INHIBITION OF CRYSTAL GROWTH IN GELS BY β-CYCLODEXTRIN

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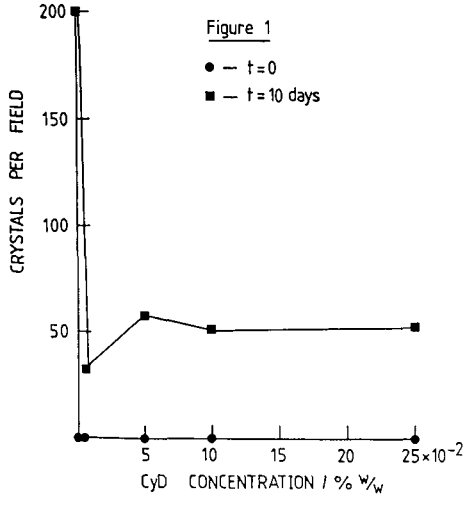
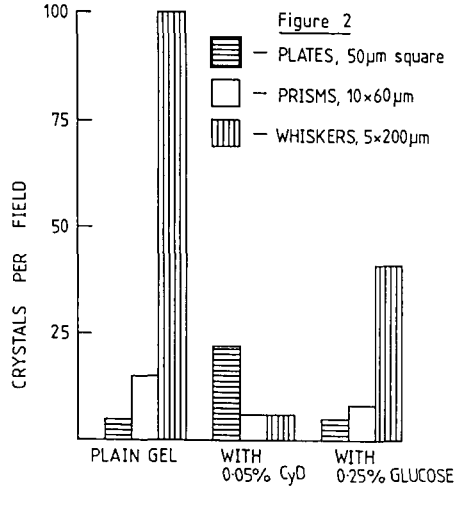
Although drugs of low solubility for topical application may precipitate in aqueous vehicles as a result of poor selection of solvent medium (Ziegenmeyer, 1982), there have been few systematic studies of crystal growth in pharmaceutical semi-solids. We report the effects of beta-cyclodextrin (CyD), a cyclic oligosaccharide usually associated with the solubilization of drugs, on the crystal growth of the poorly soluble antifungal miconazole (MCZ) in an aqueous gel.

A ternary gel of cetrimide, cetostearyl alcohol and water (0·17 : 1·54 : 18·3) was selected as a model; 1% w/w MCZ was incorporated as a solution in molten cetostearyl alcohol, and CyD dissolved in the aqueous cetrimide phase. The formulations were examined under a polarizing microscope and with a Ferranti-Shirley viscometer, immediately after preparation and over a 10 day period of storage under ambient conditions.

Whereas in plain gels acicular crystals of MCZ were observed in relatively large numbers within 24 hours of preparation, systems containing CyD had only a few crystals even after 10 days (Fig. 1). Clearly the addition of CyD had stabilised the formulation. The effect was not due to changes in gel structure, since the rheological characteristics of formulations with and without CyD were similar. Neither was it likely to be due to complexation, since the effect was apparently independent of CyD concentration (Fig. 1). It was apparent, therefore, that CyD stabilised gels by acting as a crystal poison and inhibiting the growth of MCZ; the case for this was supported not only by the few crystals present being large and well-formed, a characteristic of controlled crystallization, but also by the similar results obtained with gels containing glucose (Fig. 2). CyD has the ability to inhibit crystal growth in supersaturated semi-solid systems and thereby stabilise them, a property not previously realised.





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Ziegenmeyer, J. (1982) in "Dermal and Transdermal Absorption" eds. Brandau, R. & Lippold, B.H., Wissenschaftliche Verlagsgesellschaft, Stuttgart, pp 73-89.