Microcapsules XIV: Effects of Membrane Materials and Viscosity of Aqueous Phase on Permeability of Polyamide Microcapsules toward Electrolytes

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Abstract □ The effects of membrane materials and the viscosity of the aqueous phase on the permeability of several kinds of polyamide microcapsules toward electrolytes were studied. The permeation rate of electrolytes was higher in the microcapsule membranes consisting of polyamide molecules with a polymethylene chain than in those having an aromatic ring. The viscosity of the microencapsulated aqueous phase decreased the permeation rate of electrolytes to a great extent, indicating that the diffusion of electrolytes in the interior of microcapsules is rate determining in the permeation process.

Keyphrases □ Polyamide microcapsules—permeation rate of electrolytes □ Permeability, polyamide microcapsules—effect of membrane materials and viscosity of aqueous phase □ Microcapsules, polyamide—permeation rate of electrolytes, effect of membrane materials and viscosity of aqueous phase □ Electrolyte permeation through polyamide microcapsules—effect of membrane materials and viscosity of aqueous phase

Permeability is one of the most important properties of microcapsules when they are used in the medical and pharmaceutical fields. However, only a few papers have been published on their permeability. Chang and Poznansky (1) measured the permeability of large nylon microcapsules (200-μ mean diameter), suspended in saline solution, toward low molecular weight solutes labeled with radioisotope. The measurements were made at very early stages of the permeation, using a rapid mixing and sampling technique; the half-time for equilibration of the solutes was less than 60 sec. Takamura *et al.* (2) studied the permeation rate of various electrolytes through the membranes of polyphthalamide microcapsules (2-μ mean diameter) in quasisteady state by means of conductometry, and they reported that the permeability constant for the electrolytes is of the order of 10^{-8} cm./sec. The surprisingly low permeation rate was ascribed to the formation of a stable diffusion layer of the electrolytes in the interior of microcapsules.

Although the works cited have thrown much light on the permeability of microcapsules, many uncertainties remain with regard to the fundamentals of the permeation process. Consequently, extensive work is needed to elucidate the detailed character of the process. This paper deals with the effects of membrane materials and the viscosity of the aqueous phase on the permeability of polyamide microcapsules toward electrolytes.

EXPERIMENTAL

Materials—The diamines used in this work were *p*-phenylenediamine, piperazine, 2,5-dimethylpiperazine, and 1,6-hexamethylenediamine. Sebacoyl dichloride and *p*-phthaloyl dichloride were employed as acid dichlorides. All of these chemicals were of reagent grade. Sodium chloride and sodium sulfate (analytical reagent grade) were used for permeability experiments without further purification. Polyvinylpyrrolidone (mol. wt. 360,000) was a commercial product.

Preparation of Microcapsules—Polyamide microcapsules containing water were prepared by the same method as that described earlier (2) by making use of the interfacial polycondensation reaction between diamine in the aqueous phase and acid dichloride in the organic phase. The polyamide microcapsules prepared from the diamines with the acid dichlorides were as follows: polyphenylene phthalamide, polyphthaloyl piperazine, polyphthaloyl 2,5-dimethylpiperazine, polyhexamethylene phthalamide, and polyhexamethylene sebacamide microcapsules. All of these microcapsules were dialyzed in the same manner as already reported (2) and were dispersed in deionized water containing 1% (v/v) polysorbate 20 as the dispersing agent.

Polyphthaloyl piperazine microcapsules containing aqueous solution of polyvinylpyrrolidone were prepared, dialyzed, and dispersed in 1% polysorbate 20 solution in the same way as already mentioned. In some cases, polyphthaloyl piperazine microcapsules containing aqueous polymer solution were dispersed in polymer solution containing 1% polysorbate 20.

Estimation of Permeability—As in the previous work (2), the permeability of microcapsules was estimated from the change in electrical conductance of the mixture of microcapsule dispersion and electrolyte solution in 1% polysorbate 20 solution.

To 200 ml. of 0.05 *N* NaCl or Na_2SO_4 solution in a conductance cell immersed in a constant-temperature bath, 100 ml. of the microcapsule dispersion previously kept at the same temperature was quickly added with stirring. The conductance reading was started shortly after mixing and was taken at suitable time intervals.

The electrical conductance measurements[1] were carried out at 10 ± 0.1°. The stirring was continued throughout the measurements.

The permeability constant for the electrolyte, P, was calculated by the equation:

$$P = -\frac{2.303 C_f V_m}{C_i A t} \log \frac{C_t - C_f}{C_i - C_f} \qquad \text{(Eq. 1)}$$

which was derived in the earlier work (2) based on Fick's first law of diffusion. In this equation, C_i, C_t, and C_f are the initial, intermediary (at time t), and final concentrations of electrolyte, respectively, in the dispersion medium determined by conductance measurements; V_m is the total volume of microcapsules; and A is the total surface area of microcapsules.

The validity of Eq. 1 can be checked by plotting $\log (C_t - C_f)/(C_i - C_f)$ against time. If the plot gives a straight line, the equation strictly holds and the permeability constant can be evaluated from the slope of the line.

The permeability constant thus obtained was converted to the apparent diffusion coefficient in the microcapsule membrane, D, by the following relation given in the previous paper (2):

$$D = P\Delta x \qquad \text{(Eq. 2)}$$

where Δx denotes the membrane thickness.

Estimation of Membrane Thickness—The thickness of microcapsule membranes was calculated by the equation:

$$\Delta x = \frac{wr}{dA} \qquad \text{(Eq. 3)}$$

where w is the weight of microcapsule membranes in unit volume of dispersion, assuming the complete reaction of diamine and acid dichloride; r is the experimentally determined percent reacted of

[1] Model CM-1DB conductance meter, Toa Electric Co., Tokyo, Japan.

Table I—Apparent Diffusion Coefficients for Electrolytes in Various Microcapsule Membranes

Microcapsule	Apparent Diffusion Coefficients, $\times 10^{14}$ cm.²/sec. Sodium Chloride	Sodium Sulfate
Polyphenylene phthalamide	2.6	2.6
Polyphthaloyl piperazine	2.4	2.5
Polyphthaloyl dimethylpiperazine	3.1	3.2
Polyhexamethylene phthalamide	3.0	3.8
Polyhexamethylene sebacamide	4.4	4.9

diamine; d is the density of microcapsule membrane; and A is the total surface area of microcapsules in unit volume of dispersion.

The percent reacted of diamine was determined in the following way. Polyamide microcapsules were broken down by centrifugation, and a clear aqueous phase containing unreacted diamine was obtained. A 4-ml. portion of the aqueous phase was mixed with 3 ml. of 5% (v/v) *p*-dimethylaminobenzaldehyde solution and 1 ml. of 15% (v/v) sulfuric acid solution in methanol, and the mixture was allowed to react at 60° for 10 min. The amount of diamine remaining unreacted was determined by measuring spectrophotometrically the absorption of colored complex formed between the diamine and *p*-dimethylaminobenzaldehyde (3). The wavelengths of maximum absorption were 425, 415, and 500 nm. for the piperazine, 1,6-hexamethylenediamine, and *p*-phenylenediamine complexes, respectively. The amount of 2,5-dimethylpiperazine could not be determined by this method, because this diamine did not react with *p*-dimethylaminobenzaldehyde. Instead, 2,3-dinitrofluorobenzene was used as the coloring agent. That is, a 2-ml. portion of the aqueous phase was mixed with an equal volume of 1.2% (v/v) 2,3-dinitrofluorobenzene solution in methanol and 1 ml. of aqueous 0.1 *M* $NaHCO_3$ solution, and the absorption at 396 nm. was measured spectrophotometrically (4). In all cases, the percent reacted of diamine was calculated from its concentrations in the aqueous phase before and after microencapsulation.

The microcapsule membranes obtained by breaking down polyamide microcapsules through centrifugation were collected, washed, and dried under reduced pressure. The specific gravity of the dried sample was determined with a pycnometer. The density of the membranes was obtained by multiplying the specific gravity by the density of water.

The total surface area of microcapsules was estimated in a way similar to that adopted in earlier works (5–7).

Measurement of Viscosity—The viscosities of aqueous polyvinylpyrrolidone solutions containing sodium chloride or sodium sulfate of the concentration at distribution equilibrium were measured with a viscometer[1] at 10 ± 0.1°.

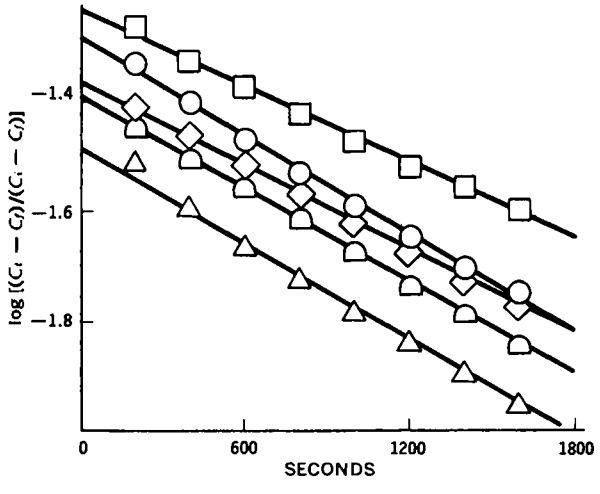

Figure 1—*Plot of log* $(C_t - C_f)/(C_i - C_f)$ *against time for the entry of sodium chloride into polyamide microcapsules. Key: microcapsules:* □, *polyphenylene phthalamide;* ◇, *polyphthaloyl piperazine;* ⬭, *polyphthaloyl dimethylpiperazine;* △, *polyhexamethylene phthalamide; and* ○, *polyhexamethylene sebacamide.*

Table II—Characteristics of Polyamide Microcapsules

Microcapsule	Membrane Density, g./cm.³	Membrane Thickness, *A*	Surface Area, m.²/cm.³
Polyphenylene phthalamide	1.38	123	1.79
Polyphthaloyl piperazine	1.37	133	2.12
Polyphthaloyl dimethylpiperazine	1.35	166	2.03
Polyhexamethylene phthalamide	1.28	167	2.21
Polyhexamethylene sebacamide	1.14	224	2.15

RESULTS AND DISCUSSION

Effect of Membrane Materials—The distribution equilibrium of electrolytes was established within 2 hr. between the inside and outside of all polyamide microcapsules studied in this work.

Figure 1 shows the plot of log $(C_t - C_f)/(C_i - C_f)$ against time for the entry of sodium chloride into polyamide microcapsules, indicating the validity of Eq. 1 between 3 and 30 min. after mixing the electrolyte solution and microcapsule suspension. The electrolyte entry into microcapsules proceeds in a quasisteady state since the permeation process is supposed to have been about 90% completed at the time when the conductance measurement is started.

The permeability constants for sodium chloride and sodium sulfate calculated by Eq. 1 were always of the order of 10^{-8} cm./sec. and were dependent on the membrane constituents. Table I lists the apparent diffusion coefficients in the microcapsule membranes converted from the permeability constants by means of Eq. 2. Inspection of the table reveals that the diffusion rate of the electrolytes is higher in the membranes consisting of polyamide molecules with a polymethylene chain than in those having an aromatic ring.

Table II gives some characteristics of the polyamide microcapsules. The data are useful in discussing the effect of the membrane constituent on the permeation rate of the electrolytes through the polyamide microcapsule membranes.

As stated previously (2), polysorbate 20 molecules are undoubtedly adsorbed on the polymer molecules constituting microcapsules,

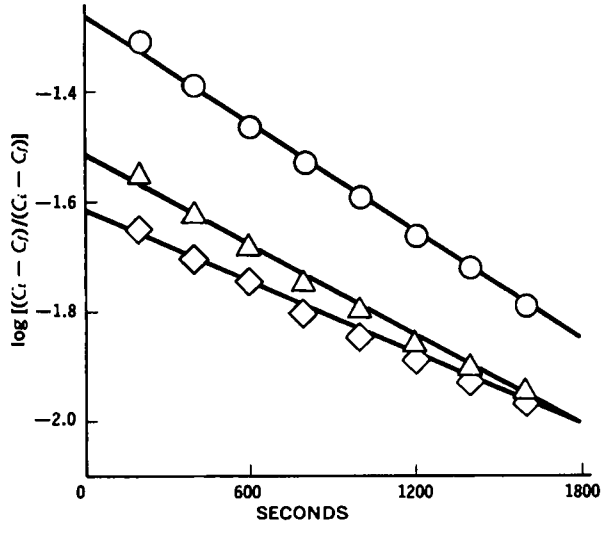

Figure 2—*Plot of log* $(C_t - C_f)/(C_i - C_f)$ *against time for the entry of sodium chloride into polyphthaloyl piperazine microcapsules in the presence of polyvinylpyrrolidone. Key (polyvinylpyrrolidone concentration, %):* ○, *0.05;* △, *0.10; and* ◇, *0.15.*

[1] Ostwald.

Table III—Effect of Viscosity of Microencapsulated and Intercapsular Aqueous Phases on the Permeability Constants of Electrolytes for the Entry into Polyphthaloyl Piperazine Microcapsules

Viscosity, cps.	—Permeability Constant, $\times 10^5$ cm./sec.— Sodium Chloride	Sodium Sulfate
1.31	1.78	1.90
1.43	1.72	1.76
1.54	1.62	1.63
1.68	1.50	1.50

Table IV—Effect of Viscosity of Microencapsulated Aqueous Phase on the Permeability Constants of Electrolytes for the Entry into Polyphthaloyl Piperazine Microcapsules

Viscosity, cps.	—Permeability Constants, $\times 10^5$ cm./sec.— Sodium Chloride	Sodium Sulfate
1.31	1.78	1.90
1.43	1.69	1.74
1.54	1.64	1.57
1.68	1.54	1.59

thereby making the membranes hydrophilic. Consequently, sodium chloride and sodium sulfate are quite likely to diffuse through the interspace filled with water of polymer chains in a random arrangement of the membranes. It is then expected that the dimension of interspace of polymer chains greatly affects the diffusion rate of the electrolytes. Since polyamide molecules having polymethylene groups are more flexible than those with aromatic rings, the dimension of interspace of polymer chains would be larger in polyhexamethylene sebacamide and polyhexamethylene phthalamide microcapsules than in polyphenylene phthalamide, polyphthaloyl piperazine, and polyphthaloyl dimethylpiperazine microcapsules.

This situation is reflected in the densities of the microcapsule membranes shown in Table II and in the diffusion coefficients for sodium chloride and sodium sulfate given in Table I. It may be inferred, therefore, that the diffusion rate of electrolytes is lower in the microcapsule membranes of high density than in those of low density.

The difference in the diffusion rate between sodium chloride and sodium sulfate would be caused either by the different hydration of chloride and sulfate ions or by the different electrostatic interaction of the two anions with polyoxyethylene chains of dispersing agent molecules adsorbed on the polyamide molecules of the microcapsule membranes. However, the former possibility is ruled out because the permeability constants for sodium sulfate are, in general, greater than those for sodium chloride, while sulfate ions are more strongly hydrated and consequently should diffuse more slowly than chloride ions in the interspace of polymer chains. This leads one to the second possibility.

As described earlier (2), anions of higher valency are likely to interact more strongly than those of lower valency with weakly cationic polyoxyethylene chains of dispersing agent molecules adsorbed on the polymer molecules constituting microcapsules. As a consequence, there would be a richer accumulation of sulfate ions than chloride ions in the microcapsule membranes. This may result in the higher permeation rate for sulfate ions than for chloride ions.

Effects of Viscosity of Aqueous Phase—Earlier (2), it was proposed that the diffusion of electrolyte in the interior of microcapsules is rate determining in the permeation process, because the formation of a stable diffusion layer of electrolyte is highly probable inside the microcapsules. If this is really the case, the viscosity of the microencapsulated aqueous phase would affect the permeation of electrolyte through the microcapsule membranes to a great extent.

Figure 2 shows the effect of viscosity of microencapsulated and intercapsular aqueous phases on the rate of entry of sodium chloride into polyphthaloyl piperazine microcapsules. The viscosity was raised by dissolving polyvinylpyrrolidone in the aqueous phases. An increase in the viscosity clearly gives rise to a decrease in the rate of entry of sodium chloride. It is quite unlikely that polyvinylpyrrolidone molecules are adsorbed on the membrane by competing with dispersing agent molecules and thus offer resistance to the entry of sodium chloride since the former molecules are far less surface active than the latter molecules.

Table III lists the permeability constants for sodium chloride and sodium sulfate when both the microencapsulated and intercapsular aqueous phases contain polyvinylpyrrolidone. Table IV gives the permeability constants for sodium chloride and sodium sulfate in the case where the polymer is present only in the microencapsulated aqueous phase. Comparison of the two tables indicates that the permeation rate of electrolytes strongly depends on the viscosity of microencapsulated aqueous phase. This would support the view that the diffusion of electrolyte in the microencapsulated aqueous phase is rate determining in the permeation process. The tables also suggest that the increase in the viscosity of the microencapsulated aqueous phase tends to diminish the difference in the diffusion rate in the microcapsule membranes between sodium chloride and sodium sulfate.

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