INFLUENCE OF EMULSION VEHICLES ON MEMBRANE PERMEABILITY

J.M.Wood, Dept. of Pharmacy, University of Manchester, U.K.

The delivery of drugs to the systemic circulation via the percutaneous route requires optimisation of the vehicle in order to maximise drug absorption, since most drugs do not readily permeate the skin. Recently, Dugard and Scott (1986) have described how the effect of the vehicle on the percutaneous absorption rate may be predicted from a knowledge of the solubility of the drug in the vehicle. The correlation between permeability coefficient and solubility was demonstrated using organic solvents. Such solvents, while useful for theoretical analysis, are not of clinical use in transdermal drug delivery.

In this work, the permeability coefficient of a synthetic membrane to a model compound (acetanilide) in aqueous solutions and in topical emulsion vehicles has been measured. The solubility of acetanilide in the solutions and the aqueous phases of the emulsions has been determined in order to ascertain whether a relationship between permeability and solubility holds for these complex, multiphase systems.

Paraffin-in-water emulsions were prepared with a phase volume ratio of 0.24. The mixed emulsifiers comprised cetostearyl alcohol (CSA) with a surfactant:- sodium dodecyl sulphate, cetomacrogol, or sodium deoxycholate (NaDC). Aqueous NaDC was initially prepared in the form of a gel, to allow its interaction with CSA. Acetanilide (0.5% $^{w}/w$) was incorporated into the emulsion after its preparation. Permeability coefficients were measured using a flow-through dialysis cell, of a similar design to that described by Bronaugh and Stewart (1985). The membrane separating the donor and receptor compartments comprised medical grade polydimethylsiloxane sheeting (Silastic, Dow Corning). Solubilities of acetanilide were measured at 25° C in the surfactant/CSA/water (ternary) systems, NaDC and cetomacrogol aqueous solutions (2% $^{w}/v$), and water.

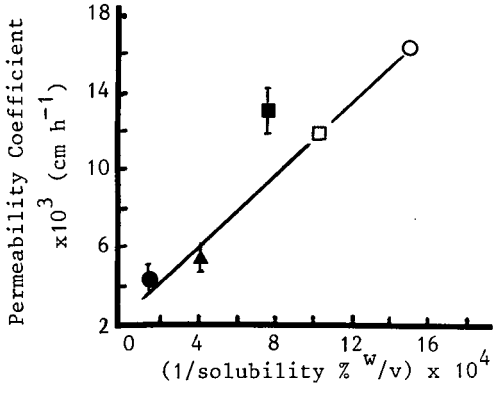

Fig.1. Correlation of P with solubility of acetanilide in: ○ water, □ cetomacrogol and NaDC solns., ■ NaDC cream, ▲ cetomacrogol cream, ● sodium dodecyl sulphate cream.

Fig. 1. shows a plot of permeability coefficient (P) as a function of reciprocal solubility. The correlation is extremely good, apart from data for NaDC cream, which gives a much higher value for P than would be predicted from the solubility. It is thought that the high permeability may be caused by release of acetanilide from the oil phase. A high interfacial tension was found to exist at the oil/water interface in NaDC emulsions, which may indicate the presence of a thinner interfacial film of emulsifier and consequently faster diffusion of solute from the oil into the aqueous phase of the emulsion.

It can be seen that, while solubility data may give a good indication of differences in membrane permeability between vehicles, some anomalies may exist with multi-component vehicles in which the drug is partitioned between different phases. *In vivo* the absorption rate may also differ from that predicted if the surfactant changes the barrier properties of the stratum corneum, or water evaporation from the vehicle changes the drug's solubility.

Bronaugh, R.L., Stewart, R.F. (1985) J. Pharm. Sci. 74 : 64-67
Dugard, P.H., Scott, R.C. (1986) Int. J. Pharm. 28 : 219-227