

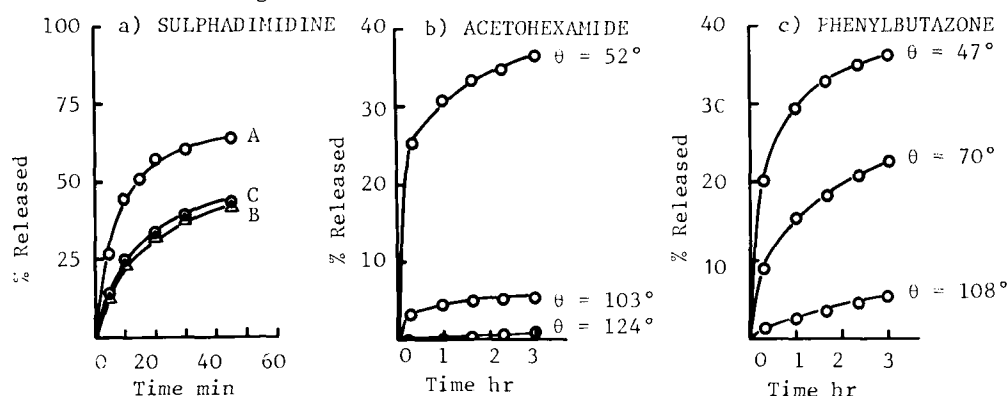
A METHOD FOR IMPROVING THE WETTING AND DISSOLUTION PROPERTIES OF HYDROPHOBIC DRUGS OF LOW AQUEOUS SOLUBILITY

G. Rowley, J.T. Pearson, M.S.H. Hussain, D.E. Hartup, B.E. Jones*, Department of Pharmaceutics, Sunderland Polytechnic, Sunderland SR2 7EE. *Eli Lilly & Co. Ltd., Basingstoke, Hants., RG21 2XA.

Hydrophilic excipients have been used to increase *in vitro* dissolution rates of poorly water soluble hydrophobic drugs. Examples include the use of hydrophilic film forming materials (Fell et al 1978) and solid dispersions (Hargreaves et al 1979). In the present study the adsorption of hexadecyl trimethylammonium bromide (HTAB) on to selected micronised drugs was measured using either a radiotracer or titrimetric method. Using maximum uptake conditions, each drug was then equilibrated with unlabelled surfactant in drug saturated aqueous solution. Known quantities of dried recovered drugs were then hand filled into hard gelatin capsules and such 'treated' samples subjected to dissolution testing using a modified B.P. method.

Fig. 1a for sulphadimidine shows that treatment (0.06% w/w HTAB adsorbed) increases dissolution (A) when compared with untreated drug (B) and a 1% w/w surfactant/drug physical mixture (C). Enhanced dissolution is also shown by acetohexamide (Fig. 1b) with a decrease in contact angle (θ) from 124° to 52° as measured by the h-c method. Rinsing with water removes surfactant and raises θ to 103° yielding a lower dissolution profile. Corresponding results for phenylbutazone are given in Fig. 1c.

Fig. 1 Dissolution results in water at 37°C



Indomethacin and sulphathiazole have also been treated by the adsorption method and some relevant parameters are included in Table 1.

Table 1. Adsorption and dissolution data for drugs of different hydrophobicity

Drugs	Contact	HTAB Adsorbed	% Released after 30 min	
	Angle θ°		Untreated	Treated
Acetohexamide	124	0.27	<1	27
Phenylbutazone	108	0.21	2	24
Indomethacin	90*	0.29	22+	44+
Sulphathiazole	53*	0.07	42	72

*Values of Lerk et al (1977) †McIlvaine's citric acid-phosphate buffer pH 6.4

Untreated acetohexamide gave 24% release after 30 min in 4×10^{-4} M HTAB as dissolution medium. This concentration is approximately one thousand times greater than that attainable by complete desorption from the treated drug. These results indicate the important contribution of adsorbed surfactant to wetting and dissolution in addition to any effect produced by residual HTAB deposited during drying.

Fell, J.T. et al (1978) J. Pharm. Pharmacol. 30 : 479-482

Hargreaves, B.J. et al (1979) Ibid. 31 : 47P

Lerk, C.F. et al (1977) J. Pharm. Sci. 66 : 1480-1481