The wetting of powders of acetylsalicylic acid, salicylic acid, phenacetin and paracetamol

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The wetting of powders of acetylsalicylic acid, salicylic acid, phenacetin and paracetamol has been assessed using methanol–water mixtures to give a range of surface tensions. The results have been interpreted in terms of the critical surface tension, adhesion tension and spreading coefficients. The critical surface tension values are surprisingly low which may be due to adsorption of the methanol at the solid surface, exposing its CH_3 group to the liquid. The adhesion tension and spreading coefficient values could be useful guides in formulation.

The wetting of powders is a preliminary step in several pharmaceutical processes, and also in the subsequent disintegration and dissolution of the product *in vivo*. According to the process under examination, different types of wetting are involved (Parfitt, 1973). The submersion of a powder as required in the dispersion process involves the spreading of liquid over the powder to effect complete wetting. The final step in this process, using the model of Parfitt (1973) involves spreading wetting, the tendency for this to occur being greater, the closer the value of the spreading coefficient, s.c., as defined below, approaches zero.

$$s.c. = \gamma_L(\cos\theta - 1)$$

where γ_L is the surface tension and θ is the contact angle of the liquid on the solid. Spreading is only spontaneous when $\cos\theta > 1$, but when θ approaches zero, density differences and agitation can complete the process.

Penetration into capillaries (e.g. in solid dosage forms) involves the replacement of a solid : air interface with a solid : liquid interface. This is immersional wetting, which will occur more readily the higher is the adhesion tension, AT, defined as

$$AT = \gamma_L \cos\theta.$$

Hence, the relation between the surface tension of the liquid and the contact angle for a particular solid needs to be known for an understanding of the wetting of powders. Recently, Lerk, Schoonen & Fell (1976) described a method for measuring the contact angles of pharmaceutical powders. We have applied this method to the study of liquids of different surface tensions, using methanol–water mixtures to obtain different values.

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MATERIALS AND METHODS

Materials

The solids used were: acetylsalicylic acid B.P. (Monsanto), salicylic acid (Analar BDH), paracetamol and phenacetin (both Reagent Grade, BDH). These were chosen to give a range of initial contact angles measured against their saturated solutions. The methanol was Analar grade (BDH).

Methods

Surface tension. This was measured by the Wilhelmy plate method using a roughened platinum plate.

Densities. Liquid densities were measured using a density bottle, and solid densities using an air comparison pycnometer (Model 930, Beckmann Instruments Ltd.).

Contact angles. These were measured by the method of Kossen & Heertjes (1965) as used by Lerk & others (1976) for pharmaceutical powders. The method consists essentially of measuring the maximum height of a drop of liquid on a presaturated compact of the powdered solid under test. Calculation of the contact angle is achieved using the following equations:—

$$\text{for } \theta > 90° \quad \cos\theta = -1 + (2 - Bh^2)\frac{2}{3(1 - \epsilon_v)}$$

$$\text{for } \theta < 90° \quad \cos\theta = 1 - \frac{2}{3(1 - \epsilon_v)}Bh^2$$

where h is the height of the liquid drop, ϵ_v is the volume porosity of the compact, and $B = \zeta_L g/2\gamma_L$ where ζ_L is the liquid density and g is the acceleration due to gravity.

The modification of Lerk, Lagas & others (1978) was adopted whereby the compact was produced in a 5 cm diameter die, removed, and saturation achieved by allowing the compact to rest on a sintered filter immersed in the test fluid. The com-

paction pressure was 31 MPa. The test liquids were saturated solutions of the appropriate solid in the methanol–water mixtures at 20° and contact angle measurements were made at least in duplicate.

RESULTS AND DISCUSSION

The relations between the liquid surface tensions and the contact angles are shown in Fig. 1, and the calculated values of the adhesion tension and spreading coefficients in Table 1 and Fig. 2. The plots of surface tension against contact angle are linear over most of the range tested, which allows the fitting of a regression line and extrapolation to $\cos\theta = 1$ to establish values for the critical surface tensions of the solids. These are given in Table 1.
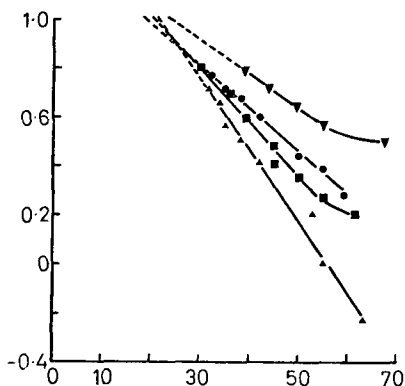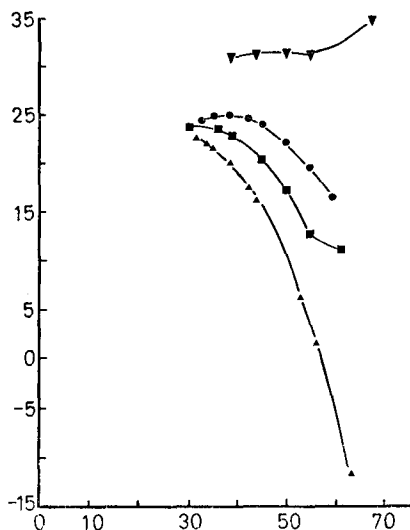

FIG. 1. The relation between surface tension and contact angle. ● = acetylsalicylic acid; ▲ = salicylic acid; ■ = phenacetin; ▼ = paracetamol. Ordinate: $\cos\theta$. Abscissa: Surface tension (mN m⁻¹).

FIG. 2. The relation between adhesion tension and surface tension. Symbols as in Fig. 1. Ordinate: Adhesion tension (mN m⁻¹). Abscissa: Surface tension (mN m⁻¹).

Table 1. *Values of the contact angles, spreading coefficients, and critical surface tensions of the materials studied.*

γ mN m⁻¹	Acetylsalicylic acid $\cos\theta$	s.c.*	Salicylic acid $\cos\theta$	s.c.*	Phenacetin $\cos\theta$	s.c.*	Paracetamol $\cos\theta$	s.c.*
67·7**	—	—	—	—	—	—	0·514	—32·9
63·3**	—	—	—0·224	—74·2	—	—	—	—
61·5**	—	—	—	—	0·202	—55·6	—	—
59·4**	0·276	—42·8	—	—	—	—	—	—
56·2	—	—	0·001	—54·7	—	—	—	—
55·0	0·389	—35·1	—	—	0·270	—41·8	0·559	—33·8
52·9	—	—	0·217	—46·6	—	—	—	—
50·0	0·436	—27·7	—	—	0·353	—32·4	0·652	—18·1
45·0	0·480	—20·9	—	—	0·403	—24·2	—	—
44·0	—	—	0·4x8	—27·7	—	—	0·724	—12·1
42·2	0·599	—17·5	0·409	—24·5	—	—	—	—
39·2	—	—	—	—	0·594	—16·0	0·788	—8·2
38·4	0·657	—13·3	0·505	—18·2	—	—	—	—
36·2	—	—	—	—	0·699	—12·4	—	—
35·2	0·714	—10·2	0·566	—13·5	—	—	—	—
34·1	—	—	0·659	—12·0	—	—	—	—
32·6	0·769	—7·9	—	—	—	—	—	—
31·8	—	—	0·718	—9·1	—	—	—	—
30·0	—	—	—	—	0·793	—6·1	—	—
	$\gamma_c = 18\cdot9$		$\gamma_c = 21\cdot6$		$\gamma_c = 20\cdot7$		$\gamma_c = 24\cdot0$	

s.c. = Spreading coefficient.
γ_c = Critical surface tension.
* Values calculated on the basis of the regression line when applicable.

The use of saturated solutions in the measurements described makes interpretation of the results in the manner used for pure liquids on non-polar, insoluble solids, more complex. Saturated solutions are required in the technique of measurement utilized in this study as the calculation of the result requires a knowledge of the surface tension of the liquid and the porosity of the compact. If both surface tension and porosity are varying due to dissolution of the compact, then the system is unstable and the results questionable. It may be argued that direct methods of measurement of contact angle on solids that will dissolve (i.e. most pharmaceutical systems of interest) are equally questionable as the surface tension of the solvent-solute mixture may vary as dissolution takes place and also the surface characteristics of the solid will change. Practically, the contact angle of a solid against its saturated solution may be the most valuable measurement, because when a solid dissolves it forms a saturated diffusion layer instantaneously (Nernst & Brunner, 1904) and it is this layer that will be in contact with the solid.

The concept of critical surface tension, γ_c, was introduced by Fox & Zisman (1950) and reviewed by Zisman (1964). Liquids with surface tensions lower than γ_c will spread on the surface of the solid whereas liquids of higher surface tension have finite contact angles. The interpretation of γ_c values is, however, subject to much discussion as the value obtained depends on the series of liquids used to make the measurements. The values of γ_c for the four drugs are surprisingly low, especially when compared with quoted values for polymers, e.g. polyethylene, 31, polystyrene, 33, polymethylmethacrylate, 39 mN m^{-1} (Zisman, 1964). These values were obtained using a series of pure liquids to obtain a range of surface tensions, but large discrepancies were obtained when mixed liquids having both polar and dispersion forces were used (Dann, 1970; Murphy, Roberts & Ross, 1972). Dann thought the discrepancies arose from the polar contributions of the solutions, and this explanation was adopted by Harder, Zuck & Wood (1971) in their study of adhesive forces in tablet coating. Murphy & others (1972), on the other hand, explained the discrepancies as caused by adsorption of a component from solution at the interfaces. In the present work, the γ_c values do not reflect the initial values of the contact angles measured against their aqueous solutions, and three of the results fall

in the range 20–24 mN m^{-1} which is said to be the critical surface tension for the methyl group (Shafrin & Zisman, 1960). It is tempting, therefore, to use the interpretation of Murphy & others (1972) that the results can be explained by adsorption of methanol at both the solid/liquid and the solid/vapour interfaces with the hydroxyl group of the alcohol orientated towards the solid, giving rise to a surface consisting of methyl groups exposed to the liquid.

In terms of processes involving wetting, the values of the adhesion tension and the spreading coefficient are important. The adhesion tension is the product of the surface tension and the cosine of the contact angle and the penetration of liquid into capillaries in a solid will proceed more rapidly, the higher its value. Reduction in surface tension will lead to a reduction in the contact angle and the relative changes involved will affect the adhesion tension and therefore the value of reducing the surface tension to aid penetration. Adsorption at the solid : vapour or solid : liquid interface will further modify this, as seen from Young's equation

$$\gamma_S - \gamma_{SL} = \gamma_L \cos\theta.$$
γ_S = solid : vapour interfacial tension.
γ_{SL} = solid : liquid interfacial tension.

The results are shown in Fig. 2. In the extreme, the curves are parabolic if the linear relation between surface tension and contact angle holds, but over the range of surface tensions used, each material behaved differently. For salicylic acid, the adhesion tension increases over the range of surface tensions used, while for aspirin and phenacetin, surface tensions below 38–40 dynes cm^{-1} (mN m^{-1}) had little effect on the adhesion tension because both curves are approaching their maxima. Paracetamol is the most hydrophilic, and the adhesion tension is virtually unaffected by changes in the surface tension of the liquid used. Thus the value of reducing the surface tension to aid penetration by means of increasing the adhesion tension depends on the initial contact angle of the powder in the systems studied. Because of maxima in the curves, reduction in surface tension beyond a certain point may have deleterious effects.

The values for the spreading coefficients (Table 1) become less negative as the surface tension falls, indicating better spreading of the liquids on all the solids with decrease in surface tension.

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