THE EFFECT OF POLYVINYLPYRROLIDONES ON THE DISSOLUTION RATE OF PARACETAMOL

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Solid dispersion systems of paracetamol and polyvinylpyrrolidone (PVP) have been prepared and this work reports their characterisation prior to their use as a model system for compression studies.

PVP 17, 30 and 90 of molecular weights 17,000, 40,000 and 700,000 g mol^{-1} respectively, were incorporated with the drug using different techniques. The methods used were mechanical mixing, coprecipitation of the two components by evaporation from ethanol, freeze drying and spray drying from aqueous solutions.

Systems containing different ratios of drug to polymer were prepared. 80/20, 60/40, 40/60 and 20/80 ratios of paracetamol/PVP dispersions prepared by evaporation from ethanol were glassy and difficult to handle. Systems containing higher drug/polymer ratios were, however, crystalline and more suitable for use. As a tablet should contain a dose of paracetamol of 500mg, systems containing a 90/10 ratio of paracetamol to PVP were used. However, X ray diffraction studies of all these products showed that they were eutectic mixtures.

Dissolution rates of these systems were assessed by a rotating disc method at 37°C (Nogami and others, 1966). The release rate of paracetamol was the same for products containing PVP 17 and PVP 30, but significantly less for those containing PVP 90. All were lower than the intrinsic dissolution rate of paracetamol. The reduction in dissolution rate for products containing PVP 17 and PVP 30 (about 6% reduction was found in these studies) would be expected, based on the results of Florence and Rahman (1975). The result for PVP 90 does not conform to the behaviour suggested by these authors that very high molecular weight molecules do not retard the diffusion of drug molecules.

Solubility studies (Table 1) showed a definite increase in paracetamol solubility with increasing PVP concentration, suggesting a complexation of the two components.

Table 1 Dissolution Rate and Saturation Solubilities of Paracetamol.

Solvent	Solubility ($mg\ ml^{-1}$)	Dissolution Rate ($mg\ min^{-1}cm^{-2}$)
Water	18.30	2.77
10% w/v PVP 17	41.59	-
10% w/v PVP 30	41.29	1.64
10% w/v PVP 90	22.45	-
1% w/v PVP 30	23.06	2.41

The dissolution rate from pure paracetamol discs into solutions containing different concentrations of the various polymers decreased with increasing solution viscosity (Table 1) but equiviscous PVP and methylcellulose solutions gave the same dissolution rate.

The viscosity of the PVP in the diffusion layer is therefore thought to be the major factor influencing the dissolution rate of paracetamol from these dispersion systems. because methyl cellulose does not complex with paracetamol. This case can also be supported by the calculated diffusion layer concentration of about 1% PVP (Collett and Kesteven 1978) which would not give a substantial rise in solubility. However, the effect of solubility appears to be present, because the dissolution rate of paracetamol from systems containing PVP 17 and PVP 30, are the same, although the viscosity of equiconcentration systems is different (PVP 30 > PVP 17).

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