PHYSICAL PROPERTIES OF BETAMETHASONE ALCOHOL-POLYETHYLENE GLYCOL 6000 SOLID DISPERSIONS

B.J. Hargreaves, J.T. Pearson and P. Connor*, School of Pharmacy, Sunderland Polytechnic, Sunderland SR1 3SD and *Glaxo Group Research Ltd., Greenford, Middlesex UB6 0HE.

Following an initial report by Sekiguchi & Obi (1961) concerning the enhanced dissolution and bioavailability achieved by using a solid dispersion of a sparingly soluble drug in a highly water soluble carrier, there has been a great deal of interest in this area (see Chiou & Riegelman, 1971 and Hajratwala, 1974). The present study forms an attempt to apply the above principle to substances of widely disparate melting point, namely, betamethasone alcohol, BMA, (solubility 88 $\mu g\ ml^{-1}$ at 25°, m.pt. 246°) and polyethylene glycol 6000, PEG, (m.pt. 61-64°). Before proceeding to *in vitro* drug release studies, it was considered essential to investigate the physical properties of BMA-PEG dispersions across the entire composition range in order to construct a complete temperature-composition phase diagram.

A series of BMA-PEG fusion formed solid dispersions were prepared under carefully controlled conditions in an inert atmosphere and subjected to hot stage polarised light microscopy and differential thermal analysis. The various phases encountered were further characterised using X-ray powder diffraction and infrared spectroscopy. In summary, it was found that preparations containing up to 3% w/w BMA exist as molecular dispersions; from 4 to 30% w/w BMA, crystallites of drug are dispersed in the PEG matrix in a situation analogous to that observed in a typical eutectic system. Above 30% w/w BMA, X-ray evidence indicates that the steroid becomes progressively amorphous up to 70% w/w; detailed examination of the melting behaviour of samples in this composition range reveals the presence of drug spherulites in the isotropic melt. Above 70% w/w BMA a transition occurs to a homogeneous glassy state. Dissolution profiles for the dispersions were obtained using a continuous flow stirring paddle apparatus similar to that described by Poole (1969) operating at 37° under sink conditions. A summary of the results obtained is presented in Table 1.

Table 1. %BMA released from BMA-PEG solid dispersions (size fraction 90-180 μm)

%w/w BMA in solid dispersion	3	20	40	60	80	micronised BMA
%BMA released after 5 min	97	89	45	37	23	7
15 min	100	98	62	59	39	17

The two extremes of the system are (a) the molecular dispersion which exhibits the most rapid drug release and (b) the glassy state, which is still capable of releasing drug at a rate superior to that observed for micronised BMA alone. In general, it is apparent that the drug release is dependent upon the position of the solid dispersion on the phase diagram, affording a potentially useful means of controlling steroid release from preparations of this type.

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