THE INFLUENCE OF β-CYCLODEXTRIN ON THE RELEASE OF HYDROCORTISONE FROM A TOPICAL CREAM BASE

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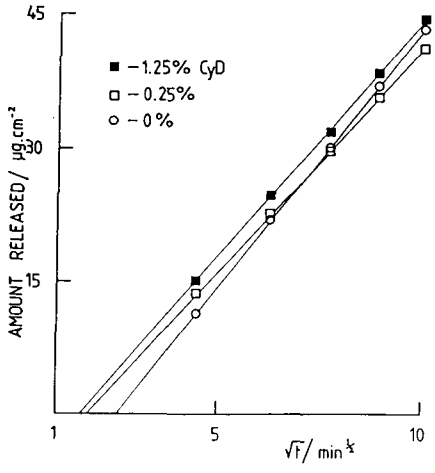
It has been shown [Otagiri, 1984] that in vitro release of steroid from hydrophilic bases can be significantly improved if the drug is incorporated as its solid cyclodextrin inclusion complex. Enhanced dissolution rate of complex over drug has been suggested as the mechanism of this effect. It remains unclear, however, how beta cyclodextrin (CyD) included as a component in the aqueous phase of a cream base will influence release of active ingredient which is incorporated separately, and not as a pre-formed complex. We have investigated this using hydrocortisone, a compound whose aqueous solubility is substantially increased in the presence of CyD [Frank, 1983].

Cetomacrogol cream B.P., without preservative, was prepared by mixing molten cetomacrogol emulsifying ointment with warm aqueous solutions of CyD. Concentrations of CyD ranged from 0.25 - 1.25% w/w, calculated on the basis of total water content. The creams were allowed to stand for 24 hours and sufficient hydrocortisone was then incorporated to give a concentration of 0.5% w/w. Drug release into 100 ml distilled water at 30°C was examined using the method of Takamura et al (1984). Hydrocortisone was assayed spectrophotometrically at 248nm. Microscopic structure of the creams was assessed on preparation and on 4 days standing using a Polyvar microscope (Reichert-Jung, Austria). Slides were prepared of both the intact and diluted (distilled water) creams. Cover slips were sealed in position on the slide with varnish.

The release profiles of hydrocortisone from cream containing 0, 0.25 and 1.25% CyD are shown below. Apparent dissolution rates per unit surface area of cream were similar both in the presence and absence of added CyD, and statistical treatment of the data showed no significant difference in release between the two sets of conditions (p=0.05). Microscopic examination of the creams immediately after preparation showed them to be well structured, with crystalline hydrocortisone dispersed evenly throughout the field. Cream containing 1.25% CyD alone showed no visible signs of alteration to cream structure, or of the presence of crystalline material, after 4 days standing. These results contrast strongly with those observed for release of drug incorporated into the base as a pre-formed solid inclusion complex [Otagiri, 1984]. Concentrations of CyD which produce large changes in aqueous solubility of hydrocortisone resulted in neither enhancement nor retardation of in vitro release from cetomacrogol cream. It is suggested that the increase in amorphous nature shown by the solid complex is the factor that confers the increase in drug release [Morita et al, 1985] rather than simple addition of CyD as an adjuvant in topical formulations.



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