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The extent of the errors associated with contact angles obtained using liquid penetration experiments

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Summary

Assessment of values for the contact angles of powders is important in many pharmaceutical processes, and the use of surface energy data estimated from contact angle determinations is gaining in popularity. Liquid penetration experiments offer one approach to obtaining an estimate of wettability, and its use continues despite practical and theoretical criticisms. This paper examines the sources and magnitude of errors that are associated with the estimate of wettability that is derived by use of the Washburn model and equation, for model particles (polymer coated glass spheres). It is necessary to ascribe one liquid as perfectly wetting and to compare the behaviour of the test liquid (for which the finite wettability is to be determined) to that of this defined liquid. The following conclusions were made: (1) the major source of error is in the measurement of penetration rates through the powder bed, with surface tension and viscosity data being far more reproducible; (2) the choice of the perfectly wetting liquid is not too critical if the test liquid wets reasonably well, but is far more important if the test liquid has a low contact angle; (3) the error in cos θ, when expressed as a percentage of the mean, was in the range of 2–6%, this being the accuracy of the experiment; (4) if the results were transformed to θ (rather than cos θ) then the error no longer reflected the accuracy of the experiment, but rather the magnitude of the contact angle, as equal changes in cos θ will result in unequal changes in θ (low contact angles showing more apparent error than large), thus it is more appropriate to quote accuracy in the cos θ domain for liquid penetration results, rather than converting to θ.

Introduction

The assessment of the wettability of pharmaceutical powders is fraught with difficulties, as a consequence of the absence of a smooth flat surface on which to make a measurement. Indirect approaches to contact angle measurements fall into two categories, these being methods involving the penetration of liquid into a loosely packed powder bed, and those in which angles are measured on a compact of the powder.

Buckton and Newton (1986a) expressed concern that the process of forming a compact can result in changes in the surface (e.g., due to plastic deformation), and thus the contact angle so measured may not relate to the properties of the original powder: factors such as surface

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roughness and porosity may also affect the results.

Liquid penetration experiments are not without problems, these include practical difficulties associated with achieving aqueous penetration into beds of hydrophobic powders (this is often circumvented by the use of binary liquid mixtures, and extrapolations to a notional behaviour for water; the validity of such experiments is questionable (see Buckton and Newton, 1985, 1986b)). Reservations also exist concerning the theoretical basis for liquid penetration experiments in which the assumption is made, based on the Washburn equation (1921), that the packed powder bed can be considered as a bundle of parallel capillaries. The validity of this model has been investigated experimentally by Yang and Zografi (1986), Yang et al. (1988) and Fisher and Lark (1979). Yang et al. (1988) demonstrated that the use of this model (i.e., the Washburn equation or its derivatives) is indeed flawed. However, it is often argued, when the powder(s) under investigation are ultimately to be used in their uncompressed form (e.g., in the process of wet granulation), that liquid penetration experiments are to be preferred to those on compressed samples (e.g., Wells and Walker, 1983).

The accurate measurement of contact angles of liquids on powders is of great importance, particularly in view of recent publications which demonstrate the value of surface energetics (estimated from contact angle data) in predicting the behaviour of drugs, excipients and their combinations (e.g., Rowe, 1990). Currently, pharmaceutical scientists and powder technologists who require a value for a contact angle have to select either a compressed powder or a penetration method, despite reservations about these techniques; consequently, they will continue to be used and therefore it remains necessary to investigate the experimental yield and its significance.

In this study the major sources of error, and the extent of propagation of such error in data manipulation, will be considered for model particles which exhibit finite contact angles in the range of 0–90°.

Materials and Methods

Solids

Spherical glass beads were chosen as model particles since they allowed the surface energy of the system to be varied without altering the packing geometry of the particles. The glass beads were monodisperse ballotini (Jencons, size 18) containing less than 20% irregular shaped particles, with a mean diameter of 66 μm. Particles with two surface energies were created by coating the ballotini with hydroxypropyl methylcellulose (HPMC) (Sigma, 2% aqueous solution at 25°C would produce a solution with a viscosity of approx. 100 cp) and polyvinylpyrrolidone (PVP) (BDH; viscosity of a 5% aqueous solution at 25°C, 2.4 cp; molecular weight, approx. 44 000) in a fluidised bed coater (Aeromatic) using a 1% aqueous solution of the coating material.

TABLE 1

Surface tension and viscosity for various liquids at 20°C

Liquid	Surface tension (mN/m)	Percent error	Viscosity (cp)	Percent error
Octane	21.25 ± 0.05	0.25	1.240 ± 0.002	0.16
Cyclohexane	23.81 ± 0.06	0.24	0.567 ± 0.0002	0.04
Ethanol	21.76 ± 0.07	0.32	1.018 ± 0.0005	0.05
Glycerol	60.22 ± 0.21	0.35	1,222 [a]	
Ethanediol	48.38 ± 0.10	0.21	19.90 ± 0.01	0.05
Propanediol	35.53 ± 0.11	0.30	58.10 ± 0.09	0.15
Diiodomethane	50.05 ± 0.11	0.21	2.820 ± 0.0001	0.04

[1] Figure from C.R.C. Handbook.

Liquids

The probe liquids were glycerol, propanediol, ethanediol (all from Sigma), diiodomethane, cyclohexane (both Aldrich), octane (Koch Light) and ethanol (Burridge). The surface tensions of the liquids were measured using a Cahn microbalance (Cahn contact angle analyser, model 312) and are given in Table 1.

Contact angle measurements

The experimental procedure was carried out as described by Buckton and Newton (1985). Tubes of 10 cm length with a uniform internal diameter (0.5 cm) were coated on the inner surface with dimethyldichlorosilane to render them hydrophobic, and thus prevent preferential wetting of the glass and hence the powder nearest the tube wall. The tubes were packed using the method reported by Studebaker and Snow (1955). A minimum of six replicates were carried out for each liquid. The viscosities of the liquids were measured at 20 ± 0.5°C with a U-tube viscometer, and their densities were assessed using a specific gravity bottle.

An important consideration during liquid penetration experiments is the problem of dissolution of the solid in the penetrating liquid, thus it is conventional to use saturated solutions. With HPMC and PVP it is obvious that saturated solutions are not acceptable due to extreme viscosity. In this work the penetration rates were extremely rapid (compared to powdered systems), perhaps due to the comparatively large size and the uniform packing, and the plots of distance of penetration squared as a function of time were very straight (correlation coefficients tending to unity), thus it was assumed that the polymers did not dissolve to any significant extent at the wetting front, and that no significant changes in either surface tension or viscosity occurred at the wetting front (as these could be expected to result in deviation from a linear penetration plot).

TABLE 2

Gradients of the plot of (length of penetration) ^{2} *with time for various liquids through packed beds of HPMC or PVP coated glass ballotini*

Liquid	HPMC-coated		PVP-coated	
	l^2/t (mm^2 s^{-1})	Percent error	l^2/t (mm^2 s^{-1})	Percent error
Octane	8.37×10^{-4} $\pm 1.6 \times 10^{-5}$	1.91	9.19×10^{-2} $\pm 1.7 \times 10^{-3}$	1.85
Cyclohexane	5.73×10^{-4} $\pm 1.0 \times 10^{-5}$	1.75	6.20×10^{-2} $\pm 1.7 \times 10^{-3}$	2.74
Ethanol	4.25×10^{-2} $\pm 8.4 \times 10^{-4}$	1.98	3.93×10^{-2} 6.9×10^{-4}	1.76
Glycerol	9.18×10^{-6} $\pm 1.9 \times 10^{-7}$	2.07	–	–
Ethanediol	2.48×10^{-3} $\pm 3.3 \times 10^{-5}$	1.33	2.85×10^{-3} $\pm 4.6 \times 10^{-5}$	1.61
Propanediol	8.37×10^{-4} $\pm 1.4 \times 10^{-5}$	1.67	7.73×10^{-4} $\pm 1.6 \times 10^{-5}$	2.07
Diiodo-methane	2.64×10^{-2} $\pm 6.6 \times 10^{-4}$	2.50	3.49×10^{-2} $\pm 6.6 \times 10^{-4}$	1.89

Results

The results in Table 1 list the surface tensions and viscosities that were measured for the test liquids, the standard deviations, and the standard deviation expressed as a percentage of the mean. The reproducibility of both the surface tension and the viscosity results was very good, with the standard deviation as a percentage of the mean not exceeding 0.35 and 0.16, respectively. Assuming that all workers have the facility to measure these physical properties to this degree of accuracy, then it is likely that the major source of error will be associated with measurements of penetration rates.

The penetration data all produced good fits to lines of distance of penetration (l) squared as a function of time (t), however, this should not be taken to imply validity of the Washburn equation (see Yang and Zografi, 1986). Data for the penetration into beds of HPMC and PVP coated particles are collated in Table 2. It can be seen that values for the standard deviations as a percentage of the mean range from 1.33 to 2.74. The values of cos θ and θ have been calculated as described above, using octane, cyclohexane and ethanol in turn as the 'perfectly wetting liquid' and are presented in Tables 3 and 4. The standard deviations for surface tension, viscosity and rate of

TABLE 3

Mean and worst cases of cos θ and θ for various liquids on HPMC using (a) octane as the perfectly wetting liquid; (b) ethanol as the perfectly wetting liquid; (c) cyclohexane as the perfectly wetting liquid

Liquid	cos θ			
	Mean value	Maximum value	Minimum value	Error (±%)
(a) Glycerol	0.087 (85.0°)	0.091 (84.8°)	0.084 (85.2°)	3.4
Ethanediol	0.477 (61.5°)	0.491 (60.6°)	0.466 (62.2°)	2.3
Propanediol	0.641 (50.1°)	0.663 (48.4°)	0.620 (48.8°)	3.4
Diiodomethane	0.698 (45.7°)	0.727 (43.3°)	0.671 (47.7°)	4.2
(b) Glycerol	0.079 (85.4°)	0.083 (85.2°)	0.076 (85.6°)	5.1
Ethanediol	0.434 (64.3°)	0.450 (63.3°)	0.420 (65.1°)	3.7
Propanediol	0.583 (50.2°)	0.607 (52.6°)	0.559 (56.0°)	4.1
Diiodomethane	0.636 (50.5°)	0.666 (48.2°)	0.605 (52.8°)	4.7
(c) Glycerol	0.079 (85.4°)	0.084 (85.2°)	0.076 (85.6°)	6.3
Ethanediol	0.435 (64.2°)	0.452 (63.1°)	0.421 (65.1°)	3.9
Propanediol	0.584 (54.3°)	0.610 (52.4°)	0.560 (56.0°)	4.5
Diiodomethane	0.636 (50.5°)	0.671 (47.9°)	0.605 (52.7°)	5.5

penetration have been selectively added to, or subtracted from the mean values for the test liquids and the perfectly wetting liquids in order to determine the maximum and minimum values for cos θ and θ that are consistent with the range of experimental error. These maximum and minimum values are presented in Tables 3 and 4, together with an error term which expresses the experimental range as a percentage of the mean.

Discussion

Choice of perfectly wetting liquid

The choice of perfectly wetting liquid is never straightforward in liquid penetration experiments (see Buckton and Newton, 1986b), and the extent to which an inappropriate choice will influence results is not fully understood. A comparison of the data in Table 3a–c reveals that for HPMC-coated particles, there is a high probability that both cyclohexane and ethanol are perfectly wetting (on the basis that the almost identical contact angle results are far more likely to be due to them both being perfectly wetting, rather than them showing partial wetting to an identical extent); octane, by comparison, yields different contact angle values if used as perfectly wetting, and thus octane probably has a finite contact angle with HPMC. The absolute extent of the error, in terms of contact angle, that is introduced by using octane as the perfectly wetting liquid (rather than either ethanol or cyclohexane) for HPMC is dependent upon the extent of wetting achieved by the test liquid. If the contact angle for the test liquid is high (e.g., glycerol) then the choice of perfectly wetting liquid is almost inconsequential (cos θ range of 0.008, Table 3a), however, if the test liquid has a low contact angle (e.g., di-

TABLE 4

Mean and worst cases of cos θ and θ for various liquids on PVP using (a) octane, (b) ethanol and (c) cyclohexane as the perfectly wetting liquid

Liquid	cos θ			
	Mean value	Maximum value	Minimum value	Error (± %)
(a) Ethanediol	0.499 (60.1°)	0.519 (58.7°)	0.480 (61.3°)	4.0
Propanediol	0.540 (57.3°)	0.564 (55.7°)	0.516 (58.9°)	4.4
Diiodomethane	0.841 (32.7°)	0.877 (28.7°)	0.806 (36.3°)	4.3
(b) Ethanediol	0.540 (57.3°)	0.562 (55.8°)	0.519 (58.7°)	4.1
Propanediol	0.584 (54.3°)	0.601 (52.4°)	0.558 (56.1°)	2.9
Diiodomethane	0.910 (24.5°)	0.948 (18.5°)	0.872 (29.3°)	4.2
(c) Ethanediol	0.461 (62.6°)	0.484 (61.1°)	0.439 (63.9°)	5.0
Propanediol	0.498 (60.1°)	0.526 (58.3°)	0.472 (61.8°)	5.6
Diiodomethane	0.776 (39.1°)	0.817 (35.2°)	0.738 (42.4°)	5.3

iodomethane) then the error is more significant (cos θ range of 0.066, Table 3a). With the PVP-coated beads, the results indicate that either none, or at most only one, of the liquids is perfectly wetting. All that can be reported with confidence is that cyclohexane has the lowest contact angle of the three tested. The principle that was noted for HPMC is also true for PVP, in that the difference in cos θ for ethanediol as a result of using the different perfectly wetting liquids is 0.041 (Table 4a), but for the test liquid with the lowest contact angle (diiodomethane) it is 0.068 (Table 4a). Thus, it can be concluded that the choice of perfectly wetting liquid is most critical if contact angles are required for test liquids that wet the sample well.

From Table 3, it can be seen that the worst case is that the error in cos θ can be as high as 0.643 (equivalent to a 24° variation in contact angle), if the error induced by choice of perfectly wetting liquid is added to that of conventional experimental errors (this is calculated as a difference between the highest and lowest values of cos θ that were calculated, i.e., 0.727 and 0.084 in Table 3a).

Errors associated with quoting results as contact angles

From Table 3a–c, it is clear that as the value of cos θ tends towards unity, the size of the error increases (in absolute terms). For example, for HPMC, the error (taken as half the difference between the maximum and minimum values) in cos θ for glycerol is approx. ± 0.004 around a mean of about approx. 0.08 (Table 3a–c), but for diiodomethane the error is in the order of ± 0.04 around a mean of approx. 0.65 (values vary depending upon the choice of the perfectly wetting liquid), i.e., the error is an order of magnitude greater (in absolute terms) for the diiodomethane. This observation is also true for the contact angle values; for high contact angles, e.g., glycerol on HPMC, the result is good to $\pm 0.2°$, but for diiodomethane, which has a low contact angle on HPMC the error is $\pm 2.2°$. Although both of these errors are acceptably low (probably due in part to the idealised model system, consisting of perfect spheres rather than less regular powders) the trend is consistent; in all cases the error increases (in absolute terms) as cos θ tends to unity (and θ tends to zero). It is interesting, however, to investigate any trends in the errors in relative, rather than absolute, terms.

The percentage spread in cos θ is presented in Table 3a–c. It is apparent that, although the errors that are observed in cos θ increase in absolute terms as the value approaches unity, the percentage error in cos θ does not follow this trend, as all results are in the approximate range of 2–5% error (irrespective of the magnitude in cos θ).

Although the percentage error in cos θ is directly related to the percentage errors of the relevant penetration values, this is not true for the error in θ. The overriding factor in determining the error in the contact angle is not the experimental error, but the magnitude of the angle. The following example can be used to illustrate this point: for diiodomethane on PVP (using ethanol as the perfectly wetting liquid, Table 4b) the percentage error in cos θ is 4.2, but the error in the contact angle is almost 22% (calculated as the difference between the maximum and minimum values divided by two (giving the error) and then expressing this value as the percentage of the mean), whilst for ethanediol the percentage error in cos θ is almost identical (4.1), but the error in the contact angle is only 2.5%. This is simply due to the shape of the cosine curve, which results in an identical change in cos θ producing different changes in θ, depending upon the gradient of the cosine curve at that point. Thus, to quote a value for a contact angle, and state that it is accurate to ± a number of degrees, does not necessarily reflect the accuracy of the experiment, but rather the magnitude of the angle. It is, therefore, perhaps more appropriate to work in the more useful cos θ values (rather than θ), and to quote the accuracy of such.

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