IS 2-PYRROLIDONE A PENETRATION ACCELERANT IN HUMAN SKIN? PARTITION COEFFICIENT AND STEADY STATE FLUX MEASUREMENTS WITH N-ALKANOLS

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Many papers report accelerant effects in percutaneous absorption but few investigate their mechanism of action (Allenby et al 1969). We are studying the accelerant 2-Pyrrolidone (2-P). Partition coefficients (Km) were measured radioactively at 30°C for a model series of primary alcohols into trypsinised, abdominal stratum corneum from 0 to 80% w/w 2-P in water. s.c.* absorbs 1-4 times its weight of the vehicle and at least two separate partition coefficients operate:-

alcohol in free vehicle $\rightleftharpoons$ (Km) alcohol in absorbed vehicle

Km bound

alcohol bound to s.c. matrix

Km can be expressed per unit dry or wet weight of s.c. but combines the two partition coefficients. In theory lipophilic alcohols should partition well into s.c. from polar solvents, and have a high Km bound. Thus Fig. 1 shows that in water Km bound is high for octanol but falls becoming negative as carbon number decreases.

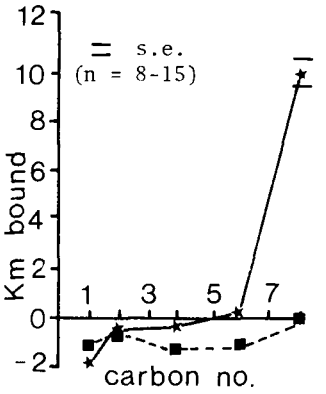

Fig.1 - Km bound vs carbon no. ● in H_2O ■ in 60% w/w 2-P/H_2O.

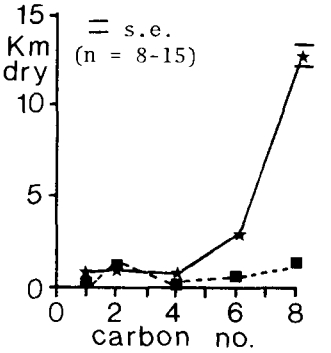

Fig.2 - Km dry vs carbon no. * in H_2O ■ in 60% w/w 2-P/H_2O.

Negative values for polar alcohols suggest that the calculation method overestimates the alcohol in the absorbed vehicle. The absorbed vehicle could be a poorer solvent for polar molecules than the free vehicle possibly because it dissolves fatty material from the s.c. Different % w/w concentrations of 2-P in water behave similarly; typical data for 60% w/w 2-P are in Figs. 1 and 2. There is little difference in Km bound between alcohols. The absorbed vehicle must be a better solvent for octanol than s.c. Fig. 2 shows that Km dry from water increases with alcohol carbon number. 2-P provides a constant value near unity indicating partitioning between like phases such as from vehicle to absorbed vehicle. Only for octanol does it remain significantly higher, 2 ($P=0.1$) due to the higher Km bound contribution. Preliminary studies in steady state diffusion showed that 2-P reduced the flux of octanol (4-21 times) and had little effect or marginally increased methanol flux (1.5 times). We conclude that 2-P is not a penetration accelerant for alcohols (C_1-C_8) at least as judged by its effect on partition coefficient and idealised steady state flux, using the same solvent in donor and receptor compartments.

*s.c. = stratum corneum

Allenby et al (1969) Br. J. Derm. 81 : Suppl. 4 47-55