IN VITRO DRUG RELEASE FROM LIPID VEHICLES

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A number of in vitro techniques are available for the study of the release of medicaments from lipid vehicles, yet few mimic the conditions which may apply in vivo when the vehicle is present as a thin layer, either as applied topically or as a thin lipid film on the rectal mucosa following fusion of a lipid suppository base. Many methods also utilise some form of membrane through which the drug must pass, thereby introducing a further artefact not present in vivo.

In the present procedure, a Zsigmondy cellulose nitrate filter was dipped into a molten base containing salicyclic acid, and after allowing excess liquid to drip off, pressed between blotting paper on a tile. The membrane was weighed and then positioned in the diffusion chamber of a Sartorius Absorption Simulator (Stricker 1971) and 100ml of aqueous phase circulated through both sides of the chamber. In this case, the aqueous phase was McIlvaine citrate-phosphate buffer, though any suitable aqueous medium can be used. Samples were removed at intervals, and assayed spectrophotometrically for salicylate.

When a 1% w/w dispersion of salicylic acid in white soft paraffin was examined in this apparatus, 25% of the acid was transferred to the aqueous phase in 120 min. In contrast, only 0.07% migrated from the same system using the method of Billups and Patel (1970). The procedure thus represents a considerable degree of transfer in a short tune. Release rates, calculated in terms of the actual weight of medicament transferred, were independent of the initial concentration of salicylic acid. The process was therefore zero order, indicative of one in which the salicylic acid is mainly present as a suspension, and migration occurs from a saturated solution in the white soft paraffin (Whitworth 1968). This postulated mechanism is in accord with the low solubility of salicyclic acid in paraffins.

Substitution of half the white soft paraffin by liquid paraffin invoked no change in release rate, even though there was a significant decrease in viscosity as measured by penetrometer, indicative that when paraffins are used as the vehicle, viscosity is not a controlling factor in drug release (Schoonen et al 1979). In contrast, substitution of white soft paraffin with various proportions of octanol or isopropyl myristate increased the release rate, and this is attributed to the increase in solubility of salicyclic acid in the vehicle. Increasing the concentration of octanol beyond 10% and that of isopropyl myristate beyond 20% had relatively little effect on release rate. It is concluded that at such concentrations, complete solution of the salicylic acid has been achieved, and small differences in release rate are probably functions of the viscosity of the lipid medium and partition coefficient. Results are presented in the Table.

Base composition Soft paraffin	(%w/w)	100	50	95	90	80	50	95	90	80	50
Liquid paraffin	(%w/w)	-	50	-	-	-	-	-	-	-	-
Octanol	(%w/w)	-	-	5	10	20	50	-	-	-	-
Isopropyl myristate	(%w/w)	-	-	-	-	-	-	5	10	20	50
Release (%) after 60 min. at 37°C		17	20	40	72	74	77	32	52	76	78
Penetrometer reading (mm) at 25°C		14	27	16	19	21	-	15	20	24	-

Stricker, H.Pharm.Ind.(1971) 33: 157-160
Billups, N.F., Patel, N.K. (1970) Amer.J.Pharm.Educ. 34: 190-196
Whitworth, C.W. (1968) J.Pharm.Sci. 57: 1540-1543
Schoonen, A.J.M. et al (1979) Int.J.Pharm. 4: 141-152