HYDRATION AND SURFACTANT EFFECTS ON METHYL NICOTINATE PENETRATION THROUGH HAIRLESS MOUSE SKIN

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The characteristics of nonionic surfactants which determine their skin penetration enhancement properties have been reasonably well established (Walters and Olejnik, 1983). The evidence suggests that surfactants containing a lauryl chain linked to an ethylene oxide chain of E10-14 are the most effective enhancers particularly with ionic permeants (Walters et al, 1984). In order to assess the reversibility of the surfactant effect and the influence of hydration, the penetration of methyl nicotinate across saline and surfactant pre-treated hairless mouse skin has been determined.

Excised abdominal skin was placed as a barrier between the two halves of a diffusion cell. The skin was then exposed to either saline or 0.5% (w/v) polyoxyethylene (10) lauryl ether (Brij 36T) for a pre-set time period followed by six rinses in saline (5 minutes per rinse). The donor chamber was then charged with 0.5% (w/v) methyl nicotinate in either saline or 0.5% Brij 36T. Samples were taken from the receptor chamber (which contained saline at all times) at intervals, for up to 7 hours, and analysed spectrophotometrically for methyl nicotinate. In all cases, following an initial lag phase, linear accumulation of methyl nicotinate in the receptor chamber occurred with time. Surfactant and hydration mediated effects on permeation are shown in Table 1.

Hydration Period (hrs)	Hydration Medium	Vehicle and Permeation Data			
		Saline		0.5% Brij 36T	
		Permeability Coefficient ($cmhr^{-1}$)$\times 10^2 \pm$SD	Lag Time (mins)$\pm$SD	Permeability Coefficient ($cmhr^{-1}$)$\times 10^2 \pm$SD	Lag Time (mins)$\pm$SD
0	-	2.79 $\pm$ 0.34	22 $\pm$ 7	5.61 $\pm$ 0.55	34 $\pm$ 9
1	Saline	2.55 $\pm$ 0.50	2 $\pm$ 0	-	-
1	0.5% Brij 36T	2.29 $\pm$ 0.31	8 $\pm$ 3	4.42 $\pm$ 0.68	20 $\pm$ 1
17	Saline	3.80 $\pm$ 0.06	6 $\pm$ 1	4.69 $\pm$ 0.08	44 $\pm$ 6
17	0.5% Brij 36T	4.24 $\pm$ 0.59	12 $\pm$ 2	5.36 $\pm$ 1.11	27 $\pm$ 4

Table 1: Hydration and vehicle mediated effects on penetration.

In the absence of surfactant, hydration of the skin barrier for 17 hours results in a slight, but significant ($P<0.001$) increase in methyl nicotinate permeation from saline, coupled with a marked decrease in lag time suggesting increased diffusivity of the permeant within the hydrated tissue. No alteration of surfactant induced permeation enhancement is evident for the hydrated tissue. The effects of the surfactant are reversible following short pretreatment times but appear to be sustained after longer periods of exposure. Whether this is simply the result of tissue hydration is as yet unclear. The data, however suggest that the mechanisms underlying the surfactant and hydration effects may be similar.

Walters K.A. and Olejnik O. (1983) J. Pharm. Pharmacol. 35:81P.
Walters K.A., Olejnik O. and Harris S. (1984) J. Pharm. Pharmacol. 36:78P.