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ENHANCED PENETRATION OF PROSTAGLANDIN E2 THROUGH HUMAN SKIN IN-VITRO

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The percutaneous penetration of PGE_2 has been studied in-vitro using dermatomed human skin mounted in diffusion cells of the Franz type. The experimental protocol was based on that of Wotton et al, (1985) and receptor phase samples analysed for prostaglandin by HPLC (Herman et al, 1987).
The ability of Azone, a novel penetration enhancer, to promote the percutaneous delivery of metronidazole has been shown to increase when it is used in conjunction with propylene glycol (Wotton et al, 1985). The mechanism by which Azone enhances is thought to involve an increase in skin lipid disorder due to the presence of the molecule in the bilayers. The diol may act as a solvent for the drug, thus increasing its concentration in the skin and enhancing its flux accordingly . The effects of these two mechanisms on the penetration of PGE_2 have been studied using Azone and Transcutol, a diether alcohol. The differing mechanisms of enhancement were also investigated by examining the effect that these two compounds have on the phase transition temperature of DPPC liposomes (a qualitative measurement of lipid order).
The unenhanced penetration of E_2 was found to be very slow but pre-treatment of the skin surface with the penetration enhancers Azone and Transcutol was found, in both cases, to facilitate improved drug flux (Transcutol producing the greater effect). These results are shown graphically in Figs 1 and 2. Azone is known to reduce the phase transition temperature of liposomes (Beastall et al, 1988) and this effect was confirmed here. The change in the phase transition temperature of DPPC liposomes in the presence of Transcutol was found to be negligible.

Figure 1

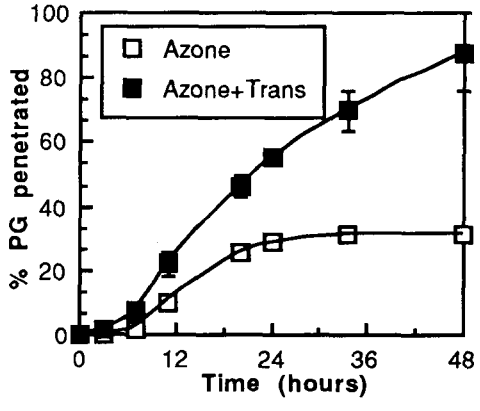
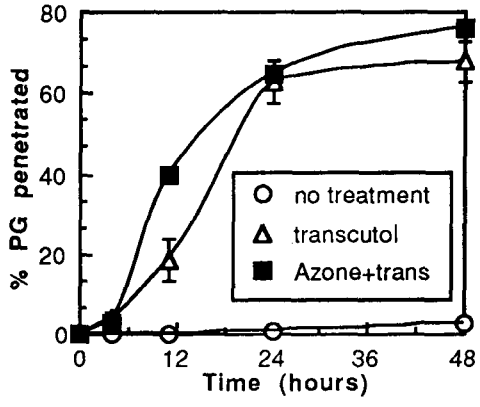


Figure 2



These results seem to indicate that there are two distinct mechanisms by which the enhancement of percutaneous absorption may be achieved. Firstly, by increasing the drug mobility in the lipid regions and secondly by raising its solubility within those regions.

Beastall J.C., Hadgraft J., and Washington C. (1988) Int. J. Pharm. 43: 207-213.
Herman, C.A., Hamberg, M., and Granstrom, E. (1987) J. Chrom. 394: 351-362.
Wotton, P., Møllgard, B., Hadgraft J. and Høelgaard, A. (1985) Int. J. Pharm. 24: 19-26.