ENHANCED ABSORPTION THROUGH CADAVER SKIN OF SODIUM SALICYLATE BY LONG CHAIN ETHOXYLATED AMINES

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The enhanced percutaneous absorption of sodium salicylate by Bis(2-hydroxyethyl)oleylamine has been previously reported (Hadgraft et al, 1985). Related compounds to this amine (Polyoxyethylene(5)oleylamine and oleylamine, Akzo U.K. Ltd.) have been investigated in an attempt to ascertain structural features that may be important influences upon penetration enhancement properties.

In vitro experiments were conducted using full thickness human caucasian abdominal skin obtained at autopsy from the region of the midline excision. Steady state permeation of Salicylate was monitored from a donor compartment containing 1 ml of pH 5 0.01M sodium salicylate. Salicylate appearance in the receptor compartment (pH 7.4 buffer) was monitored using an HPLC technique. Experiments were conducted over a period of at least 92 hours. Skin samples were pretreated with 50 µl of 0.1M ethanolic solutions of the proposed enhancers three hours prior to application of the salicylate dose. Control experiments were conducted in parallel, where skin samples were pretreated with 50 µl of absolute ethanol.

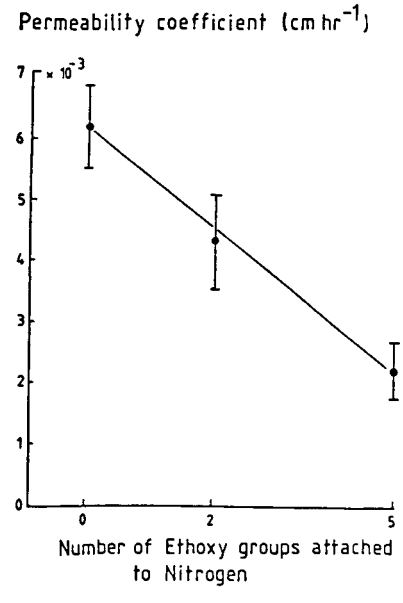

FIG. 1

Steady state permeation profiles were obtained, from which permeability coefficients were calculated. In the control cells, no salicylate permeation was detected. Mean permeability coefficients (± S.E.) plotted as a function of the degree of ethoxylation of the enhancers are shown in Fig. 1.

Increasing the degree of ethoxylation reduces the efficiency of these compounds to act as penetration enhancers. This may be due to the corresponding decrease in lipophilicity caused by addition of polar ethylene oxide groups which may influence their partitioning into the stratum corneum and subsequent interaction with endogenous lipids. It is possible that these compounds may act by interacting with and fluidising the intercellular lipids of the stratum corneum, to increase the percutaneous absorption of salicylate via the intercellular channels.

Hadgraft, J. et al (1985) J. Pharm. Pharmacol. 37: 82P.