THE DISSOLUTION OF HYDROPHOBIC DRUGS IN MEDIA CONTAINING HYDROPHILIC POLYMERS

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The dissolution from suspensions of drug particles in media containing hydrophilic polymers will depend on both the properties of the adsorbed polymer film at the particle-media interface and the bulk viscosity of the dissolution media. Florence and others (1973) showed that for the dissolution of simple electrolytes into hydrophilic polymers, it was possible to relate the dissolution rate constant, k, to an 'effective' viscosity and that the relationship was independent of the chemical structure of the polymer.

The drugs selected for this study are nystatin and sulphadimidine in order to examine the effect of a) film thickness on particle dissolution rate b) polymer fractions on the equilibrium solubility and c) the viscosity of the dissolution media on k.

The dissolution of nystatin particles of surface area 17.8 m^2g^{-1} in 0.1g dl^{-1} of polyvinylpyrrolidone (PVP) solutions was determined in a stirred beaker at 37°. The dissolution rate was reduced as the molecular mass of PVP increased from 10,000 to 44,000; any further increase had no effect on the rate. These results are related to PVP adsorbed film thicknesses as determined by hydrodynamic volume changes. The increase in the relative viscosity of the media (η_r) was negligible, hence the observed differences in the dissolution rate result principally from changes in the film properties. At 0.1g dl^{-1}, saturation of the adsorption sites occurs and hence the polymer segment density is independent of the polymer fraction. The only variable factor will be the film thickness, which will control the diffusion path length for drug molecules from the particle surface to the dissoluting media.

Equilibrium solubilities of nystatin at 37° were measured in PVP concentrations over the range 0.1 to 0.5g dl^{-1}. Increased solubility was observed for all fractions, although greater effects were obtained with the lower molecular mass fractions. This may be due to increasing excluded volume effects with increasing PVP molecular mass.

Bulk viscosity effects were assessed by employing compressed discs of sulphadimidine and measuring dissolution rates according to the method of Florence and others (1973). A sampling procedure was employed and the drug assayed at 260nm. When k was plotted as a function of η_r, a different curvilinear relationship was obtained for the five PVP fractions compared with the three fractions of sodium carboxymethyl-cellulose (SCMC). Data obtained for different concentrations of the same polymer were coincident with the original curves. Furthermore, the addition of electrolyte to SCMC which causes coiling of the polymer chain and hence a decrease in η_r, produced data which again fell on the same curves. This would suggest that although changes in the length of the polymer chain, the concentration of the polymer in the media and the conformation of the molecule all result in changes in η_r, the effect on dissolution rate may be predicted from a knowledge of η_r.

Florence, A.T., Elworthy, P.H. & Rahman, A. (1973)
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