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Studies on Microcapsules. XIII. Effect of Span 85 and pH of Aqueous Phase on the Formation of Polyamide Microcapsules

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The effects of the pH of aqueous phase containing piperazine and the concentration of Span 85, a nonionic surfactant with chemical description of sorbitan trioleate (Atlas Power Co., U.S.A) on the formation of polyphthalamide microcapsules were systematically investigated by the interfacial polycondensation method in the organic phase containing *p*-phthaloyl dichloride. The presence of Span 85 facilitated the formation of microcapsules by increasing the transfer of undissociated diamine molecules into the organic phase in the pH range 9.0–12.0, outside of which Span 85 did not significantly contribute to the formation of microcapsules. An increase in the pH in this range gives rise to an increase in the number of undissociated diamine molecules, promoting the transfer of diamine.

It is known that the partition of diamines between water and a water-immiscible organic liquid is important for the formation of polymers by interfacial polycondensation reaction.[1] The same holds for the formation of microcapsules by the interfacial polycondensation method.[2–4]

On the other hand, the partition coefficients of diamines were found to be affected favorably in an organic phase in the presence of Span 85, a nonionic surfactant.[2] Diamine molecules should exist in an undissociated form so that they can be transferred into an organic phase. This indicates that the partition might be significantly reduced near a pH equal to the pK value of diamines. Actually, when $NaHCO_3$ was present instead of Na_2CO_3 the partition of diamines was unfavorably affected, and hardly any microcapsules were formed.[5]

Since the findings are still scanty, a systematic study is needed to understand the effects of the pH of aqueous phase and the Span 85 concentration in organic phase on the formation of microcapsules. Thus, the effects of the pH of aqueous phase containing piperazine, a diamine, and the Span 85 concentration in a chloroform-cyclohexane mixture containing *p*-phthaloyl dichloride on the formation of polyphthalamide microcapsules were systematically examined.

Experimental

Determinarion of Apparent Partition Coefficient of piperazine. The apparent partition coefficient of piperazine was determined at various pH in the same way as in the preparation of micrlcapsules.[2] Ten milliliters of 0.40 M piperazine (diethylenediamine) was added to 10 ml of 0.90 N Na_2CO_3–$NaHCO_3$ in a 500 *ml* round bottom flask surrounded by ice. The Na_2CO_3–$NaHCO_3$ mixture was used with varying the mixing ratio but keeping constant the total concentration at 0.90 N. One hundred milliliters of mixed organic solvent (cholroform-cyclohaxane, 1 : 3 vol), containing 0–7 vol% Span 85 was added to the solution as an emulsifying agent. The mixed solution was then mechanically emulsified with a Chemistirrer (Tokyo Rika Kikai Co., Tokyo, Model B-100) at 521 r. p. m. for 5 min to yield a water-in-oil emulsion.

Immediately after stirring was stopped the emulsion was centrifuged at 13000 g for 10 min to remove the aqueous phase from the organic phase. The concentration of piperazine in the organic phase was then determined by titration with HCl solution in an isopropanol-ethyleneglycol mixture (1 : 1 vol) using BTB-BCG mixed indicator.[6] The

** To whom all inquiries should be addressed.
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2) M. Koishi, N. Fukuhara, and T. Kondo, *Chem. Pharm. Bull.* (Tokyo), **17**, 804 (1969).
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partition coefficient of piperazine was calculated from its initial concentration in the aqueous phase and final concentration in the organic phase.

Determinarion of the percentage of Reacted Piperazine. The determination was carried out as follows. The mixture of the aqueous phase and the organic phase was mechanically emulsified under the same conditions as in the determination of apparent partition coefficient. One hunderd milliters of 0.04 *M* *p*-phthaloyl dichloride solution in the mixed organic solvent was added to the emulsion obtained, and the resulting microcapsule suspension was centrifuged at 29000 g for 10 min after stirring was continued for 3 min. Centrifugation caused the breakdown of microcapsules and a clear aqueous phase was obtained.

A 5 m*l* portion of the aqueous phase was mixed with an equal volume of *p*-dimethylaminobenzaldehyde solution in methanol containing 30 vol% H_2SO_4. The amount of piperazine remaining unreacted was determined by measuring the absorption of colored complex at 425 mμ spectrophotometrically.[7] The percentage of reacted piperazine was calculated from its initial and final concentrations in the aqueous phase.

Measurement of Viscosity of Ploymer Solution. The measruement of viscosity of polymer solution was carried out in a way similar to that described previously.[4] Each microcapsule suspension prepared under various conditions was centrifuged to break down the microcapsules and the microcapsule membrane obtained was collected, washed, and dried under reduced pressure. The dried sample was dissolved in *m*-cresol. For each sample solution thus prepared, the relative viscosity was measured at 30 °C with a dilution type Ubbelohde viscometer. The reduced viscosity was then plotted against the polymer concentration and the intrinsic viscosity was graphically estimated by extrapolation to zero conecntration.

Determination of CMC of Span 85. The determination of critical micelle concentration of Span 85 was carried out by the method of Ross and Olivier.[8] 5m*l* of iodine solution (70 mg/*l*) in the mixed organic solvent was added to an equal volume of each Span 85 solution of various concentrations around its CMC in the same solvent. The transmittance of the solutions was then measured at a wavelength of 360 mμ using the mixed solvent as a reference. The CMC was graphically determined as the break point of transmittance *versus* concentration curve.

Results and Discussion

Apparent Partition Coefficient. The dependence of apparent partition coefficient of piperazine on the pH of aqueous phase at several Span 85 concentrations in the organic phase is shown in Fig. 1.

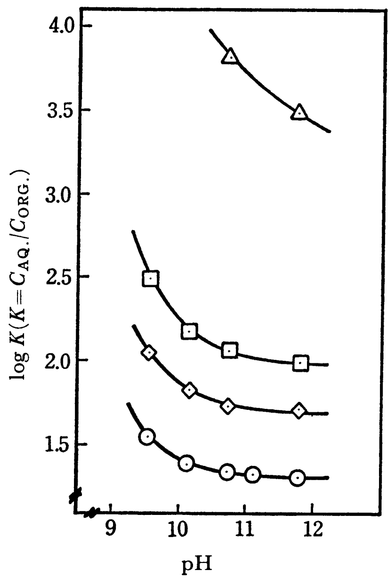

Fig. 1. The dependence of apparent partition coefficient of piperazine on the pH of aqueous phase at several Span 85 concentrations in the organic phase. Span 85 concentrations: (△) 0%, (□) 1%, (◇) 2%, and (○) 5%.

At any concentration of Span 85 in the organic phase, the apparent partition coefficient decreased first and then levelled off as the pH of aqueous phase increased, indicating that the transfer of piperazine from the aqueous to the organic phase initially inincreases but approaches a saturation value as the hydrogen ion concentration in the aqueous phase decreases.[9] This results from the fact that the p*K* values of piperazine are 5.57 and 9.81. Increases in the pH of aqueous phase will cause an increase in the number of unprotonated piperazine molecules and a transfer would be favored. The transfer would stop increasing when all the piperazine molecules in the aqueous phase take the unprotonated form above pH 10.0. This trend of a transfer of substances with pH-dependent dissociable groups in their molecules is frequently observed.[10–12]

It was reported that the transfer of piperazine or 1,6-hexamethylenediamine from aqueous Na_2CO_3 solution to a chloroform-cyclohexane mixture is facilitated by the presence of Span 85 in the organic solvent.[2] We see from Fig. 1 that the presence of Span 85 in the organic phase increases the transfer of piperazine irrespective of the pH of aqueous phase and the amount transferred increases as the Span 85 concentration increases. Although the exact role of Span 85 in facilitating the transfer of piperazine is not yet fully understood, a portion of piperazine transferred should exist in the solubilized form in Span 85 micelles since the concentrations of Span 85 we used lie beyond its CMC (9.3×10^{-2}%).

Percentage of Reacted Piperazine. The percentage of reacted piperazine with *p*-phthaloyl dichloride at

TABLE 1. PERCENTAGE OF REACTED PIPERAZINE

pH / Span 85 (vol%)	9.54	10.13	11.77
0	8	—	34
1.0	42	75	87
2.0	54	74	90
5.0	79	—	89
7.0	87	—	—

7) C. Menzie, *Anal. Chem.*, **28**, 1321 (1956).
8) S. Ross and J. P. Olivier, *J. Phys. Chem.*, **63**, 1671 (1959).
9) Transfer of piperazine was not noticeable below pH 9.0.

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various pH and Span 85 concentrations is given in Table 1.

The percentage was greatly affected by both the pH of aqueous phase and the Span 85 concentration in organic phase. Since the interfacial polycondensation reaction occurs on the organic solvent side of the interface of water and organic solvent,[1] the percentage of reacted piperazine should be related to its apparent partition coefficient. The relation between the percentage and its apparent partition coefficient is illustrated in Fig. 2. The relation is linear for all the pH values and the slope of straight line increases with increasing pH. At a pH of about 12, the straight line becomes vertical, suggesting that the percentage is practically independent of the transferred amount of piperazine above this pH.

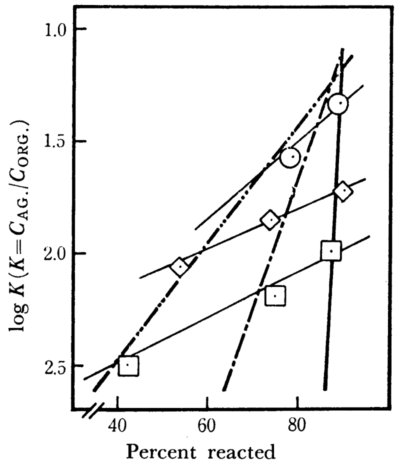

Fig. 2. The relation between the percent reacted of piperazine and its apparent partition coefficient. Span 85 concentrations: (□) 1%, (◇) 2%, and (○) 5%. pH of aqueous phase: (—··—) pH 9.54, (—·—) pH 10.13, and (—) pH 11.77.

We see also that the apparent partition coefficient increases, and consequently, the percentage decreases as the pH of aqueous phase lowers at any Span 85 cancentration in the organic phases. Since the apparent partition coefficient drastically rises below pH 9.0 irrespective of Span 85 concentration (Fig. 1), it would be inferred that the percentage greatly falls below this pH. In fact, polyphthalamide microcapsules were not formed appreciably below pH 9.0, however high the Span 85 concentration. This indicates a very low percentage. This would mean that the lower limit of pH for the formation of microcapsules making use of polycondensation reaction between a diamine and an acid dichloride lies around a value equal to the pK of the diamine used.

Intrinsic Viscosity of Polymers Constituting Microcapsules. The intrinsic viscosities of polymers constituting polyphthalamide microcapsules prepared under various conditions are given in Table 2.

A close relation is clearly observed between the intrinsic viscosity of polyphthalamide and the percentage by comparison with Table 1. A polymer with high intrinsic viscosity or high molecular weight is obtained at high percentage while a low intrinsic viscosity corresponds to a low percentage. Typical photomicrographs of microcapsules prepared under the conditions pH 9.54 of aqueous phase and 1 vol% of Span 85 in the organic phase, and pH 11.77 and 5 vol% of Span 85, are shown in Photos. 1 and 2, respectively.

Table 2. Intrinsic viscosity of polymers constituting microcapsules

pH / Span 85 (vol%)	9.54	10.31	11.77
1.0	0.20	0.31	0.56
2.0	—	0.35	0.43
5.0	0.53	—	0.55

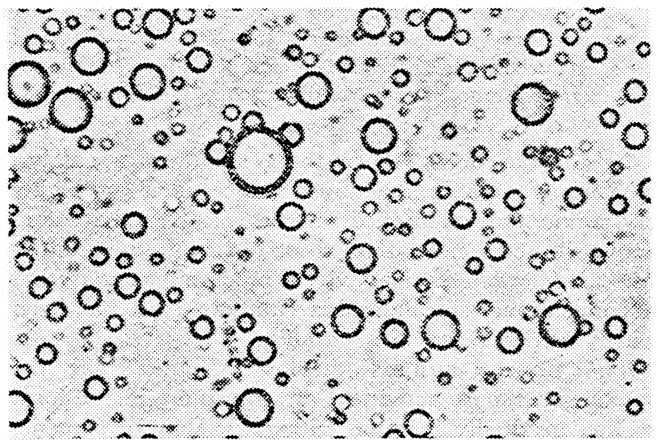

Photo. 1. Photomicrograph of polyphthalamide microcapsules prepared at pH 9.54 of aqueous phase and 1 vol% of Span 85 in the organic phase (×600).

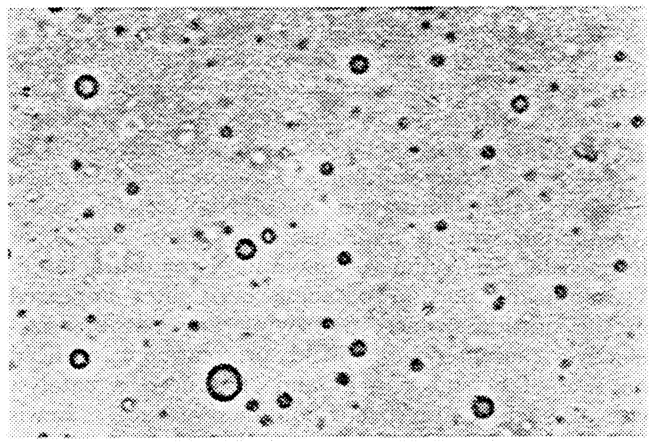

Photo. 2. Photomicrograph of polyphthalamide microcapsules prepared at pH 11.77 of aqueous phase and 5 vol% of Span 85 in the organic phase (×600).

Microcapsules were generally larger in size if they were prepared at low pH and Span 85 concentration as compared with those prepared at high pH and Span 85 concentration. Formation of large microcapsules was also reported[4] for the case in which the oil soluble reactant concentration in organic phase was reduced or the temperature at which polycondensation reaction takes place was lowered. It might be concluded that large microcapsules are formed by the mechanism discussed[4] whenever polymers with low intrinsic viscosity are produced.