MODIFICATION OF HYDROPHOBIC DRUG SURFACES BY ADSORPTION

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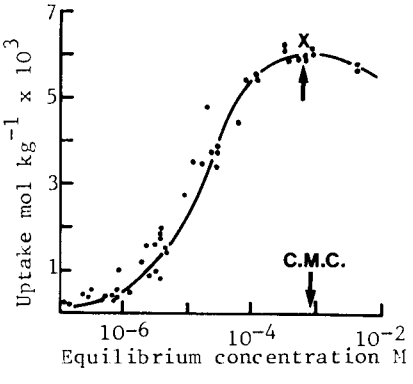
Drug physical properties together with formulation and manufacturing processes are known to affect drug dissolution rate. For example, enhanced dissolution of poorly water soluble hydrophobic drugs has been achieved by crystallisation from surfactant solutions (Chiou et al 1976) and high speed milling with hydrophilic excipients (Lerk et al 1978). Decreased dissolution due to the presence of nonionic surfactant in sulphanilamide granules has recently been reported (Heng and Wan 1985). The present work investigates the adsorption of cationic surfactant on to drugs selected for their low aqueous solubility and hydrophobic nature.

Known quantities of micronised acetohexamide, phenylbutazone, sulphadimidine and sulphathiazole were equilibrated in their respective saturated aqueous solutions containing hexadecyl trimethylammonium bromide (HTAB) radiolabelled with 1-14C surfactant. Initial concentrations in the range 1 x 10^{-6} - 1 x 10^{-2}M were used in HTAB treated glassware under standard conditions of agitation and temperature. After equilibration and centrifugation, surfactant depletion was determined using a liquid scintillation technique.

Using the classification of Giles et al (1974), isotherms were generally of the 'co-operative' S type; specific data for phenylbutazone at 30°C is given in Fig.1.

Fig. 1 HTAB adsorption on phenylbutazone 30°C



Adsorption at low HTAB concentrations is due to electrostatic attraction between the cationic head groups and negative sites on the drug surface as inferred by particle microelectrophoresis. Further adsorption by hydrophobic interactions occurs as HTAB concentration increases after charge reversal (range 1 x 10^{-6} - 5 x 10^{-4}M, depending on the drug). Adsorption reaches a maximum in the region of the critical micelle concentration (c.m.c.) 8.9 x 10^{-4}M in saturated phenylbutazone at 30°C.
Using specific surface areas (gas adsorption) and a mean literature molecular cross sectional area of 0.362nm² for HTAB ("end on" orientation), maximum overall percentage surface coverage (point X, Fig. 1) was calculated: acetohexamide 42%, phenylbutazone 40%, sulphadimidine 22% and sulphathiazole 20%. Such values must be interpreted with caution due to the possible existence of surfactant clusters in S type systems and 'hemi-micellar' nature of the proposed adsorption mechanism (Somasundaran et al 1964).

Sedimentation studies revealed that de-flocculation occurred due to improved wetting in HTAB solutions sufficiently concentrated to exceed charge reversal. These observations support the view of molecular orientation gained from the adsorption data and, together with contact angle determination on recovered drug samples, confirm the increase in the hydrophilic nature of the drug surface.

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