscosity of a polymer in a particular solvent[12] correlates with the diffusion coefficient of the polymer in the solvent. However, the diffusion coefficient of low molecular weight molecules in polymer solution should be affected by the local frictional factor rather than the macroscopic viscosity of the solution.[13] Our experimental results indicated only a minor decrease in diffusion coefficient in the 8 to 10% PMDG concentration range although the viscosity of the solution underwent drastic changes. This is a rather convincing demonstration that macroscopic viscosity is not the controlling factor in our system.

The diffusion coefficient of mandelic acid through the liquid membrane and especially its dependence on the concentration of the polypeptide can be explained using the free volume theory of Cohen and Turnbull.[14] The dependence of the diffusion coefficient on the average free volume, f, of the menbrane is given by eq 6, where A is a frequency factor and B is a measure of the minimum hole size for the jump process. If the free volumes of the polymer and the solvent are additive, then

$$D = A\exp(-B/f) \tag{6}$$

$$f = f_p\varphi + (1 - \varphi)f_s \tag{7}$$

where φ is the volume fraction of the polymer in the solution, and f_p and f_s are the free volume of the pure polymer and the solvent, respectively. In eq 7 the contribution of mandelic acid to the total free volume was neglected because the concentration of the diffusant was low, less than 4% by volume in all cases. Combining eq 1 and 2 and substituting $\beta = f_s - f_p$, eq 8 is obtained. This equation can be

$$D = A\exp(-B/(f_s - \varphi\beta)) \tag{8}$$

further rearranged to yield eq 9, where D_s is the diffusion

$$D = D_s\exp\left(-\frac{B\beta\varphi}{f_s(f_s - \varphi\beta)}\right) \tag{9}$$

Table I
Comparison of Permeation and Diffusion Coefficients of D, L, and DL-Mandelic Acids[a]

	$P \times 10^7$	$D \times 10^7$
D-Mandelic acid	1.50 ± 0.05	3.3 ± 0.1
L-Mandelic acid	1.48 ± 0.06	3.3 ± 0.1
DL-Mandelic acid	1.37 ± 0.05	3.4 ± 0.1

[a] The volume fraction of PMDG in the liquid membrane was 23% and the experiments were done at 22°. P and D are in cm²/sec.

coefficient of the diffusant in the pure solvent

$$D_s = A \exp(-B/f_s)$$

At low volume fraction of the polypeptide, when $\varphi\beta < f_s$, the diffusion coefficient can be approximated by eq 10. It is

$$D = D_s \exp(-B\beta\varphi/f_s^2) \quad (10)$$

this low concentration region where the logarithmic plot of the diffusion coefficient *vs.* volume fraction of the polypeptide should be linear. This has indeed been observed for both the diffusion coefficient obtained from the time lag, D, and the average diffusion coefficient $\bar{D}$. It should be mentioned that many other models, not directly imposing free volume concepts, could also represent the change in D with the volume fraction of the polymer.

The change in the slope of the logarithmic plot of the diffusion coefficient (see Figures 5 and 8) of mandelic acid occurs in the vicinity of 12 to 14% PMDG by volume. It reflects a major alteration in the structure of the liquid membrane which occurs when the polypeptide solution undergoes the biphasic to liquid crystalline phase change. We note that the viscosity of the polypeptide solution also decreases around this concentration range.

Separation of Optical Isomers. One of our objectives was to investigate the possibility of effecting a separation of optical isomers by the process of diffusion of DL mixtures through an asymmetrical environment. The cholesteric state of polypeptide, which results in an enormous optical activity of the cholesteric phase,[11] might cause preferential diffusion of one enantisomer. No measurable separation of isomers of DL-mandelic acid was achieved in our work. Indeed when the diffusion coefficients of L- and D-mandelic acids through PMDG solutions were separately measured and compared, the results were identical for the two isomers at any given PMDG concentration (see Table I). Klein, *et al.*,[15] studied the permeation of mandelic and tartaric acids through saturated solutions of optically active polymers. They also reported that optical resolution of the acids was not achieved during the permeation.

Klein, *et al.*,[15] suggested that the lack of separation of optical isomers was due to the absence of free interacting groups in the polymer. The interacting groups must bind with an optical isomer at three separate points, according to Buss, *et al.*, in order to differentiate between the isomers.[16] The same explanation could apply in our case since the centers of the asymmetry of the polymer, *i.e.*, the α carbon of the polypeptide, are embedded in the α-helical backbone and therefore are not in an optimum position for direct interaction with the diffusants.

Summary

The transport behavior of mandelic acid through the liquid PMDG membranes, especially the dependence of the diffusion coefficient on the concentration of the polypeptide in the membrane, was studied. The permeation properties of the liquid membranes undergo a distinct change in a concentration region where the polypeptide solution undergoes a phase transition from the biphasic to the liquid crystalline state. The change of the permeation properties is indicative of a major morphological alteration of the membrane structure upon formation of a continuous liquid crystalline phase and is a consequence of the changes of the free volume of the system.

The fact that the permeation and the diffusion coefficients of the D, L, and DL isomers are identical with each other at every concentration of the polypeptide, including the concentration in which the liquid membrane is in the cholesteric state, indicates that the effective dimensions of the available holes required for the diffusional jumps are greater than the size of the diffusing species.

Acknowledgment. The authors wish to acknowledge the many helpful suggestions by Professor W. J. Kauzmann and Dr. R.-J. Roe during the course of this work.

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