

# Assessment of the wettability and surface energy of a pharmaceutical powder by liquid penetration

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The use of a technique involving the assessment of the rate of penetration of a liquid into powder beds has been critically evaluated as a method for characterizing the wetting and surface energy of a hydrophobic powder (amylobarbitone). The choice of the perfect wetting liquid has been assessed, and the possible use and value of extrapolation techniques to indicate the theoretical result for water have been explored. Values of 99.5 and 102.8 obtained for the contact angle, and 25.7 and 26.9 mNm<sup>-1</sup> for the critical surface energy, were the best estimates obtainable by this technique. Previously reported limitations of the Washburn equation have been considered.

An understanding and characterization of how a powder is wetted is fundamental to several pharmaceutical processes. The surface energy of a solid is the best measure of wettability and can be derived from measurements of the angle of contact, which represents an equilibrium of energies at a three phase interface. Contact angles determined preferably for a homologous series of liquids of known surface energy allow extrapolation to a value of surface energy which corresponds to a zero contact angle, this value being what is known as the critical free surface energy (or the critical surface tension,  $\gamma_c$ ) of the solid (Fox & Zisman 1950). This approach clearly relies on accurate determination of the values of the contact angle. These values can be obtained for solids of suitable topography by application of methods such as the sessile drop (Fox & Zisman 1950), tilting plate (Adam & Jessop 1925), and plate rise (Neumann & Tanner 1970). However, when the sample exists as a powder, which does not have a continuous smooth surface, direct determinations are not possible so indirect methods must be used. The techniques most frequently cited fall into two categories, those involving liquid movement into a bed of powder (see Bartell & Osterhof 1927; Washburn 1921; Studebaker & Snow 1955), and those involving measurements on a compressed disc of powder (see Heertjes & Kossen 1967; Zografis & Tam 1976). When the powder is compressed as a tablet, the latter methods may be of value, but if the powder is to be used loosely packed, as in the formulation of hard gelatin capsules or the dispersion of powders in liquids, it is unrealistic to measure

the contact angle on a compressed surface the formation of which could provide a different surface energy from that of the original powder. It would therefore seem logical to try to use liquid penetration experiments to assess the wettability of a powder.

In an early report on liquid penetration techniques, Bartell & Osterhof (1927) used a method by which the pressure required to prevent penetration was measured. In practice, this proved difficult and offered no advantage over the work of Washburn (1921) which advocated unopposed penetration of a liquid into a powder bed. Washburn (1921) combined the capillary driving force for a cylindrical tube with the Poiseuille equation for viscous drag in conditions of steady flow. The theory was extended by Levine & Neale (1975), who used a model of a bed of spherical particles, rather than the assemblage of parallel capillaries used by Washburn (1921). The Levine & Neale theory, however, was highly idealized, and, in general, the basic equation of Washburn is used as adapted by Studebaker & Snow (1955)

$$\cos \theta = \frac{\gamma_{LV1} \eta_2 \text{gradient}_2}{\gamma_{LV2} \eta_1 \text{gradient}_1} \quad (1)$$

where  $\gamma_{LV}$  is the surface tension,  $\eta$  is the viscosity, and the gradient is of a graph of the distance of penetration squared ( $l^2$ ) as a function of time ( $t$ ) for a perfectly wetting liquid (suffix 1) and an imperfectly wetting liquid (suffix 2),  $\theta$  being the contact angle.

## MATERIALS AND METHODS

The powder used was amylobarbitone BP, a hydrophobic powder with a volume geometric mean diameter of 77  $\mu\text{m}$  and a geometric s.d. of 1.29  $\mu\text{m}$ .

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The liquids used were Analar grade or equivalent, and where appropriate were treated with molecular sieves to ensure dryness. The water used was triple distilled from an all glass apparatus.

The method of packing the tubes was as reported in the literature (Studebaker & Snow 1955). Tubes of 15 cm length with a uniform internal diameter of 1.0 cm were coated on the inner surface with the hydrophobic material, dimethyldichlorosilone, to prevent preferential wetting of the glass and hence the powder nearest the tube wall. The prepared tubes were clamped vertically and illuminated with a fibre optic cold light source, thus preventing uneven flow due to the heating of the penetrating liquid. A saturated solution of the solid in the liquid, was added from a burette, and the time taken for the liquid front to reach various points through the bed was measured (temperature was  $20 \pm 1^\circ\text{C}$ ). A digital readout travelling cathetometer was used to observe the liquid front and measure the distance moved. If the liquid passage was not uniform, poor packing was suspected and the result was rejected. A minimum of six and a maximum of ten replicates were performed for each liquid. The viscosities of the liquids were measured at  $20 \pm 0.05^\circ\text{C}$  with a U-tube viscometer, and their densities measured with a Parr digital densitometer (DMA 35). Surface tensions were measured with a Wilhelmy plate and results quoted are averages of at least five determinations (Table 1).

Table 1. Physical properties of liquids saturated with amylobarbitone, rate data for penetration of various liquids into a bed of amylobarbitone, and the value of  $\cos \theta$  obtained using equation 1.

Liquid used	$\gamma$ ( $\text{mNm}^{-1}$ )	Viscosity ( $\text{mNsm}^{-2}$ )	Gradient of $P^2 t^{-1}$	Corr coef.	$\cos \theta$
Hexane	19.9	0.3162	0.3055	0.999	0.6573
Cyclohexane	27.8	1.1188	0.1170	0.999	0.6376
Octane	23.1	0.6774	0.2141	0.999	0.8502
Toluene	29.3	0.5955	0.1757	0.999	0.4836
Methanol	25.9	1.5250	0.1086	0.999	0.8659
Ethanol	25.4	2.4066	0.0515	0.999	0.6608
Propanol	26.2	3.5330	0.0344	0.999	0.6282
Butanol	26.2	5.1729	0.0295	0.999	0.7914
Pentanol	27.5	5.5956	0.0229	0.999	0.6309
Hexanol	27.7	6.6611	0.0210	0.999	0.6176
Ethyl Acetate	27.0	0.7118	0.1184	0.998	0.4227
Isopropyl- Alcohol (IPA)	25.0	3.9744	0.0354	0.999	0.7621
50% IPA	28.6	4.1192	0.0472	0.999	0.9206
40% IPA	29.2	3.5466	0.0608	0.999	1.0000
30% IPA	30.7	2.9186	0.0476	0.998	0.6128
25% IPA	32.7	2.5628	0.0404	0.998	0.4288
20% IPA	36.0	2.1824	0.0395	0.999	0.3242
15% IPA	39.0	1.7837	0.0322	0.998	0.1944
10% IPA	43.2	1.5159	0.0221	0.998	0.1050
30% Ethanol	38.0	2.3240	0.0400	0.999	0.3561
25% Ethanol	40.4	2.3491	0.0350	0.999	0.2750
20% Ethanol	43.0	1.9460	0.0310	0.999	0.1900
17% Ethanol	43.7	1.7643	0.0250	0.999	0.1367
15% Ethanol	45.9	1.6605	0.0200	0.999	0.0980
12% Ethanol	45.5	1.5088	0.0150	0.999	0.0674

## RESULTS AND DISCUSSION

### Choice of perfectly wetting liquid

When the equation of Studebaker & Snow (1955) (eqn 1) is to be applied, it is necessary to have a perfectly wetting liquid with which to compare the values for the liquid of unknown wetting properties. It was suggested (Studebaker & Snow 1955), that if the results for any two liquids when substituted into equation 1, yielded a value of one for  $\cos \theta$ , they should be assumed to be perfectly wetting. This is on the basis that it is more probable that two liquids showing the same degree of wetting on the powder are in fact both perfectly wetting, than both partially wetting to the same extent. In this particular work it was not possible to describe any one liquid as perfectly wetting, thus it was necessary to look at the possible magnitude of error that could be introduced in the calculated value of the contact angle, by assuming that the *best* wetting liquid was perfectly wetting. To study this, the values obtained from the determinations on a selection of liquids which ranged from that which gave the best wetting performance (40% isopropyl alcohol in water) to the worst wetting performance (ethyl acetate) were substituted into eqn 1 as the perfectly wetting liquid. For each liquid, values of  $\cos \theta$  were determined for the ethanol-water and the isopropyl alcohol-water dilution series, and in each case the plot of  $\cos \theta$  against % alcohol was extrapolated to zero alcohol concentration, and a theoretical value of  $\theta$  for water obtained (Table 2). As the maximum variation in the calculated value of the contact angle is only 13 degrees between the best wetting liquid and the worst wetting pure liquid studied, it is clear that the choice of the perfectly wetting liquid is not too critical when such an extrapolation technique is used. Therefore, for the rest of this work 40% isopropyl alcohol in water was taken as a perfectly wetting liquid for amylobarbitone. Table 3 shows the values of  $\theta$  obtained when different solvents were assumed to be perfectly wetting, together with the value of  $\cos \theta$  obtained for each of the solvents when 40% isopropyl alcohol is taken as perfectly wetting.

### Extrapolation techniques

With many hydrophobic powders, such as amylobarbitone, spontaneous penetration of water into the powder bed will not occur. To obtain an indication of the contact angle of water on the powder an extrapolation technique may be employed. The most suitable method would be to use a homologous series of pure liquids, such as the straight chain alcohols, and then extrapolate to a theoretical state of zero

Table 2. Values of  $\cos \theta$  obtained using various liquids as the 'perfectly wetting' liquid, and using the two alcohol-water extrapolation series as the other liquid, in equation 1.

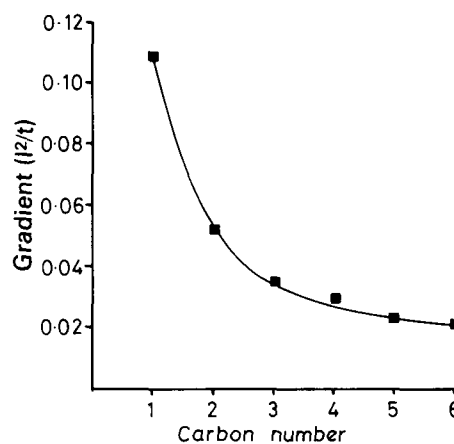
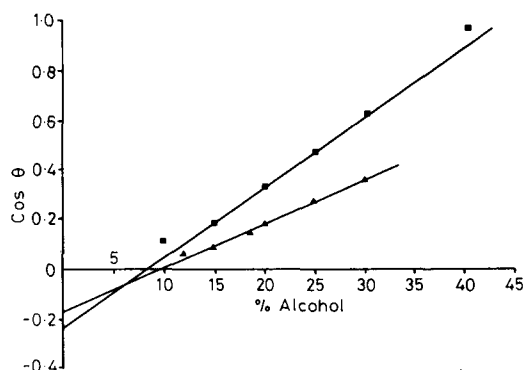
Other liquid	Perfectly wetting liquid						
	40% IPA	Ethyl acetate	Toluene	Cyclohexane	Butanol	Methanol	100% IPA
25% Ethanol	0.2750	0.6520	0.5699	0.4322	0.3488	0.3183	0.3616
20% Ethanol	0.1900	0.4495	0.3929	0.2979	0.2405	0.2194	0.2493
17% Ethanol	0.1367	0.3234	0.2826	0.2144	0.1730	0.1578	0.1793
15% Ethanol	0.0980	0.2318	0.2026	0.1557	0.1230	0.1132	0.1286
Intercept*	-0.1642	-0.3909	-0.3417	-0.2590	-0.2091	-0.1908	-0.2168
30% IPA	0.6128	1.4498	1.2672	0.9611	0.7756	0.7077	0.8041
25% IPA	0.4288	1.10143	0.8867	0.6724	0.54276	0.4952	0.5626
20% IPA	0.3242	0.7672	0.6706	0.5086	0.4104	0.3745	0.4255
15% IPA	0.1975	0.4718	0.4124	0.3128	0.2524	0.2303	0.2617
Intercept	-0.2219	-0.5057	-0.4420	-0.3352	-0.2706	-0.2469	-0.2771

\* When values of  $\cos \theta$  are plotted as a function of % ethanol, the intercept corresponding to 0% ethanol has been taken as  $\cos \theta$  for water.

Table 3. The rank order of the estimates of  $\theta$  obtained from the values of  $\cos \theta$  for water (taken as the intercept in Table 2) and values of  $\cos \theta$  obtained for each solvent using 40% isopropyl alcohol as the perfectly wetting liquid.

Liquid taken as 'perfectly wetting' from Table 2	$\theta$ calc from IPA extrapolation	$\theta$ calc from ethanol extrapolation	$\cos \theta$ if 40% IPA is taken as 'perfect wetting'
40% IPA	102.8	99.5	1.0000
Methanol	104.3	101.0	0.8659
Butanol	105.7	102.1	0.7901
100% IPA	106.1	102.5	0.7621
Cyclohexane	109.6	105.0	0.6376
Toluene	116.2	110.0	0.4836
Ethyl acetate	120.4	113.0	0.4227

carbon number. With a series of alcohols, the extrapolation of the plot of the gradient of the square of the distance of penetration ( $l^2$ ) as a function of time ( $t$ ), as a function of carbon number of the alcohol, to the theoretical zero carbon number, could not be made (Fig. 1). It was also impossible to extrapolate the graph of  $\cos \theta$  for the alcohols, as a function of carbon number, to a zero carbon number. Owing to these problems with an homologous pure liquid system, use of binary liquid mixtures was considered. Theoretical problems arise because of the complex nature of the system, as well as the possibility of the liquids partitioning at the solid liquid interface during the penetration process. The straight line portions of the ethanol-water, and the isopropyl alcohol-water mixtures, when plotted as % alcohol as a function of  $\cos \theta$ , were extrapolated to 0% alcohol (Fig. 2). The use of extrapolation on two different organic liquid-water mixtures provides a check on the validity of the results and it is notable that despite the theoretical concern about the process, both alcohol-water systems yield approxi-

Fig. 1. The gradient of the plot of distance of penetration squared ( $l^2$ ) as a function of time ( $t$ ), as a function of the carbon number of the straight chain alcohols.Fig. 2. Apparent  $\cos \theta$  as a function of % alcohol.  $\blacktriangle$  = ethanol-water. For straight line portion correlation = 0.995, intercept = -0.165,  $\theta = 99.5$ .  $\blacksquare$  = isopropyl alcohol-water. For straight line portion correlation = 0.993, intercept = -0.222,  $\theta = 102.8$ .

mately the same value of  $\theta$ , the ethanol extrapolation giving 99.5, and the isopropyl alcohol extrapolation 102.8.

#### Modified Zisman plots

In discussion of the wetting of solids in terms of surface energy, the term critical surface tension ( $\gamma_c$ ) is often used as a characteristic of the solid. Originally, this was determined as a plot of  $\cos \theta$  as a function of the surface tension of a series of liquids ( $\gamma_{LV}$ ), extrapolating to a value of  $\cos \theta = 1$  (Fox & Zisman 1950). Good (1980) noted that  $\cos \theta$  as a function of  $\gamma_{LV}^{-1/2}$  is more appropriate. There must be considerable concern in that the values of  $\cos \theta$  obtained for the pure solvents in this work do not yield a straight line when plotted in such a manner. Both solvents in the alcohol-water series form such a plot (Fig. 3) and both yield almost identical values of

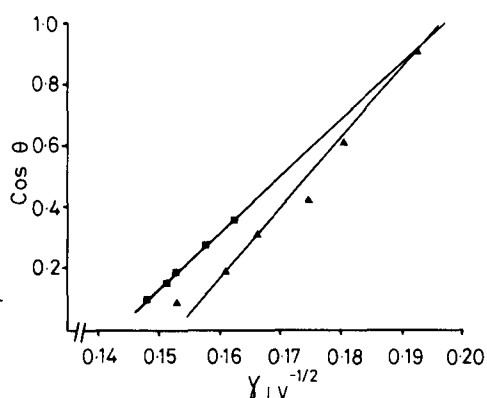


FIG. 3. Modified Zisman Plot,  $\cos \theta$  as a function of  $\gamma_{LV}^{-1/2}$ ;  $\blacktriangle$  = ethanol-water,  $\blacksquare$  = isopropyl alcohol-water.

$\gamma_c$  when the best line of fit has been calculated, the ethanol series giving  $25.7 \text{ mN m}^{-1}$  and the isopropyl alcohol series giving  $26.0 \text{ mN m}^{-1}$ . These findings are supported by the work of Hansford et al (1980), who reported that a pharmaceutical powder (griseofulvin) of similar hydrophobicity to amylobarbitone, yielded values of 92.8 to 101.9 for  $\theta$  by a liquid penetration technique, and  $20\text{--}30 \text{ mN m}^{-1}$  for  $\gamma_c$ , calculated from an ethanol-water dilution series.

#### Limitations of the Washburn equation

The failure to be able to produce a modified Zisman plot for the pure liquids suggests that the Washburn equation (eqn 2) does not fully describe the process. Carli & Simioni (1979) proposed an explanation of

the limitations of the Washburn equation, the usual form of which is

$$l^2 = \frac{R \gamma_{LV} \cos \theta t}{2\eta} \quad (2)$$

(where  $R$  = capillary radius).

As the volume of penetrated liquid is directly proportional to penetration length (Washburn 1921), eqn 2 can be written as

$$V = k^m t^m \quad (3)$$

(where  $V$  = volume of penetrated liquid, and  $k$  and  $m$  are constants). For equation 2 to be valid,  $m$  must equal 0.5. Schicketanz (1974), and Carli & Simioni (1977, 1979) have shown that this is not always so. Re-presentation of equation 3 as

$$\log V = m \log K + m \log t \quad (4)$$

makes it possible to obtain the value of  $m$  from a double logarithmic plot of the distance of penetration as a function of time. Such plots have been produced for the pure alcohols and the two dilution series, and values of  $m$  are presented in Table 4. It is

Table 4. Gradients of the double logarithmic plots of penetration as a function of time for the pure alcohols, and the alcohol-water mixtures. Correlation coefficients were 0.999 for each graph.

Penetrating liquid	Gradient	Penetrating liquid	Gradient
Methanol	0.495	20% ethanol	0.604
Ethanol	0.546	25% ethanol	0.530
Propan-1-ol	0.495	10% IPA	0.617
Butanol	0.509	15% IPA	0.504
Pentanol	0.520	20% IPA	0.474
Hexanol	0.520	25% IPA	0.495
12% ethanol	0.596	30% IPA	0.508
15% ethanol	0.579	40% IPA	0.548
17% ethanol	0.619	50% IPA	0.496

clear that the assumption of Washburn (1921) holds true, particularly in the case of the pure alcohols, as  $m$  is approximately equal to 0.5.

It seems therefore that the Washburn equation (1921) does hold true in the present work, and may offer a theoretical explanation of the penetration process. However, there seems to be a further limitation to the equation to prevent application to modified Zisman plots for pure liquids.

#### CONCLUSIONS

If data obtained from experiments involving liquid penetration are to be used to determine contact angles, it must be assumed that measurements of the movement of the solvent front, are measurements of

the three phase interface. That is, the vapour phase has already passed ahead of the solvent front to wet the powder. If such vapour phase wetting has not occurred, it is unlikely that  $l^2$  as a function of  $t$  will yield a straight line. This fact can be observed in the work of Cook (1978) who found that penetration of dimethylformamide into a bed of griseofulvin would not produce a linear relation, unless the bed had been previously saturated with vapour.

The results we obtained in the present work proved to be reproducible, and yielded straight lines for  $l^2$  as a function of  $t$ , with correlation coefficients in the region of 0.999, consequently it would appear that the fundamental Washburn relationship does apply for all the liquids studied.

It can be concluded that values of  $\theta$  for water on a hydrophobic powder cannot be obtained from extrapolation of the carbons of a series of straight chain alcohols to a point of zero carbon number, also it is not possible to obtain a value of  $\gamma_c$  from a modified Zisman plot with such liquids.

The use of alcohol-water binary liquid systems does allow a value of  $\theta$  and  $\gamma_c$  to be obtained, and, despite reservations about such systems, the results are numerically in the correct order of magnitude.

Application of a liquid penetration technique employing alcohol-water mixtures for the assessment of surface energy of a pharmaceutical powder, may be limited for very hydrophilic drugs, owing to high solubilities leading to viscous solutions which

will not penetrate the powder bed. However, for such drugs, spontaneous penetration of a saturated solution in water is likely to occur and thus a value for surface energy could be obtained directly.

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