26P

PHYSICAL STRUCTURE OF DRUG DISPERSIONS IN PVP DETERMINED BY LOW FREQUENCY DIELECTRIC SPECTROSCOPY AND X-RAY POWDER DIFFRACTION

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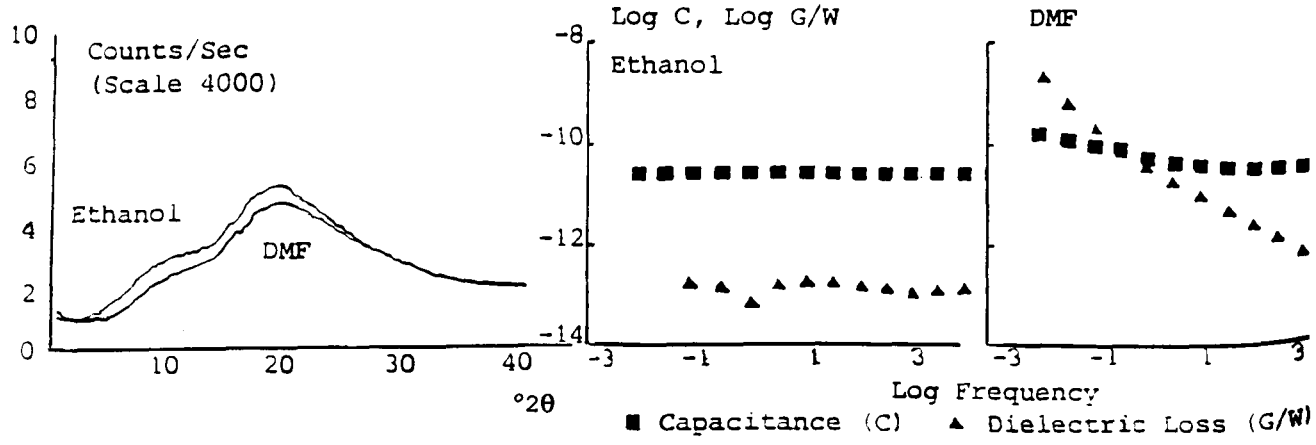
It has frequently been reported that the dissolution rates of poorly water soluble drugs may be enhanced by dispersion within polyvinylpyrrolidone (PVP), and that such dispersions are amorphous (Chiou and Riegelman, 1971). This study concerns the analysis of dispersions containing a poorly water soluble (<0.0001mg/ml), poorly bioavailable benzodiazepine derivate, using X-ray powder diffraction and low frequency dielectric spectroscopy. The latter technique has been successfully applied to the study of polyethylene glycol solid dispersions (Chatham, 1985, Craig, 1989) and therefore may be of relevance to PVP systems. Ten%^{w}/w dispersions were prepared by dissolving 150mg of drug and 1.35g of PVP 40 (Sigma) in 50ml of either ethanol or dimethylformamide (DMF). The solvent was evaporated in a rotary vacuum at 40°C, followed by storage at 60°C in a vacuum oven for 20 hours. 120mg samples of the residue were then compacted at 1.5kN into 10mm diameter discs. Pure PVP control samples were prepared in an identical manner. Low frequency dielectric spectroscopy studies were conducted as previously described (Barker et al, 1989). The results were analysed in terms of the capacitance (C) and the dielectric loss (G/w), indicating the energy stored and lost respectively. X-ray diffraction studies indicated that pure PVP and PVP/drug dispersion samples were all amorphous as shown in Figure 1. The dielectric spectra for the two drug dispersions are shown in Figure 2. The pure PVP samples showed similar differences in dielectric spectra when using the two manufacturing techniques. The corresponding X-ray diffraction spectra for the dispersions are essentially identical.

Figure 1. X-ray Diffraction.

Figure 2. Dielectric Response.



The dielectric spectra show considerably greater differences between the two samples than the X-ray diffraction spectra. These differences may be due to changes in orientation of the drug and carrier or possibly due to the formation of different solvates. In either case, the studies indicate firstly that the structure of the dispersions may be affected by the solvent used in the manufacturing process, and secondly that dielectric spectroscopy is sufficiently sensitive to detect these changes.

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