# LONG TERM HYDRATION EFFECTS ON PERMEABILITY OF HAIRLESS MOUSE SKIN

J.R. Bond and B.W. Barry, Postgraduate School of Studies in Pharmacy, University of Bradford, Bradford, West Yorkshire, BD7 1DP, U.K.

As a model for human skin, hairless mouse skin has been much used over the past 10 years, due in part to restricted availability of human skin. Several workers (Durrheim et al 1980, Stoughton 1975) have demonstrated similarities in permeabilities of the two skin types, for various compounds. More recently, interest in long-term (7 days or more) percutaneous drug delivery systems has developed.

This study aimed to characterise the effects of prolonged hydration upon the permeability of hairless mouse skin, as would be induced by such devices. Freshly excised, full-thickness hairless mouse skin was mounted into the diffusion cells of an automated diffusion apparatus (Akhter et al 1984). The steady state permeability of the skin to the model compounds water (polar) and hexanol (nonpolar) at 31 ± 1°C was then measured, constantly over the first 48h of hydration and then by a daily diffusion run on days 3 to 10. By utilising a dual label technique, the penetration of $^3H$ water and $^{14}C$ hexanol could be monitored simultaneously.

Figure 1 shows that over the first 2 days of hydration, permeability changes little. Between 2 and 4 days, larger increases occur, more pronounced for water than for hexanol. From 4 days onwards, a dramatic increase in permeability is seen for both permeants.

These marked increases are too great to be due just to hydration of the stratum corneum. It was thought that the stratum corneum barrier was actually disrupted and removed by 8 days of hydration. To test this concept, permeabilities were measured after either tape stripping 30 times, or 8 days of hydration. Table 1 shows that hydration for 8 days does in fact have a similar effect to mechanical removal of the stratum corneum.

In conclusion, therefore, we suggest that hairless mouse skin may not be the model of choice for testing percutaneous absorption where long-term hydration occurs.

Fig. 1. Permeability coefficients of hairless mouse skin to water and hexanol, after increasing time of hydration.

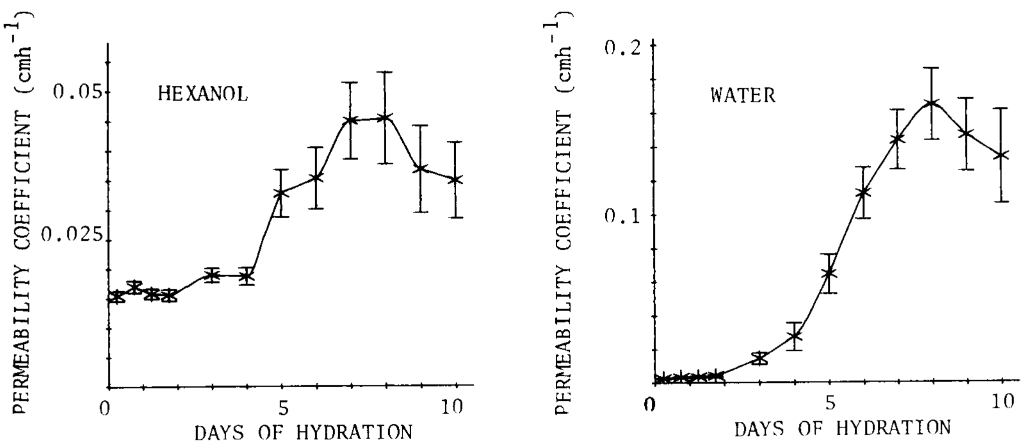


Table 1. Permeability coefficients (x $10^3$ cmh$^{-1}$) of tape-stripped and 8-day hydrated hairless mouse skin to water and hexanol. Figures in parentheses are standard error of mean.

| | Water | Hexanol |
|---|---|---|
| Hydrated skin (n=6) | 124 (24) | 48.6 (9.3) |
| Stripped skin (n=5) | 111 (14) | 35.4 (2.1) |

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Durrheim, H., Flynn, G.L., Higuchi, W.I., Behl, C.R. (1980) J. Pharm. Sci. 69, 781-786.
Stoughton, R.B. (1975) in "Animal Models of Dermatology" Maibach, H. (Ed.) Churchill Livingstone, New York, 121-132.