A POTENTIAL MODEL FOR STUDYING ABSORPTION THROUGH ABNORMAL STRATUM CORNEUM

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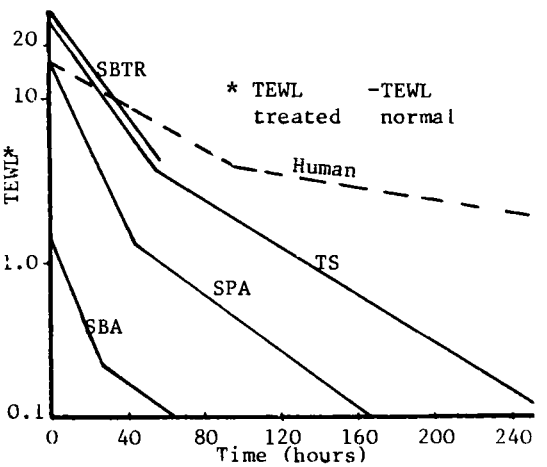
Diffusion across the keratinized stratum corneum (the outermost layer of the epidermis) is generally accepted as the rate limiting step during percutaneous absorption. When the stratum corneum is absent or abnormal, the skin has been shown to be more permeable to water (by measurement, Spruit 1969) and to other molecules (by observation of increased biological responses, Davies et al 1979 and Hallam 1978). Such increased permeability is significant for toxicological assessment and development of topical therapy. A well-characterised model of abnormal skin has been developed to study the permeability of abnormal skin to different classes of chemicals. The water permeability of rat skin has been measured in vivo immediately following mechanical alteration of the epidermis and during regeneration of a diffusion barrier. In these experiments 7-week old rats of Alderley Park (Wistar derived) strain were anaesthetised and four standard methods were used to induce an abnormal epidermis; blunt-edge scalpel blade abrasion (SBA), medium grade sandpaper abrasion (SPA), adhesive-tape stripping (TS) and suction blister-top removal (SBTR). The permeability was assessed by in vivo measurements of transepidermal water loss (TEWL) using a 'Ventilated Chamber' technique: dry nitrogen was passed through a cup lightly held on the skin and the water content of the effluent gas was monitored by a Shaw moisturemeter.

The mean TEWL of normal rat skin was 0.51 mg $cm^{-2}hr^{-1}$ (SEM 0.04, n = 25) similar to that through human skin (c. 0.4 mg $cm^{-2}hr^{-1}$; Spruit 1969, Dugard unpublished results). Each procedure gave a reproducible initial increase in water permeability and pattern of barrier regeneration. The magnitude of the initial increase in permeability was in the order SBTR (corrected for area of lesion) > TS > SPA > SBA. A subsequent rapid decrease in permeability, responsible for the major portion of barrier regeneration, was followed by a more gradual return to a 'normal' rate of water loss. When log (increased TEWL) values were plotted against time the barrier regeneration appeared bi-phasic and a half-time was calculated (Table) for the initial phase of the barrier formation. When human skin was altered by TS (Spruit 1969) a similar bi-phasic regeneration of the permeability properties also occurred (Fig) but the rate of change in permeability ie regeneration of the barrier properties was slower than observed in the rat (Table). This rat model will be used to assess the factors governing absorption through mechanically altered skin. It may be possible to link the permeability of disease-affected human skin and the animal model by non-invasive water loss measurements.

TABLE

Treatment	$t_{\frac{1}{2}}$ (hr)
SBTR	21.0
TS	18.7
SPA	10.3
SBA	9.7
Human TS	c. 40

Spruit, D. (1969) Ph.D. Thesis, Univ. Nijmegen
Davies, M.G. et al (1979), Br. Med. J. 1: 661
Hallams, G. (1978), Acta Derma (Stockholm), 58: 413-419



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