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THE WETTING AND DISSOLUTION RATE OF PHENOBARBITONE POWDERS

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ABSTRACT

The wetting of phenobarbitone powders by solutions of sodium lauryl sulphate has been measured. Large changes in contact angle and adhesion tension occur at low surfactant concentrations followed by more gradual changes at higher concentrations. The dissolution rates of phenobarbitone from capsules reflect these changes showing that initially, dissolution is penetration rate limited.

INTRODUCTION

The wetting of a solid has been divided into three types (1) namely, adhesion, immersion and spreading. The distinction between the three types of wetting depends on the various interfaces gained or lost during the process. To obtain

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reasonable dissolution rates from capsules, penetration of liquid into the capillaries of the powder fill is required, a process of immersional wetting. Here, solid, vapour interface is exchanged for solid liquid interface, but the extent of the liquid surface remains unchanged. The change in free surface energy for this process, W_i, is given by: $W_i = -\gamma_{LV} \text{Cos}\,\theta$ where γ_{LV} is the liquid vapour interfacial tension and θ is the contact angle of the liquid on the solid. For the process to occur spontaneously, W_i must be negative, i.e. must be below 90^o, and the process will occur more readily, the higher the value of $\gamma_{LV} \cos\theta$, the adhesion tension. Many drugs are hydrophobic in nature and penetration of liquid into the capillaries of such powders will be limited. This limited penetration may be overcome by mixture with a hydrophilic component and/or the use of surface active agents. *In vivo*, a capsule will first encounter gastric juice which itself is surface active, having a surface tension between 35 and 50mNm^{-1}(2). This report examines the influence of surface tension on the contact angles and dissolution rates of phenobarbitone from capsules.

MATERIALS AND METHODS

Phenobarbitone was separated by air jet sieving (Alpine Process Technology Ltd., U.K.) into three size fractions, 180 - 250µm, 53-90µm and less than 45µm. Sodium lauryl sulphate solutions (B.D.H. Ltd., U.K., Specially Pure) were made up in glass distilled water (surface tension 72.6 mNm^{-1}).

Suface tension measurements were carried out by the drop volume method using an Agla syringe, and applying the correction factors of Harkins & Brown (3) in the calculations.

Contact angles were measured using the h-ε method and a direct method. The h-ε method was carried out as detailed by Lerk et al (4). The direct method used was that described by Fell and Efentakis (5). Compacts were prepared using a 1.92cm. dia. flat-faced punch and die set at a compaction force of 40 KN. All surface tension and contact angle measurements were made with the appropriate solution saturated with phenobarbitone.

Solubility of the phenobarbitone in the sodium lauryl sulphate solutions was measured by shaking excess powder with the appropriate solution in a water bath at 37°C. Samples were analysed (after filtration) by u.v. spectrophotometry at time intervals until no further increase in reading was obtained. Dissolution rates were measured by the method described by Newton and Rowley (6). No. 5 hard gelatin capsules were filled with 100mg. of the appropriate powder and placed in stainless steel wire spirals in 750ml. of dissolution medium at

$37^{o}C$. Stirring was effected at 100 r.p.m. by a four flat-bladed paddle 4cm in diameter situated 3cm above the capsule. 5ml. samples were removed at suitable time intervals, filtered through membrane filters (0.8μm Millipore Ltd., U.K.) and analysed spectrophotometrically. 5ml. of fresh medium was replaced in the dissolution vessels, after the removal of each sample.

RESULTS AND DISCUSSION

The relation between sodium lauryl sulphate concentration and surface tension is shown in Figure 1. The concentrations chosen were below the critical micelle concentration to avoid solubility increases which may have made interpretation of the dissolution rate data more difficult.

Plots of contact angle against surface tension are shown in Figure 2. Similar plots were obtained for all the particle sizes showing no effect of particle size on contact angle as observed previously by Lerk et al (4). The plots show an initial rapid drop in contact angle with a small change in surface tension, followed by a more gradual drop as the surface tension is lowered. This relation is not a consequence of using a compacted powder system. The relation for sodium lauryl sulphate solutions on a smooth teflon surface (Fig. 2) follow

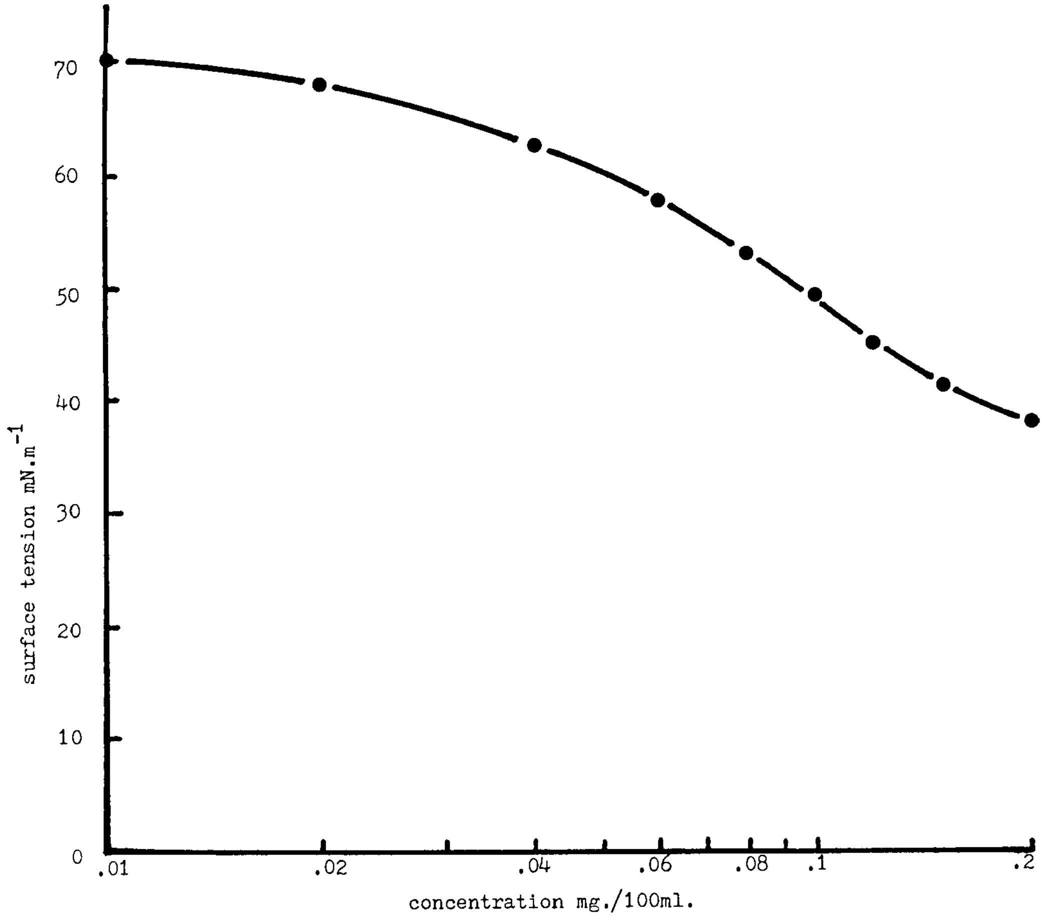

Fig. 1. The relation between surface tension and concentration of sodium lauryl sulphate solutions.

the same pattern. The results for the direct method of determining the contact angle follow the same pattern as those obtained by the h-ε method, but are somewhat lower. This could be a consequence of the Wenzel (7) relationship for contact angles on rough surfaces

$$\cos\theta' = r\cos\theta$$

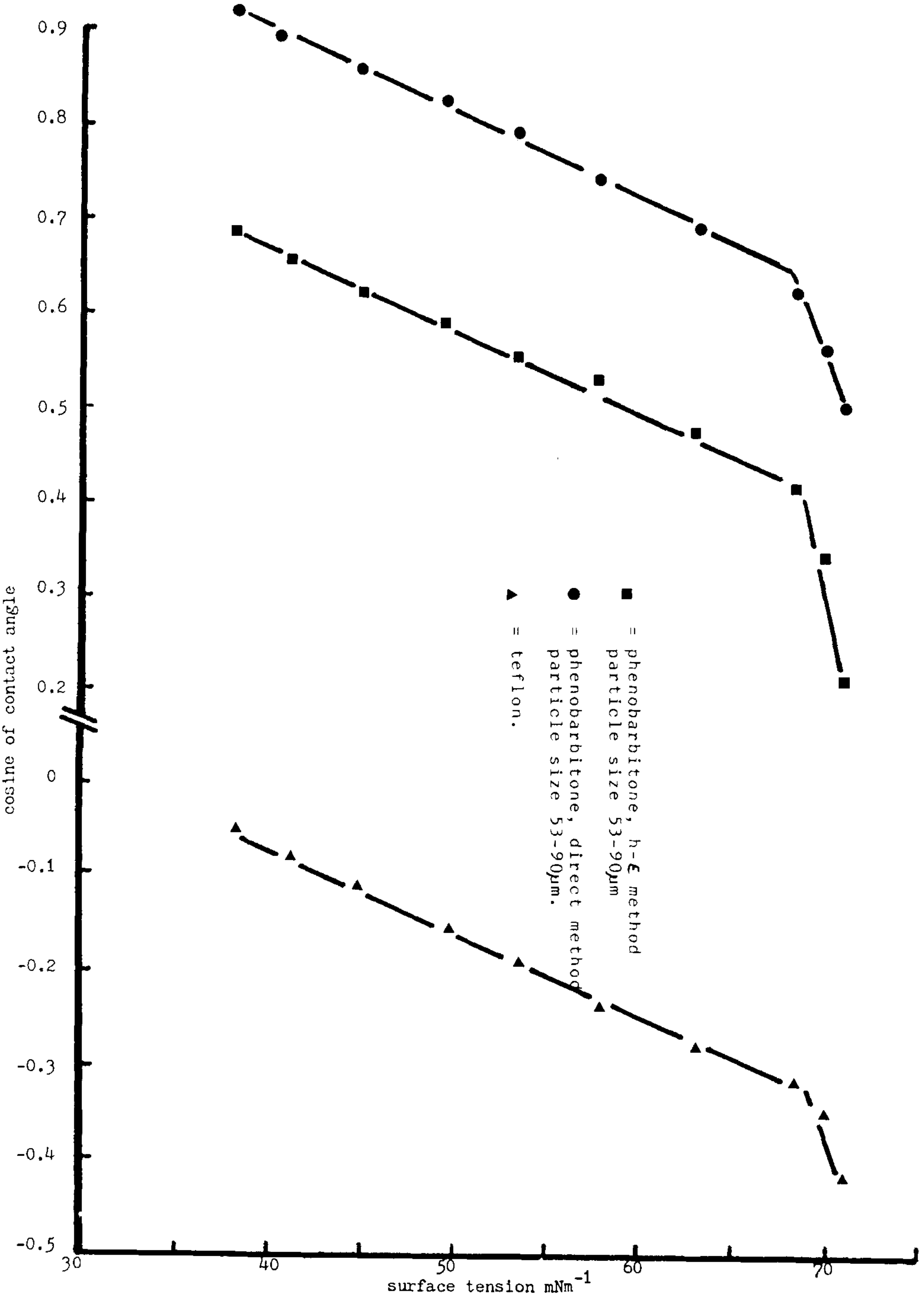

Fig. 2. The relation between surface tension and contact angle.

where θ' = the observed contact angle

θ = the real contact angle

r = the roughness factor.

The equation predicts that for contact angles beow 90^o, roughening the surface will lead to a lower contact angle. If the contact angle determined by the h-ε method is assumed to be the true contact angle, then a lower angle would be expected from a direct measurement on a rough surface.

The Young equation (8) relating the contact angle to the three interfacial tensions involved is:

$$\text{Cos} = \frac{\gamma_{sv} - \gamma_{sL}}{\gamma_{Lv}}$$

where γ is the interfacial tension and the subscripts s, L and v are the solid, liquid and vapour phases respectively.

Adsorption of surface active agents at any of these three interfaces will modify the contact angle. Adsorption at the liquid vapour interface and the solid liquid interface will reduce the contact angle, whereas adsorption at the solid vapour interface tends to increase the angle due to the lowering of γ_{sv}.

The dissolution rate studies all gave similarly shaped plots of % dissolved against time, allowing the use of a T_{50} (time for 50% of the material to be dissolved) for comparison. Assuming a powder bed to be analogous to a bundle of capillary tubes, the rate of penetration into the powder is given by the Washburn equation (9).

$$l^2/t = \frac{\gamma_{Lv} r \operatorname{Cos} \theta}{2\eta}$$

where l = the distance of penetration

t = the time of penetration

γ_{Lv} = the surface tension of the liquid

θ = the contact angle.

r = the capillary radius

η = the liquid viscosity.

If the capillary radius and the liquid viscosity are constant, the rate of penetration will be governed by $\gamma_{Lv}\operatorname{Cos}$, the adhesion tension. For rapid penetration, ideally there should be a low contact angle and a high surface tension. The change in adhesion tension with the surface tension of the sodium lauryl sulphate solutions is shown in Figure 3. The most dramatic changes in the adhesion tension occur at the low surfactant concentrations where small changes in surface tension give rise to larger changes in the contact angle (see Fig. 2). The

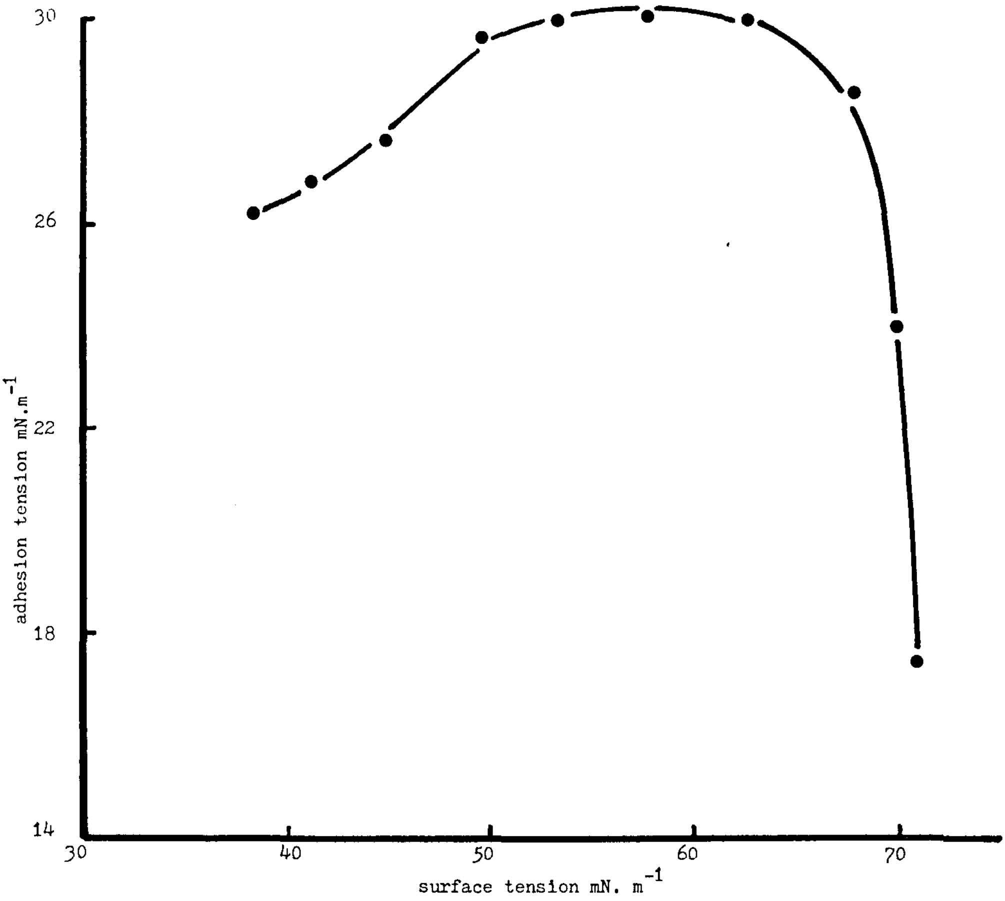

Fig.3. The relation between adhesion tension and surface tension.

linear nature of the relation between the cosine of the contact angle and the surface tension for the higher surfactant concentrations leads to the parabolic nature of the adhesion tension, surface tension plot and produces a fall in adhesion tension at the higher surfactant concentrations.

Plots of T_{50} against the surface tension of the dissolution medium are shown in Fig. 4. It can be noted that the plots

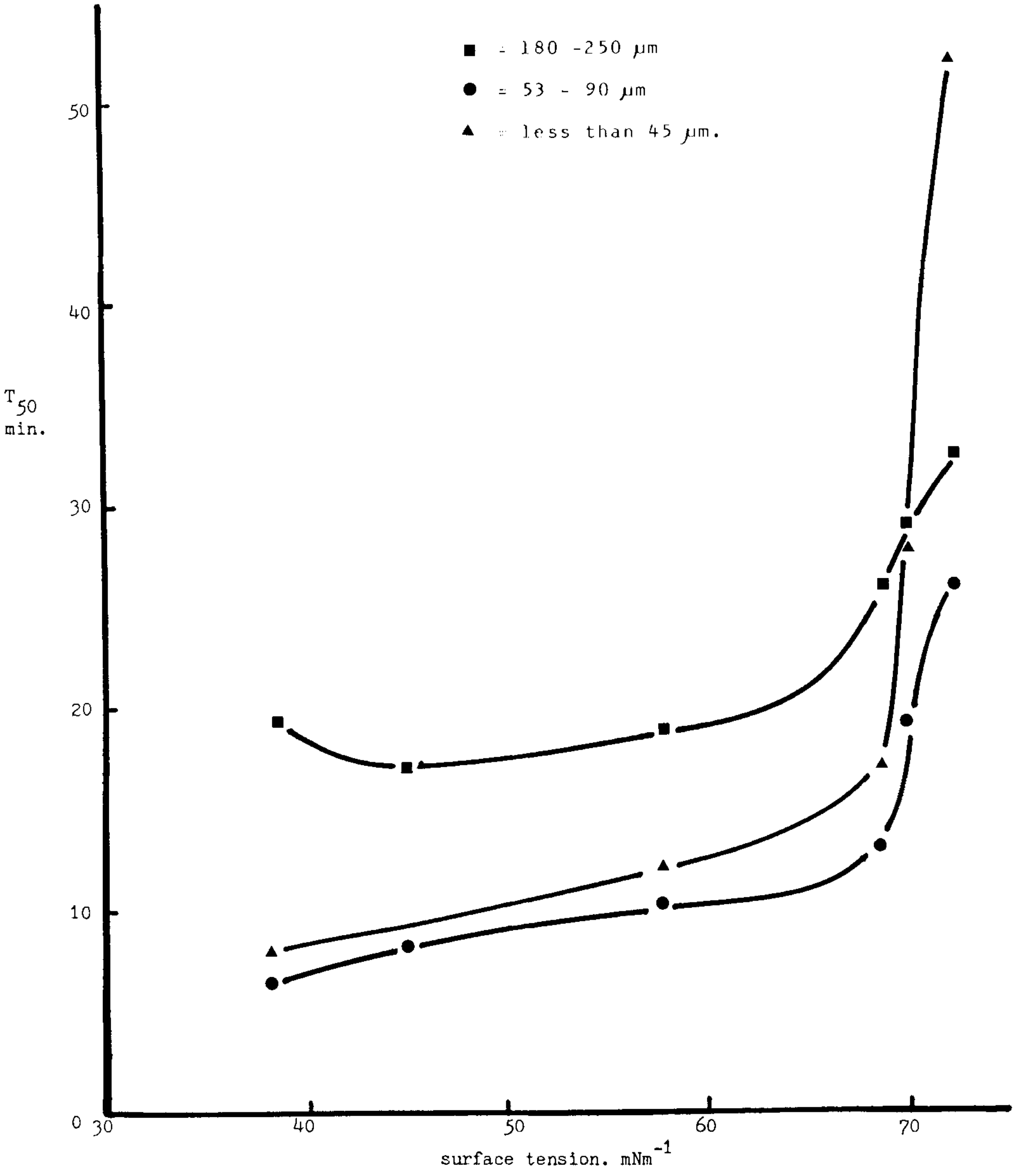

Fig. 4. The relation between dissolution rate (T_{50}) and surface tension.

closely reflect the changes in adhesion tension, the maximum changes in dissolution rate occurring at the low surfactant concentrations. Changes in solubility are not involved in these studies, the solubility of the phenobarbitone remaining constant throughout the range of surfactant solutions employed.

The particle size effects are similar to those noted by Finholt (2). Only when the powders are well wetted can the higher surface areas of the smaller particles become effective. Even at the highest surfactant concentration used, the potential of the smallest particle size powder is not realized. Initially the dissolution rate is penetration limited and improvement in the rate of penetration by an increase in the adhesion tension improves this. However, further factors such as disintegration and deaggregation are important if maximum dissolution rates are to be achieved.

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