FACILITATED PERCUTANEOUS ABSORPTION OF SODIUM SALICYLATE

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The facilitated transport of sodium salicylate across artificial lipid membranes by long chain amines has been previously described (Hadgraft et al. 1984). We have now applied this system to skin membranes using both full thickness human skin in vitro, and an in vivo Rabbit model. Some of the results obtained are reported here, using Ethomeen S12 (Bis(2-hydroxyethyl) oleylamine, Akzo Chemie U.K.Ltd.) as the facilitating molecule.

Full thickness human abdominal skin was used in all glass Franz type diffusion cells. The receptor compartment contained isotonic pH 7.4 phosphate buffer at 37 C. The skin membrane was pretreated with 50ul of 0.1 M (■) or 0.01 M (O) EtS12 dissolved in ethanol. The ethanol evaporated to leave the skin impregnated with EtS12 . The donor compartment contained 1ml of 0.01M sodium salicylate at pH 5 . Salicylate appearance in the receptor phase was monitored using HPLC. The steady state permeation profiles of salicylate are shown in Fig. 1. (In control cells containing skin pretreated with 50 ul ethanol no salicylate permeation was detected). For the in vivo experiments a similar approach was used to pretreat the skin before application of oily cream BP containing sodium salicylate 10% w/w to the rabbit ear. Blood samples were removed at appropriate intervals from the marginal vein of the opposite ear and following an extraction procedure plasma salicylate levels were determined using HPLC. The plasma concentration versus time profiles are shown in Fig. 2. (n=3 rabbits) for skin pretreatment with ethanol (▲), 0.01M EtS12 (O) and 0.1M EtS12 (■) .

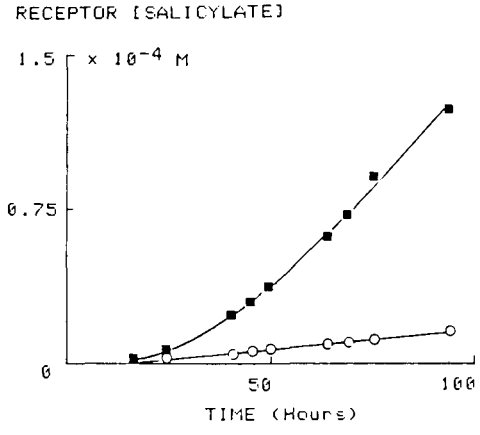

Fig. 1

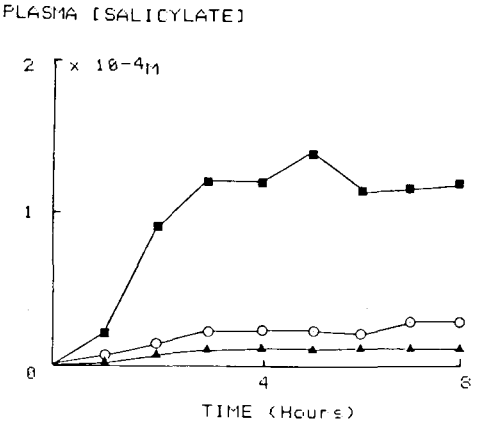

Fig.2.

The results show that EtS12 facilitates the transport of salicylate across both types of skin membrane and at the concentrations used appears to produce no irritation by itself to the rabbits ears. Related chemicals have been used in cosmetic preparations and therefore we consider long chain alkanolamines to be potentially useful penetration enhancers for anionic drugs.

Hadgraft, J., Wotton, P.K., and Walters, K.A. (1984). J.Pharm. Pharmacol. : 36 Supp 22P.