The use of the Washburn method in determining the contact angles of lactose powder

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Summary

This paper studies the contact angles of lactose powder determined by the Washburn method based on liquid intrusion into the powder bed. The liquids used were water, methanol, 1-propanol, 1-butanol, 1-octanol and n-hexane. Liquid intrusion was studied with saturated solutions. Liquid flow to the powder column was controlled with a technique allowing constant liquid flow with zero hydrodynamic pressure. Packing of the lactose powder into glass tubes was done manually by tapping in a vertical motion. The packing of the powder columns was studied with different packing times (3, 6 and 12 min) and different size fractions ($> 212~\mu$m, 106–$212~\mu$m and $< 106~\mu$m) of lactose. Packing time was not found to be critical with optimal shaped lactose particles and the shortest packing time, 3 min, was adequate. Liquid intrusion rate diminished with diminishing particle size. The intrusion rates of the liquids varied significantly. The slope values of intrusion distance squared vs intrusion time were 0.798 (n-hexane), 0.414 (methanol), 0.179 (water), 0.123 (1-propanol), 0.099 (1-butanol) and 0.036 (1-octanol). n-Hexane was found to be the best wetting liquid. Estimating the n-hexane contact angle to be 0°, the following values for the other liquids were obtained: water 61.7°, methanol 38.7°, propanol 39.2°, butanol 33.4° and octanol 36.2°.

Introduction

The wettability of a solid material is important in pharmaceutical technology when considering the manufacturing processes and the properties of the end product (Nogami et al., 1966; Rowe,

1990). Wetting of a solid is required in granulation, pelletization and tablet coating. Wetting is also important in disintegration and dissolution of solid dosage forms. The contact angle has usually been used in characterizing the wettability of pharmaceuticals (Buckton and Newton, 1986a; Lippold and Ohm, 1986).

Typically the contact angles have been determined from systems having a more or less smooth surface by the sessile drop method (Zografi and Tam, 1976; Ohm and Lippold, 1985). In practice

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this requires compression of the powder to a tablet. These results cannot be used to characterize the wettability of the powders as the compression process can dramatically alter the physical properties of the particles resulting in a different type of surface (Buckton and Newton, 1986b; Kiesvaara and Yliruusi, 1991b). Because powders are the usual raw materials in pharmaceutical technology it is important that the analysis result has an emphasis on powder characteristics.

Washburn (1921) introduced the basic theory for determining the contact angle of a liquid and a solid from liquid intrusion data. After that many different methods for assessing the wettability of a powder have been presented and discussed in literature (Lerk et al., 1976; Stamm et al., 1984; Buckton et al. 1986, 1987; Buckton 1988, 1990; Buckton and Beezer, 1988; Kaya and Koishi, 1988). Despite the limitations of Washburn method (Carli and Simioni, 1979; Buckton and Newton, 1985, 1986a; Yang and Zografi, 1986) it is used extensively in the assessment of wettability, being low-cost and the measuring system easy to assemble. The powder column can be placed either into a vertical or a horizontal position. In the vertical position liquid intrusion can occur either upwards or downwards (Studebaker and Snow, 1955; Hansford et al., 1980).

In this study we will describe the use of the Washburn method in contact angle determinations, and generally evaluate the suitability of the method in pharmaceutical powder technology.

Materials and Methods

Materials

The material used was lactose (Ph. Eur.). A fraction of 100–300 μm (Orion-Farmos Pharmaceuticals) was used in packing and liquid intrusion studies. Three sieve fractions; greater than 212 μm, 106–212 μm and smaller than 106 μm, were used to study the liquid intrusion rate into the powder columns. The intrusion was determined with six liquids. Of the liquids, methanol, 1-propanol, 1-butanol, 1-octanol and n-hexane were p.a. grade. The water was triple distilled.

Solutions saturated with lactose were prepared and used in intrusion studies in order to avoid breaking of the powder column structure due to dissolution.

To minimize differences between the powder particle surfaces in different measurements, lactose powder was stored in a standard humidity atmosphere ($20 \pm 2°C$, $53 \pm 1\%RH$) for 24 h prior to liquid intrusion studies. The standard atmosphere was formed in an exsiccator with saturated sodium dichromate solution ($Na_2Cr_2O_7 \cdot 2H_2O$, J.T. Baker).

Methods

The morphological characterization of the material was made by scanning electron microscopy (Jeol JSM-840A, Japanese Electron Optical Ltd, Tokyo, Japan). Crystal properties of lactose were studied by X-ray powder diffraction (XRPD) (Siemens 500D, Siemens AG, Karlsruhe, Germany). The measuring parameters were: tube voltage 40 kV and CuKα radiation (1.541 Å). Measuring speed was 1°/min. The particle size distribution was determined by the laser diffraction method (Series 2600c Droplet And Particle Sizer, Malvern Instruments, Malvern, U.K.); the specific surface area was measured by the nitrogen gas adsorption method (BET, single point) (Flowsorb II 2300, Micromeritics Instrument Corporation, Norcross, GA, U.S.A.). The surface tensions of the liquids were determined with a surface tension balance (Digital Tensiometer Krüss K10T, Krüss GmbH, Hamburg, Germany) using the ring method. The kinematic viscosities of the liquids were measured by capillary viscosimetry (Ubbelohde Microviscosimeter, Schott Geräte GmbH, Germany). The densities of the liquids were determined by accurately weighing 25.0 ml of the liquid. The dispersion and polar components of the liquids were calculated with the geometric-mean method (Wu, 1973; Ohm and Lippold, 1985) using a computer program described elsewhere (Kiesvaara and Yliruusi, 1991a). The contact angles of the liquids were measured on a solid paraffin surface with an experimentally assessed surface free energy of 24.3 mN/m (Nurminen et al., 1991).
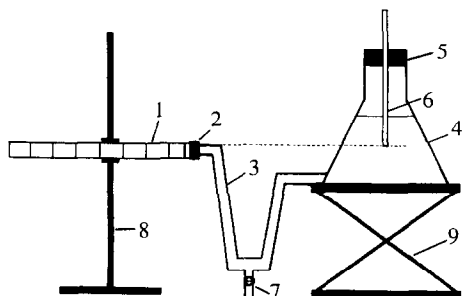
Fig. 1. Diagram of the equipment. See text for corresponding numbers.

Washburn equipment

A diagram of the Washburn equipment is presented in Fig. 1. The equipment has two major parts: the horizontal sample tube packed with powder, and the liquid reservoir with flow control. The Washburn tube (1) made of glass with length of about 200 mm and internal diameter of 10 mm was heat siliconized in order to make the surface hydrophobic. A millimeter scale from 0 to 150 mm was engraved on the tube. The other end of the tube was closed with a glass sinter (2), pore size 160–200 μm (No. 0). A silicone rubber tube (3) with a diameter of 5 mm connected the Washburn tube to the liquid reservoir (4). The glass reservoir was closed with a rubber stopper (5) penetrated by a glass capillary tube (6). The lower end of the glass capillary tube was adjusted to the level of the upper side of the powder column. As the liquid flows from the reservoir, the glass tube supplies air to compensate for the volume of the used liquid. This arrangement reduces the hydrostatic pressure to zero at the level of the lower end of the glass capillary tube. Thus the liquid flow into the powder bed is free and controlled only by the capillary forces in the powder bed.

A valve (7) was added to the tube to allow for the rapid formation of the equilibrium hydrostatic pressure right from the beginning of the liquid intrusion. A laboratory stand (8) was used to hold the Washburn tube. The liquid reservoir was placed on an adjustable laboratory tray (9) to facilitate the vertical alignment.

Packing of the columns

The packing of lactose powder into the glass tubes was made by manually tapping in a vertical

motion using an amplitude of 10 ± 2 mm and a frequency of 190 ± 5 taps per min. Packing times of 3, 6 and 12 min were used. The number of repetitions was six.

Powder contact angle measurements

Liquid penetration in the powder bed was monitored by recording the length of the liquid front intrusion as a function of time. The basic equation of the Washburn technique is (Washburn, 1921):

$$l^2 = \frac{\gamma \times \cos \Theta \times r \times t}{2 \times \eta} \qquad (1)$$

where l is length of liquid intrusion, γ denotes liquid surface tension (mN/m), Θ is the contact angle, r represents the pore radius and η is liquid viscosity.

Assuming the contact angle of the best wetting liquid is known, the contact angles of the other liquids with respect to the best wetting liquid can be calculated with the following modification of Eqn 1 (Studebaker and Snow, 1955):

$$\cos \Theta_1 = \left[\frac{\gamma_1 \times \eta_2 \times k_2}{\gamma_2 \times \eta_1 \times k_1} \right] \times \cos \Theta_2 \qquad (2)$$

where k is the slope of the l^2 vs t linear intrusion curve. Subscripts 1 and 2 refer to the best wetting liquid and to the liquid under examination, respectively.

Results and Discussion

The morphological characterization of lactose powder made from SEM micrographs showed that the particles are nodular corresponding to the typical shape of lactose. According to XRPD analysis the material is well crystallized. The specific surface area of lactose powder (fraction 100–300 μm) is 1.38 m^2/g. The relative volume size distribution of the material is presented in Fig. 2. The median of the distribution is 220 μm. The distribution is log-normal by shape, being optimal for this type of experiment, also repre-
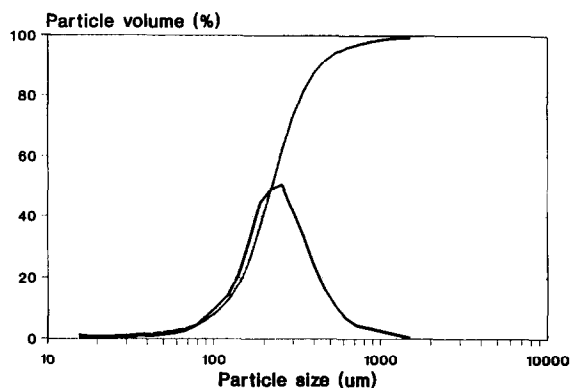
Fig. 2. Particle size distribution of lactose powder.

Liquid	Θ (°)		γ_L (mN/m)	γ_L^D (mN/m)	γ_L^P (mN/m)
	Mean	SE			
Water	110.4	0.8	72.8	23.1	49.7
Methanol	33.5	1.4	22.8	18.0	4.8
Propanol	29.1	0.7	23.9	20.6	3.3
Butanol	27.6	1.1	24.6	22.1	2.5
Octanol	26.7	1.2	28.5	(30.0)	(−1.5)
Hexane	0	0	18.7	(14.4)	(4.3)

Parentheses indicate an inconsistent result.

senting the form of distribution often encountered in pharmaceutical powders. The size distributions of the lactose fractions presented in Fig.
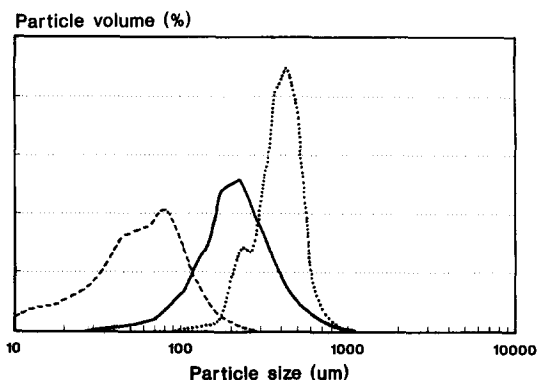

Fig. 3. Particle size distributions of lactose powder sieve fractions. > 212 μm (dot), 106–212 μm (solid), < 106 μm (dash).

3 exhibit more irregular shapes due to sieving. The median values differ significantly, being 355, 220 and 50 μm for size fractions greater than 212, 106–212 and less than 106 μm, respectively.

The contact angles on solid paraffin surface, surface tensions and calculated dispersion and polar components of the liquids are presented in Table 1. The values are very close to those given in literature (Weast, 1982; Ohm and Lippold, 1985). Water has the highest polar component. Starting with methanol, the polar component decreases as the length of the hydrocarbon chain increases.

The surface tension, the cosine of the contact angle and the surface free energy value of the solid paraffin surface include an error so that the mathematical treatment yields inconsistent results. This manifests as a negative polar compo-

TABLE 2

The densities and dynamic viscosities at 24 ± 0.2°C, and contact angles (Θ) (n = 10) on solid paraffin surface, the surface tensions (γ_L) (20 ± 0.2°C) and dispersion (γ_L^D) and polar (γ_L^P) components of the liquids saturated with lactose

Liquid	Density (g/cm³)	Dynamic viscosity (mN s m^{-2})	Θ (°)		γ_L (mN/m)	γ_L^D (mN/m)	γ_L^P (mN/m)
			Mean	SE			
Water	1.09	1.96	107.6	0.7	58.2	17.0	41.2
Methanol	0.78	0.55	39.9	0.8	22.8	16.7	6.1
Propanol	0.80	1.86	26.8	1.2	23.9	21.1	2.9
Butanol	0.81	2.66	28.6	1.0	24.6	22.0	2.6
Octanol	0.82	7.86	30.4	0.9	27.3	26.6	0.7
Hexane	0.66	0.29	0	0	18.7	(14.4)	(4.3)

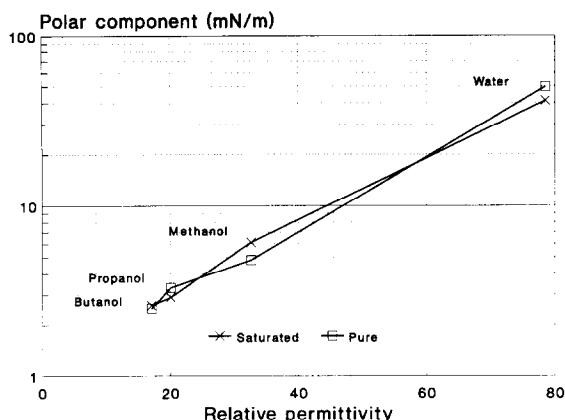Parentheses indicate an inconsistent result.

Polar component (mN/m)

Fig. 4. Polar component vs relative permittivity of both pure and lactose saturated water, methanol, propanol and butanol.

component of both pure and lactose saturated liquids and the relative permittivity (Weast, 1982) (Fig. 4). Liquids with non-existent polarity, octanol and hexane, are not presented in the graph (Tables 1 and 2) because of the logarithmic scale. In rank correlation level the relationship is well understood as the relative portion of the electronegative hydroxyl group determines the polarity of the liquid.

The densities and dynamic viscosities of the liquids used in contact angle calculations are presented in Table 2. The density values are slightly higher compared to the pure liquid values due to dissolved lactose (Weast, 1982). The effect of dissolved lactose on the viscosity of the liquids is significant, with water for example, the viscosity is twice as great as with pure water.

Table 2 also lists the contact angles on solid paraffin, the surface tensions and the calculated dispersion and polar components of the liquids saturated with lactose. Only slight differences, apart from the significant decrease of the surface tension and the components of water, are observed when comparing with the values in Table 1. This is due to the great solubility of lactose in water and smaller solubility in the other liquids.

The effect of particle size of the powder on liquid intrusion is presented in Fig. 5. The intru-

nent with octanol, hexane has a polar component although the contact angle on the paraffin surface is zero degrees. It can be assumed, though, that as the contact angle of hexane is zero degrees, the polar component is also negligible. The inconsistent values are given in parentheses in Tables 1 and 2. It is evident that a similar deviation is present also in the values calculated for the other liquids.

It is interesting to observe a linear correlation between the logarithm of the measured polar

Time (seconds)
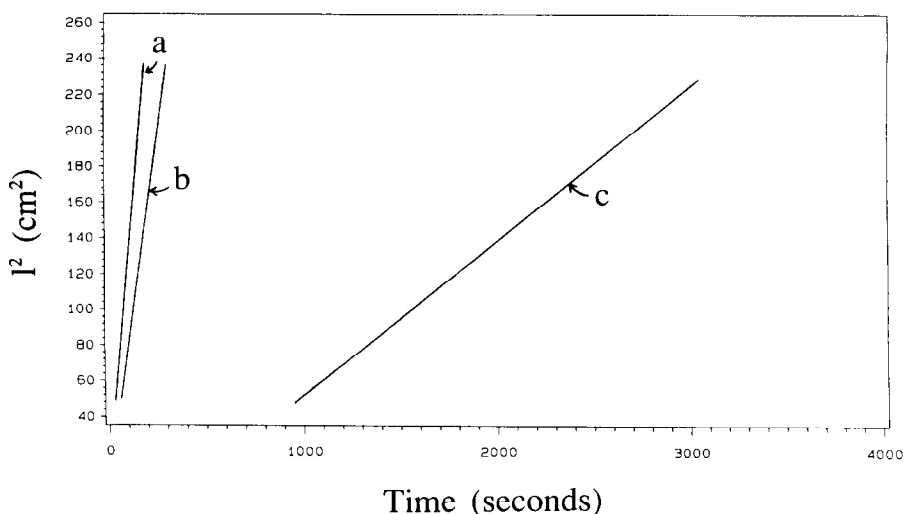
Fig. 5. The slope of distance squared vs time of different size fractions of lactose; > 212 μm (a), $106-212$ μm (b) and < 106 μm (c).

sion into the two greatest fractions is clearly faster than into the smallest fraction. This can be attributed to a small particle size and a continuous particle size distribution in the lower end enabling a more effective degree of packing. The fraction of particles less than 10 μm in diameter amounts to up to six percent according to Fig. 3. Because the liquid properties remain the same, the mathematical treatment results in different contact angles for the size fractions; the greater the intrusion rate the smaller the contact angle.

The beginning of the liquid intrusion did not generally yield a straight line when l^2 was plotted against time. The packing method generates an impulse that mostly affects near the sinter in the bottom of the tube causing heterogeneous and loose packing of the particles. Therefore, a steady flow of the liquid is reached only after some distance. The data used in calculations is obtained from the linear part of the penetration curve.

The data in Table 3 show that with different packing times the resulting powder column exhibits a similar structure. The shape of the particles in terms of packing properties is close to optimal. The most compact powder bed and smallest capillaries were, surprisingly enough, obtained with the shortest packing time. As a result, a packing time of three minutes was used in the final contact angle determinations. The regres-

TABLE 3

Linear regression parameters of water intrusion into lactose powder bed for different packing times

Packing time (min)	k (cm^2 s^{-1})		b (cm^2)		r
	Mean	SE	Mean	SE	
3	0.179	0.005	4.62	1.51	0.999
6	0.187	0.005	−2.24	1.41	0.998
12	0.184	0.008	3.53	1.92	0.999

k, slope; b, intercept; r, regression coefficient; $n = 12$. The number of data points in regression analysis is 11.

sion coefficients for the curves are by and large equally good and thus all packing times studied can be considered acceptable. The packing times can be classified by the slope values, however, and thus it seems necessary to determine the optimal packing time for individual powder systems.

A typical example of intrusion data for contact angle determination is presented in Fig. 6. The graph contains all data points with least squares fits from six parallel studies. Although the points of each parallel study deviate from each other to some extent, the numerical slope values used in calculations are relatively near one another. The parameters of the least squares fit of liquid intrusion data and the calculated contact angle values
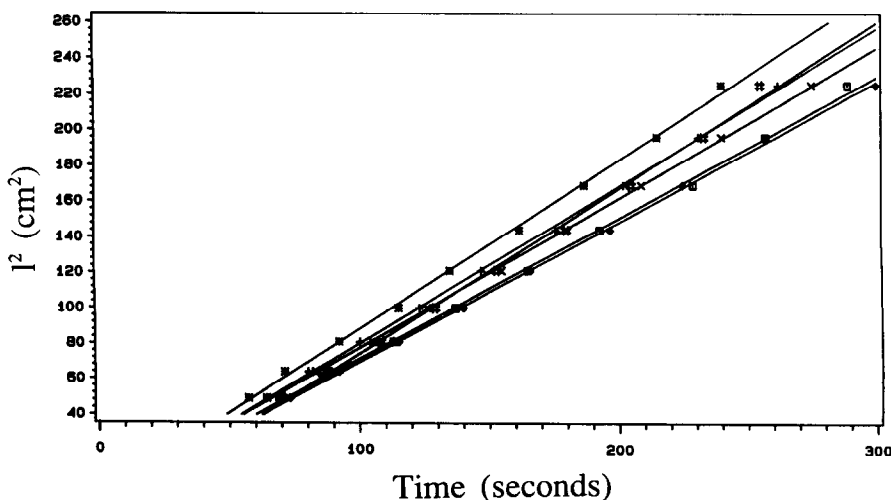

Fig. 6. Methanol intrusion into lactose (100–300 μm) powder bed; data of six parallel studies with linear least-squares fits.

TABLE 4

Linear regression parameters of liquid intrusion into lactose powder bed and the calculated dynamic contact angles of the liquids

Liquid	k (cm^2 s^{-1})		b (cm^2)		r	θ(°)		n
	Mean	SE	Mean	SE		Mean	SE	
Water	0.179	0.005	−1.31	1.51	0.999	61.7	0.7	12
Methanol	0.414	0.010	0.02	0.97	0.995	38.7	1.5	6
Propanol	0.123	0.005	0.49	0.77	0.994	39.2	2.4	6
Butanol	0.099	0.003	−1.43	1.08	0.999	33.4	2.1	6
Octanol	0.036	0.001	−7.26	3.02	0.995	36.2	2.4	6
Hexane	0.798	0.020	−11.2	2.09	0.999	0	0	6

The number of data points in regression analysis is 11. Hexane is the best wetting liquid with estimated contact angle of 0°. k, slope; b, intercept; r, regression coefficient.

are presented in Table 4. All the liquids studied behaved quite well during the intrusion; the advancement of the liquid front was easily monitored. The difference in penetration rate with the fastest and the slowest liquid is noticeable. It took octanol 90 min to advance 14 cm, while hexane needed only 4 min. The variance in intrusion rate is greatest with the fastest liquids. The good correlation coefficients indicate steady intrusion of all of the liquids.

Water has clearly the highest dynamic contact angle value with lactose powder (Table 4). The alcohols all have approximately equal contact angles about two thirds of the water contact angle. Although there is no clear trend among the alcohols, it can be observed that the higher the liquid polarity, the higher is the contact angle value. This results from a greater dissolution into a polar liquid increasing the viscosity of the liquid. Thus the resulting numerical contact angle is greater.

Water has the poorest wettability judged by the contact angle, but it still wets lactose faster than propanol, for instance, although the difference between the contact angles is 13°. This is a most important advantage of the dynamic liquid intrusion method compared with the static sessile drop method, that does not reveal the rate of wetting. The rate of wetting is important in studying of manufacturing processes, whereas the static contact angle can be utilized when ranking alternative excipients, for instance, for a drug formulation, where the interface should remain stable for the entire shelf-life of the drug product.

The water contact angles previously measured on lactose tablets were about 10° (Kiesvaara and Yliruusi, 1991b). Although the results from a static and a dynamic method are not directly comparable, the difference in the contact angle values implies a difference between the powder particle and tablet surfaces.

Technically the Washburn method for determining the relative rate of wettability and contact angles of a powder is applicable. The use of a horizontal powder column simplifies the mathematical treatment by making the use of the gravity term in the Washburn equation unnecessary.

The intrusion rate constant k is a good measure of powder wettability because it includes liquid viscosity. All the liquids studied can be ranked by this parameter. The contact angle is already more difficult to determine, requiring knowledge of the best wetting liquid and its contact angle.

It is evident that the results are very much dependent on both the powder properties; packing and contact angle, and liquid viscosity and surface tension.

The repeatability of the packing technique must be confirmed as constant structure of interparticle space of the powder bed is determining factor in obtaining valid results. This means that when comparing results from previous batches, for instance, the particle morphology and size distribution must be taken into account. Processes like milling affect the wettability by altering the morphology, size distribution and the surface properties. The method also yields different contact angles for the different size fractions of a powder because the intrusion rate is different. The liquid intrusion method can thus be used to measure and quantify changes caused by processes.

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