BENZYL ALCOHOL VAPOUR DIFFUSION THROUGH HUMAN SKIN : DEPENDENCE ON THERMODYNAMIC ACTIVITY IN THE VEHICLE

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Development of new drugs and formulations for topical use often requires multiple, lengthy diffusion experiments with limited supplies of human skin. Here we try to relate a readily measured, physical characteristic of the drug in its vehicle to percutaneous absorption, with the eventual prospect of optimising rates withoutdoing any diffusion experiments.

Factors affecting the passive diffusion of molecules through the skin are combined in Fick's Law, $J=KmD\Delta C/h=kp\Delta C$, where J is the steady state flux: partition coefficient (Km), diffusion coefficient (D) and membrane thickness (h) give the permeability constant (kp); ΔC is the change in penetrant concentration across the barrier. Higuchi (1960) postulates that the concentration term should be replaced by thermodynamic activity for non-ideal penetrant-vehicle mixtures; we tested this with the model compound, benzyl alcohol.

Headspace gas chromatography was used to find the benzyl alcohol vapour concentration at equilibrium for 0.5 mole fraction binary mixtures with model solvents; isopropyl myristate (A), toluene (B), isophorone (C), propylene carbonate (D), butan-1-ol (E) and butyl acetate (F). The activity (a) of these mixtures was found from peak heights by comparison with those for neat benzyl alcohol vapour (taken as a = 1).

Benzyl alcohol vapour flux from the same mixtures was measured through dermatomed, human abdominal skin (≃0.4mm, 4 replicates) using diffusion cells at $30^{o}C$, (Fig. 1). Receptors contained 50% v/v aqueous ethanol, maintained at<10% penetrant saturation and samples were analysed by GC.

Fig. 2 shows that steady state vapour flux increases linearly with the activity found by headspace analysis. In conclusion, for such non-ideal mixtures, where the vehicle is presumed to have no effect on the skin's barrier function, the rate of percutaneous absorption from a vapour is proportional to thermodynamic activity, as determined by headspace analysis.

Fig. 1

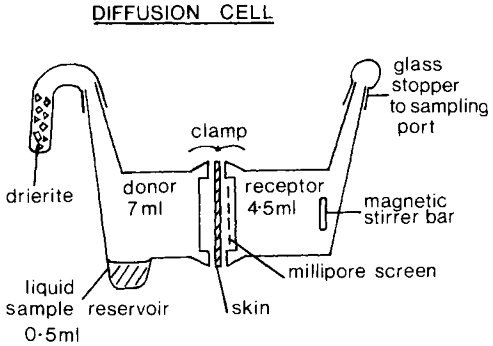

Fig. 2

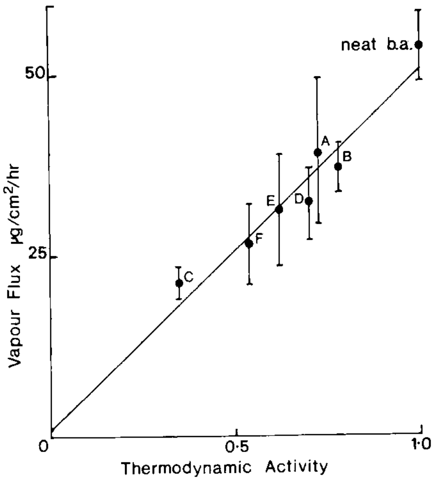

Fig.2 Vapour flux of benzyl alcohol through human epidermis from 0.5 mole fraction binary mixtures with several vehicles, versus their benzyl alcohol activity. The regression correlation coefficient is 0.967, the mean of 4 cells is shown, ± the standard deviation.

Higuchi, T. (1960). J.Soc. Cosmet. Chem. 11: 85 - 97

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