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GELUCIRE BASES AS SEMI-SOLID MATRICES FOR DELIVERY OF METOCLOPRAMIDE

Reed, C.M., Rogerson, A., Jolliffe, I.G., Reckitt & Colman Pharmaceuticals, Dansom Lane, Hull, UK, HU8 7DS.

The buccal route of administration can, in many circumstances, offer many advantages over the oral route, particularly if acid degradation or first-pass metabolism compromise drug bioavailability. In addition drugs such as the antiemetic metoclopramide could benefit from buccal administration as swallowing of tablets could be avoided (a distinct advantage during bouts of nausea). However one of the major drawbacks of the buccal route is the relatively small surface area of the buccal mucosa. Thus incorporation of drug into semi-solid matrices has been investigated (Jones et al 1986). This current work describes the use of Gelucire bases, which display a range of melting point and HLB values, as potential sustained-release delivery systems and assesses the influence of propylene glycol (PG) on the rate of drug diffusion, with the ultimate aim of reducing the size of the dosage form.

Previous work in this laboratory had indicated that the melting point of the base had a greater influence on the rate of drug release than its HLB value (unpublished). Consequently G44/14 and G37/02 (these numbers representing their melting point and HLB values) were melted, 3.3mg of metoclopramide incorporated, then cooled and stored overnight.

The stratum corneum is recognised as being the rate-limiting barrier to transdermal drug absorption. Following removal of the stratum corneum, the remaining dermis displays excellent correlation with excised buccal mucosa, in terms of its permeability to water and various drugs (Galey et al 1976). The diffusion of metoclopramide from various Gelucire bases was determined across dekeratinised hairless mouse skin using a glass diffusion cell with pH 7.4 buffer maintained at 37°C. Incorporation of PG (1% w/v) during mixing was responsible for a marked increase in drug diffusion (flux increased from 0.07mgcm^{-2}hr^{-1} to 0.13mgcm^{-2}hr^{-1}) such that some 70% of a 3.3mg dose was absorbed in 6 hours (fig 1). This was effected without an accompanying increase in drug dissolution rate, suggesting that the two-fold enhancement in penetration may be a consequence of direct PG action on the tissue.

Thus the use of PG in semi-solid dosage forms of this nature may be able to safely enhance absorption, thus allowing sustained release of drug, and formulation of dosage forms of acceptable size, to be possible simultaneously.

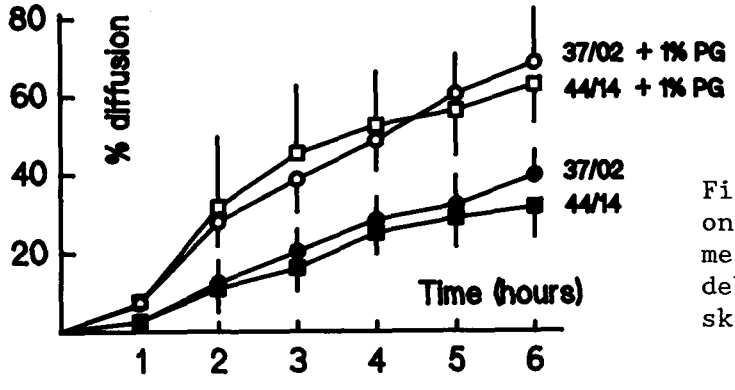

Fig 1 : The influence of 1% PG on the diffusion of metoclopramide across dekeratinised hairless mouse skin.

Jones E. et al, (1986) European Patent Application, 215635
Galey, W.R. et al (1976) J.Invest.Dermatol. 67: 713-717