A POTENTIAL MODEL FOR STUDYING ABSORPTION THROUGH ABNORMAL STRATUM CORNEUM

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Following superficial mechanical alteration of rat skin, the water permeability barrier undergoes a bi-phasic regeneration: an initial rapid decrease in permeability (responsible for the major proportion of barrier regeneration) is followed by a more gradual return to normal (Scott and Dugard 1981[a]). Spruit (1969) reported a slower but otherwise similar bi-phasic regeneration in human skin. We proposed (Scott and Dugard 1981[b]) that altered rat skin could form a "model" for studying factors governing absorption through physically modified skin. In vivo measurements of [^{3}H]mannitol absorption have been made to extend the assessment of the properties of the "model".

The model design selected was rat skin altered by 15 applications of adhesive tape and allowed to recover for 0 and 24 hours (first phase of water barrier regeneration) and 96 hours (second phase) before application of test material. Initially, the pattern of excretion of tritium was characterised by urine analysis after i.v. dosing of [^{3}H]mannitol. In skin absorption measurements an aqueous solution of [^{3}H]mannitol was applied under occlusion to the skin and hourly urine samples collected for 24 hours. Adequate urine production was ensured by water-loading the rats by oral dosing of 10% glucose in 0.9% saline. Rats were allowed food and 10% glucose-saline ad libitum and were housed in restraining cages which separated urine and faeces.

The results are presented in the Table. Because tritium is rapidly excreted following i.v. administration of [^{3}H]mannitol, urine analysis is suitable for assessing rates of absorption through skin. [^{3}H]mannitol was slowly absorbed through normal skin and skin damage caused a large increase in absorption rate. In contrast to the epidermal barrier to water loss, no regeneration of a barrier to [^{3}H]mannitol had occurred by 24 hours after damage but by 96 hours a reduction in permeability was apparent.

The "model" has been used to quantify the absorption through altered skin of a range of molecules with different physico-chemical characteristics. Generally, the more slowly a molecule penetrates normal skin the greater is the factor of increase through abnormal skin. The rat skin model will be used to aid toxicological assessments of the hazard of chemicals contacting abnormal skin and to quantify the maximum possible absorption of topical drugs applied to diseased skin.

Tritium accumulation in urine following [^{3}H]mannitol dosing

Skin type	Accumulated applied dose (%) in urine at (time after dosing)			Factor of increase above normal skin	
	3(h)	6(h)	24(h)	3(h)	24(h)
iv	75	76	80	-	-
Normal	0.07	0.14	0.42	-	-
0 h recovery	34	44	52	420	140
24 h recovery	31	40	50	400	130
96 h recovery	0.36	0.79	1.8	4	4

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