8. SUMMARY

Summary :

1. The object is to study ion exchange resin-cinchona alkaloid system and the usefulness towards practical application.

2. The ultraviolet absorption spectra of quinine, quinidine, cinchonine and cinchonidine in aqueous alcohols (methanol, ethanol and n-propanol) have been studied. The spectra of quinine and quinidine are distinctly different from those of cinchonine and cinchonidine.

On comparing the ultraviolet absorption of alkaloids in water and in alcohols, the values of maxima of quinine and quinidine are almost unaffected and the value of log ε (ε = extinction coefficient), is either not affected or affected by small amount. Same is true for cinchonine and cinchonidine except that first maximum (at lower wavelength) is significantly shifted to lower wavelength side when solvent is changed from water to alcohol.

3. The equilibrium exchange between cinchona alkaloid (quinine, quinidine, cinchonine and cinchonidine) sulfates in dilute aqueous solution and cation exchange resins has been studied. The variables studied include the relative degree of crosslinking of the resins, the ionic form of the resins and different particle size in hydrogen form of the resin.

The effect of the degree of crosslinking is significant. The value of P_R (the percent resin capacity exchanged at equilibrium) for all the alkaloid sulfates decreases as X increases. This is so for each of the ionic form of the resin. Also P_R values of quinine sulfate and quinidine sulfate for a resin in a particular ionic form are significantly lower than

those for cinchonine sulfate and cinchonidine sulfate for the same resin in the same ionic form.

The values of P_R for resin for optical isomers quinine and quinidine are almost same and same is true for optical isomers cinchonine and cinchonidine. The exception seems to be lower crosslinked resin X2 in ammonium form for which the values of P_R for optical isomers are somewhat different. The value for the levo isomer being higher than that for dextro isomer.

Average value of P_R for resins of fine mesh (200/400) is higher than that for the same resins of larger mesh (60/80). Also for resin X2, P_R increases with decrease in P_A (the percent exchange of alkaloid base, at equilibrium), for resins X4, X8 and X12, P_R increases when P_A decreases for usually fine mesh (200/400), but is practically constant, when P_A decreases for larger mesh (60/80).

The comparison of values of P_R for equilibrium exchange of quinine sulfate for resins of same particle size (60/80 mesh) in hydrogen and ammonium form indicates that the value of P_R , for X2, is higher ; for X4, is almost same and for X8, is less for resin in ammonium form than that in hydrogen form. For the equilibrium exchange of cinchonine sulfate with same resins, the values of P_R are higher for ammonium form than those for hydrogen form.

For resin IR-200, which probably has X about 20, but has an expanded structure, the value of P_R in hydrogen form is practically constant and independent of P_A ; but for resin

in ammonium form, the value of P_R decreases to some extent as P_A increases. Also the value of P_R for hydrogen form of the resin is somewhat higher than average value of P_R in ammonium form of the resin.

4. The equilibrium uptake of quinine and quinidine on sulfonic acid cation exchange resins in aqueous methanol and ethanol has been studied.

With increase in X, the value of P_R decreases. The values of P_R, for resin X8, in aqueous methanol and ethanol do not appear to be much different. However in aqueous methanol, the value of P_R is somewhat higher for quinine than that of quinidine. As the percent methanol content of the solvent medium is increased from 0 to 40% , the equilibrium uptake of quinine increases ; but in 100% methanol, the equilibrium uptake is less than that in water.

For the resin IR-200, the value of equilibrium uptake is almost same for 0% and 100% methanol ; but it is higher in 10 to 40% aqueous methanol. For quinidine also, the values of P_R in 40% and 60% aqueous methanol are greater than those for 0% methanol i.e. quinidine sulfate in water (pH $\backsim$ 7).

5. A study of the rates of exchange of quinine sulfate in aqueous solution with the resin Dowex 50W X4 has been carried out. The study includes the effect of the concentration of external solution, temperature and the particle size of the resin.

It was observed that the value of k (second order rate constant) obtained was practically independent of the

value of initial concentration of quinine sulfate solution. Also it is inversely proportional to the average particle diameter, 'a', of the resin. The results of this study, together with those of earlier work, indicate that rates of exchange of four cinchona alkaloid (quinine, quinidine, cinchonine and cinchonidine) sulfates are almost same within about 5% for resin X^4. Also the value of apparent energy of activation is almost same for resins of degree of crosslinking 1 to 4, and is 3.06 K-cals. .

6. A column study of exchange behaviour of quinine sulfate with resin X^4 was carried out. The variables studied include flow rate, particle size of the resin, ionic form of the resin and solvent medium.

7. Cinchona bark was analysed and digested with N/100 sulfuric acid with constant stirring ; filtered and passed through a resin (X^4 or IR-200)-column in ammonium form. The effluent was collected and reused as solvent after adjusting its pH to its original value. This was continued till the resin column was saturated or all the alkaloid material from the bark used, was taken up. The column was then washed with distilled water, backwashed and 50% aqueous ethanol (50 cc.) was passed. Then the alkaloids were eluted with N/10 ammonical ethyl alcohol. The effluent was concentrated by distillation, evaporated to dryness on a water bath, dried at 100°C and weighed. The percentage of major alkaloids present was estimated by the conventional methods aided by ultraviolet absorption. The procedure was repeated with N/10 sulfuric acid and also

for hydrochloric acid of concentrations N/10 and N/100.

The uptake of alkaloids from cinchona febrifuge and totaquina was studied similarly.

The maximum amount of alkaloid material obtained for 100 meq. of the resin was 15 gm for resin Dowex 50W X4 and 8 gm for resin Amberlite-200.

Publications :

1. Studies with ion exchange resins on cinchona alkaloids III : Exchange rates ; J.Pharm.Sci., 58, 1550 (1969).
2. Ion exchange resins on cinchona alkaloids IV : Effect of resin particle size on equilibrium exchange and column studies ; J.Pharm.Sci., 60, 319 (1971).