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Note

The wetting of powders by bile salt solutions and gastric juice

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Abstract

Contact angle studies using bile salt solutions and gastric juice have been carried out on phenobarbitone, a model hydrophobic powder. Interpretation of the results according to the method of Lucassen-Reynders (*J. Phys. Chem.*, 67 (1963) 969–972) shows that the predominant interfacial adsorption of the surface active components changes with concentration. The physical properties of the gastric juice samples were essentially similar except for surface tension. For a given surface tension, gastric juice wets the hydrophobic powder better than the bile salts.

Keywords: Wetting; Contact angle; Gastric juice; Bile salt; Adhesion tension

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The important role of wetting in several pharmaceutical processes has led to extensive studies on the determination and characterization of the wettability of pharmaceutical materials (Parsons et al., 1992; Buckton, 1993). In the dissolution of drugs from tablets and capsules, solvent penetration into capillaries must occur to ensure adequate solid/solvent contact. This process is one of immersional wetting, the free energy change (W_I) occurring being given by

$$W_I = -\gamma_{LV}\cos\theta$$

where γ_{LV} is the liquid surface tension and θ denotes the contact angle of the liquid on the solid. For this process to occur spontaneously, W_I must be negative and hence θ must be less than 90°.

Hydrophobic powders will exhibit limited aqueous penetration. This may be overcome, for example, by mixture with a hydrophilic component, or the use of surface active agents (Lerk et al., 1976; Mohammad and Fell, 1983). Surprisingly, wetting studies have not been carried out using the initial solvent for drugs, namely gastric juice. This paper reports such studies using phenobarbitone as a model hydrophobic compound. Comparison is made with pure solutions of bile salts which are known to reflux from the duodenum into the stomach (Rhodes et al., 1969).

Phenobarbitone (Sigma, Poole, UK) was sieved to obtain a 53-90 μm size fraction. Bile salts (a mixture of sodium cholate and sodium deoxycholate) were also obtained from Sigma. Hard paraffin was of B.P. quality. Gastric juice was obtained from eight patients admitted to Hope Hospital, Salford and measurements were conducted using the fresh samples. Contact angles

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were measured by direct microscopic observation of a drop of liquid on a compressed disc of powder. The compaction pressure was 20 MPa although compaction at different pressures did not influence the results. All liquids were saturated with phenobarbitone to prevent dissolution. Surface tension measurements were carried out using the drop volume method and applying the correction factors of Harkins and Brown (1919). Liquid densities were determined with a density bottle at 22°C. Viscosities were measured using a capillary viscometer.

The use of a sessile drop on a compressed powder for the determination of contact angles is open to criticism. The problems have been reviewed by Buckton (1993). For a series of barbiturates, changes in the measured contact angle with increasing compaction pressure leading to a limiting value have been observed (Buckton and Newton, 1990). The final value was correlated with the onset of plastic flow of the material. In the current study, the pressure chosen was sufficient to make a stable compact. Further increases in pressure did not alter the measured angle. Although the values obtained may not be truly representative of the original powdered material, they are reproducible, represent compacted material and allow conclusions on the influence of surface active agents to be drawn.

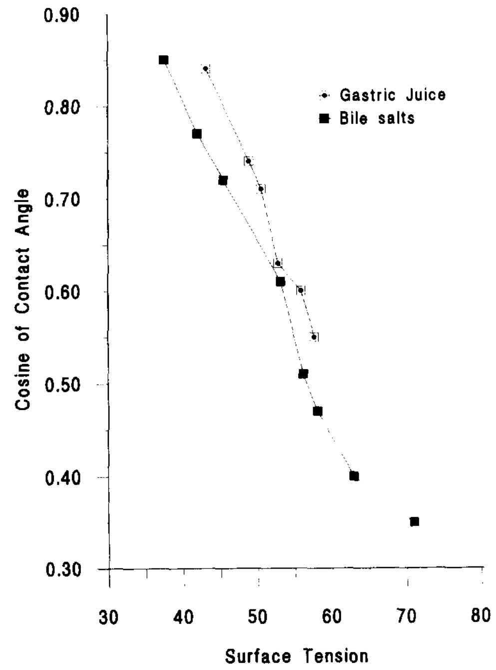

Fig. 1. The relation between surface tension (mN/m) and the cosine of the contact angle of bile salt solutions and gastric juice on phenobarbitone.

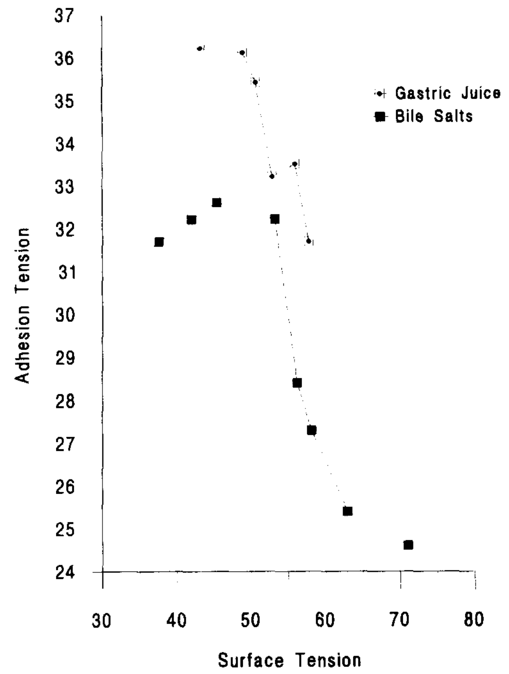

Fig. 2. The relation between surface tension (mN/m) and the adhesion tension (mN/m) for bile salt solution and gastric juice on phenobarbitone.

The relationship between surface tension and the contact angle for solutions of bile salts is shown in Fig. 1. There is a linear decrease in the cosine of the contact angle with surface tension. This is a slightly different result from that obtained previously with sodium lauryl sulphate (SLS) (Mohammad and Fell, 1983) in that with SLS, small changes in surface tension gave large changes in the contact angle followed by a more gradual change as the surface tension was further reduced. This may be due to different patterns of surfactant adsorption. One approach to examining this is that of Lucassen-Reynders (1963). Combining the Young and Gibbs equation gives

$$\frac{d(\gamma_{LV}\cos\theta)}{d\gamma_{LV}} = \frac{\Gamma_{SV} - \Gamma_{SL}}{\Gamma_{LV}}$$

where Γ_{SV}, Γ_{SL} and Γ_{LV} represent the surface excess of surfactants at the solid vapour, solid liquid and liquid vapour interfaces, respectively.

A plot of adhesion tension ($\gamma_{LV}\cos\theta$) against surface tension indicates the type of adsorption. Negative slopes indicate that the adsorption is greater at the solid liquid interface than the solid air interface. Positive slopes indicate the reverse. Zero slope shows that adsorption at solid liquid and solid air interfaces are equal. Fig. 2 shows the relationship between the adhesion tension and surface tension for bile salt solutions on phenobarbitone. At low concentrations adsorption occurs mainly at the solid liquid interface whereas at higher concentrations, the adsorption at the solid-air is equal to or predominates over that at the solid-liquid interface. This is in contrast to the adsorption on a completely non-polar surface, paraffin, where a negative slope throughout the concentration range implies that adsorption at the solid liquid interface predominates (Fig. 3).

The physical properties of the samples of gastric juice are shown in Table 1. Except for surface tension, the other physical properties determined lay within a fairly narrow band.

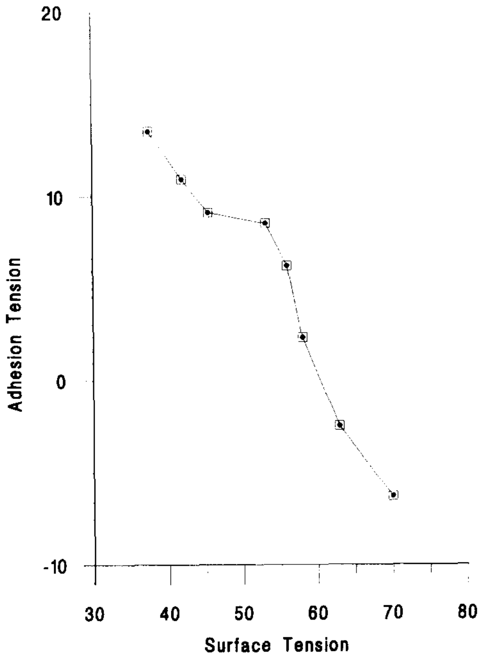

Fig. 3. The relation between surface tension (mN/m) and the adhesion tension (mN/m) for bile salt solutions on paraffin.

Table 1
Physical properties of the samples of gastric juice

Sample no.	Viscosity (mN m^{-2}S)	Density (g/cm)	pH	Surface tension (mN/m)
A	1.163	1.0014	2.01	43.14
B	1.0238	1.0018	1.53	43.85
C	0.997	1.00	1.23	48.83
D	1.208	1.00	1.66	50.45
E	1.0476	1.001	1.25	51.14
F	1.0029	1.008	1.38	52.67
G	0.973	1.00	1.38	55.75
H	1.029	0.999	1.6	57.56

The relation between the surface tension of the gastric juice and its contact angle on phenobarbitone is shown in Fig. 1. For a given surface tension, gastric juice wets phenobarbitone better than the bile salt solution. The graphs of the change in contact angle with surface tension are, however, parallel, implying a similar pattern of adsorption for the two materials. This naturally leads to a similarity in the adhesion tension, surface tension curves (Fig. 2).

The adhesion tension is the driving force for liquid penetration into powder beds, which may be the rate limiting step in drug dissolution. This will be particularly the case for hydrophobic systems e.g., capsule fills mixed with magnesium stearate. In these cases, dissolution may be influenced by the surface tension of the gastric juice.

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