Interaction Between Polyvinyl Alcohol and Procaine Hydrochloride

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The interaction between procaine hydrochloride and polyvinyl alcohol was studied in terms of a determination of the activity coefficient of chloride ions in aqueous solution by means of membrane electrodes. γ_{Cl^-} shows a discontinuity in solution of procaine hydrochloride as a function of the dilution. This discontinuity is enhanced and shifted toward diluted range when amounts of polyvinyl alcohol are present in solution and also a polyelectrolyte behavior is observed.

INTERACTION of macromolecules with chemicals is of great and increasing interest, particularly in the field of compounds with pharmacological activity. Local anesthetics (8–10), steroidic hormones, barbiturates, penicillins, salicylates, and sulfonamides were studied in connection with their interactions with macromolecules (1–7). In some cases the complex formation between several local anesthetics and macromolecules determines a sharp increase in potentiating both duration and intensity of local anesthetic activity (13).

The results obtained by studying the interaction of procaine hydrochloride (PrHCl) and polyvinyl alcohol (PVA) are reported.

EXPERIMENTAL

Materials.—Procaine hydrochloride reagent analytical grade was supplied by Carlo Erba, S.p.A., Milan, Italy. Polyvinyl alcohol from Polymer Consultants, Ltd., London, England, had a molecular weight of 128,000, according to light scattering measurements carried out in our laboratory. Dialyzer tubing of cellulose was supplied by A. H. Thomas Co., Philadelphia, Pa. All other reagents were analytical grade.

Procedure.—Membrane equilibrium dialysis and potentiometric measurements were carried out at room temperature; viscosity and conductivity measurements were performed in a thermostatic bath at 25°.

The solutions of procaine hydrochloride and procaine hydrochloride–polyvinyl alcohol investigated were brought into equilibrium across a dialyzing membrane. For this purpose, two arrangements were set up: (*a*) conventional bags containing the mixed solution of polymer and drug dipped into a vessel containing the drug solution was shaken from time to time, and (*b*) the dialyzing membrane (of about 55 mm. in diam.) was clamped tightly between the flanges of two half cells with a capacity of approximately 50 ml. each. The solution of procaine and procaine + polymer contained in the two half cells was stirred continuously with two glass rods, squeezed at the tips, and running at the same speed into the solution. Both systems were maintained at room temperature until equilibrium was established. Before and after the experiments, the procaine concentration at the two sides of the membrane was determined by measuring the optical densities at 290 mμ with a Beckman (DU) spectrophotometer.

The activity of chloride ions of the solutions containing procaine hydrochloride was determined with positively charged membranes (Permaplex A20). The apparatus and detailed procedure for these potentiometric determinations have been described elsewhere (11).

Conductometric measurements performed in thermostatic bath at 25° ± 0.01 were recorded with a Philips a.-c. bridge, using a cell that allowed the dilution of the stock solution about 15 times.

RESULTS AND DISCUSSION

The membrane equilibrium dialysis measurements obtained in the study of the interaction with polyvinyl alcohol are shown in Fig. 1. The ordinate represents the ratio between the concentration of drugs at the two sides of the membrane at equilibrium; the variation of concentration of polymer is reported on abscissa. The slope of the straight line obtained clearly indicates that an interaction takes place between drug and polymer chain.

Figure 2 shows the activity coefficient of chloride ions (lower) and the specific conductivity (higher) determined in simple PrHCl solution as a function of the PrHCl concentration.

The simpler and more intuitive explanation of such phenomenon could be the existence of small aggregates of PrHCl molecules in water solution above a certain concentration. In fact, the discontinuity and the trend of the plots are similar to that of laurylsulfate and/or similar colloidal electrolytes in the concentration range where the critical micelle concentration takes place (11).

When PVA is added, the plot below the critical point becomes sharply parallel to the abscissa, and the discontinuity is shifted towards lower concentrations of PrHCl (Fig. 3). This shift is also proportional to the concentration of PVA in solution. The localization of the concentration where the break takes place was determined by conductometric and potentiometric measurements; in both cases the agreement was very good.

Below the critical point, the behavior of the activity coefficient is invariant with the concentration and typical of polyelectrolytes (12), while (as previously mentioned) the trend of the plot in absence of polymer in diluted solution is very similar to that of simple electrolytes.

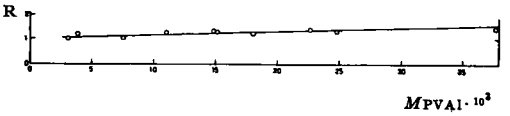

Fig. 1.—Membrane equilibrium dialysis measurements. The ordinate represents the ratio of drug on both sides of the membrane at equilibrium; the abscissa represents the concentration of polymer.

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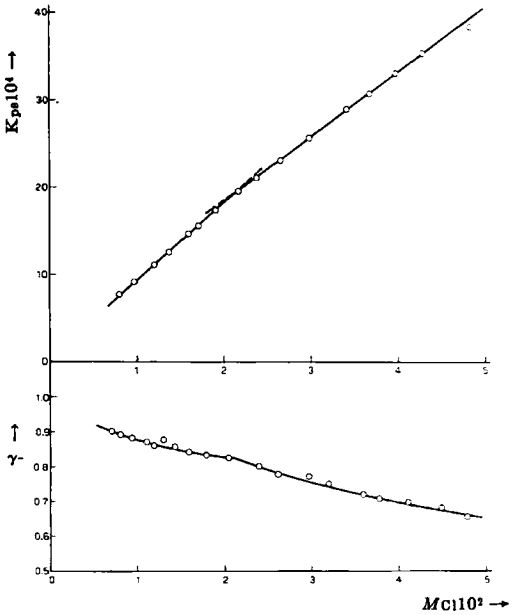

Fig. 2.—The activity coefficient of chloride ions (lower) and the specific conductivity (higher) determined; simple PrHCl solution is shown as a function of PrHCl concentration.

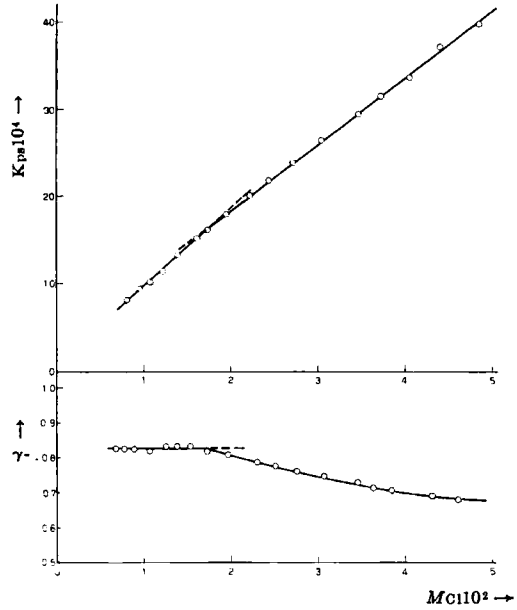

Fig. 3.—Activity coefficient of chloride ions (lower) and specific conductivity (higher) determined in PrHCl solution (PVA also being present) as a function of PrHCl concentration.

In a previous paper (10) Higuchi and co-workers showed that when PrHCl was admixed with polyvinylpyrrilidone (PVP) no interaction takes place. To confirm our potentiometric results, this experiment was reproduced. The determination of activity coefficient of chloride ions with membrane electrodes was perfectly identical to the values of PrHCl in water, thus confirming the lack of interaction.

In conclusion, the results reported here indicate that an interaction takes place between PrHCl and PVA and that the determination of the activity coefficient can be considered a useful method to provide information about interactions between drugs and macromolecules.

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