

IN-VITRO COMPARISONS OF THE PERMEABILITY PROPERTIES OF HUMAN AND HAIRLESS MOUSE SKIN

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Drugs and other chemicals are routinely applied to the skin of laboratory animals in order to assess dermal toxicity and product efficacy. However when interpreting the results an assumption is made that laboratory animal and human skin penetration is similar. As yet there is no one species whose cutaneous diffusion barrier, to a range of permeants, has been shown to be identical to that of man. The object of this study was to compare the permeability properties of human skin with that of hairless mouse. A range of chemicals were selected with different physico-chemical characteristics and applied to the skin in solution. Experiments were performed *in vitro* using excised whole skin (epidermis and dermis) mounted in glass diffusion cells. With the exception of toluene, all penetrants were radio-labelled. The 'total amount penetrated' was followed as a function of time, and permeability constants (Kp units: $\text{cmhr}^{-1} \times 10^3$) were calculated from the pseudo-steady state linear region of the curve. All experiments were done at 30°C ($\pm 1.0^\circ\text{C}$), and the results are tabulated below (Table 1).

There were statistically significant differences ($p < 0.001$) in the rates of permeation between hairless mouse and human skin, for all the compounds measured. Consequently the results indicate that when attempting to extrapolate to the human situation from animal percutaneous absorption experiments, care must be taken to ensure the proposed 'model' is representative. Rates of penetration between laboratory animal and human skin depend to a large extent on the physico-chemical nature of the permeant and can be extremely variable, eg. of paraquat (>1000 fold difference).

TABLE 1: MEAN VALUES FOR HUMAN AND HAIRLESS MOUSE WHOLE SKIN.

| | WATER | MANNITOL | ETHANOL | TOLUENE | PARAQUAT |
|---------------------------|---------------------------------------|----------------------------|----------------------------|---------------------------|--------------------------------|
| | Kp UNITS $\times 10^3$ cm/hr \pm SD | | | | |
| HUMAN WHOLE SKIN | 0.78 ± 0.39 n=21 | 1.36 ± 0.56 n=11 | 2.07 ± 0.68 n=28 | 0.15 ± 0.04 n=6 | 0.0073 ± 0.0060 n=10 |
| HAIRLESS MOUSE WHOLE SKIN | 2.43 ± 0.77 n=21 | 4.28 ± 0.33 n=9 | 7.47 ± 3.70 n=20 | 1.68 ± 0.14 n=7 | 10.66 ± 4.27 n=10 |