EFFECTIVENESS OF SKIN PENETRATION ENHANCERS PROPYLENE GLYCOL, AZONE, DECYLMETHYLSULPHOXIDE AND OLEIC ACID WITH MODEL POLAR (MANNITOL) AND NONPOLAR (HYDROCORTISONE) PENETRANTS

S.L. Bennett* and B.W. Barry, Postgraduate School of Studies in Pharmacy, University of Bradford, Bradford, West Yorkshire, BD7 1DP, U.K.
*Present address: Glaxo Group Research Ltd., Greenford, Middlesex, UB6 OHE, U.K.

The vehicle used to apply a drug to the skin can significantly affect the percutaneous absorption of the medicament. Recently much interest has centered on penetration enhancers - compounds which promote the passage of a drug through skin. Our aim was to investigate the effect of four penetration enhancers on the permeation of polar and nonpolar materials. Thus mannitol a highly polar compound (octanol/water partition coefficient log K = -2.47) and hydrocortisone a fairly nonpolar material (log K = 1.61) were chosen as model penetrants. The penetration enhancers selected - propylene glycol (PG), Azone (A), decylmethylsulfoxide (DCMS) and oleic acid (OA) - have been shown to promote the penetration of selected compounds (Stoughton & McClure, 1983; Cooper, 1980; Cooper, 1984).

An 'in vivo mimic' experiment with an automated diffusion apparatus (Akhter et al, 1984) was used. After full-thickness human skin from autopsy had been prepared, partially hydrated, and mounted in diffusion cells, the cells were left for 3 days for the skin to reach hydration equilibrium at 22 ± 1°C, 60 ± 5% R.H. A film of radioactive test penetrant was then deposited from a 30 µl acetone solution containing 500 µg of the material; permeation was monitored by scintillation counting for 60 h. Then 20 µl acetone (control), 10 µl PG or 10 µl PG containing another penetration enhancer were each applied to 3 cells and permeation was again monitored.

The results (Table 1) are summarised as ratios of the amount and flux of penetrant related to values for the control (acetone). PG alone had little effect on mannitol permeation but increased hydrocortisone penetration. Mannitol data indicate that all 3 enhancers in combination with PG produced large effects. PG+A and PG+DCMS dramatically increased mannitol permeation whereas promotion due to PG+OA was somewhat lower. Hydrocortisone data showed smaller increases with PG+DCMS producing less enhancement than PG alone. PG+A and PG+OA which had an enhancement effect although a proportion of this was due to the PG.

Table 1. Effects of potential penetration enhancers on skin permeation, expressed as ratios of control treatment with acetone.

Treatment	Mannitol		Hydrocortisone	
	(i)	(ii)	(i)	(ii)
PG	1.3 ± 0.89[a]	0.77 ± 0.37	29 ± 11	51 ± 15
PG + 2% A	450 ± 280	970 ± 640	53 ± 21	200 ± 80
PG + 15% DCMS	260 ± 210	640 ± 580	8.6 ± 4.1	16 ± 5.4
PG + 5% OA	81 ± 52	83 ± 72	61 ± 24	240 ± 96

(i) Ratio = $\frac{\text{total drug penetrated in 60 h after treatment}}{\text{total drug penetrated in 60 h after deposition from acetone}}$

(ii) Ratio = $\frac{\text{maximum flux after treatment}}{\text{maximum flux after acetone control}}$

[a]Mean ratio ± standard error of mean

The table shows that enhancement effects are more prominant with mannitol than with hydrocortisone. This is partly because mannitol has a very low partition coefficient and a high hydrogen binding capability and thus penetrates skin very poorly; these factors permit penetration enhancers to show dramatic responses.

In summary, PG+A, PG+DCMS and to a lesser extent PG+OA, increased the permeation of the polar compound and PG, PG+A and PG+OA increased the penetration of the nonpolar compound.

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