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Application of time-dependent sessile drop contact angles on compacts to characterise the surface energetics of sulfathiazole crystals

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Abstract

The time-dependent wetting of sulfathiazole compacts with sessile water drops was evaluated using video microscopy. The influence of sulfathiazole crystalline form, particle size, pre-saturation with water, humidity and compaction pressure on the droplet spreading kinetics and contact angles are reported. The rate and extent of droplet spreading decreased for compact surfaces of high microscopic roughness; this was determined by atomic force microscopy (AFM). Pre-saturation of powder compacts with water (pre-saturated with sulfathiazole) enhanced droplet spreading and enabled pseudo-equilibrium contact angles to be determined for up to 10 min. Sessile-drop contact angles on both sulfathiazole powder compacts and single crystals are compared with particle contact angles determined by liquid penetration. This study has led to an improved understanding of the influence of physical heterogeneities and the face-specific surface chemistry of individual crystals on the wetting characteristics of pharmaceutical compacts. © 2002 Elsevier Science B.V. All rights reserved.

Keywords: Sulfathiazole; Compacts; Wettability; Contact angle; Sessile drop; Porosity; Surface roughness

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1. Introduction

The sessile drop technique has been widely used to measure contact angles between solid, liquid and vapour phases and characterise the surface chemistry of solids (Good, 1979). According to Young's theory, the equilibrium contact angle, θ_Y, is related to the interfacial tensions of the solid–vapour, γ_{sv}, solid–liquid, γ_{sl}, and liquid–vapour, γ_{lv}, as given by:

$$\cos \theta_Y = \frac{\gamma_{sv} - \gamma_{sl}}{\gamma_{lv}} \qquad (1)$$

The sessile drop technique is commonly used for estimating the surface energy of pharmaceutical powders (Buckton, 1993). However, such powders require compression into compacts (discs) prior to the application of a sessile drop and this approach may be problematic due to the introduction of porosity and changes in the surface energy. Neumann and Good (1979) reported that

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the presence of capillaries in compressed powder compacts, in most cases, led to sessile drop penetration over time. A stable drop may only be obtained if the contact angle is sufficiently high ($\theta > 90°$), thus reducing the driving force for liquid penetration into the capillary, as given by the Laplace pressure (ΔP):

$$\Delta P = \frac{2\gamma_{\mathrm{lv}}\cos\theta_{\mathrm{p}}}{r} \tag{2}$$

where r is the capillary radius and θ_{p}, the liquid penetration particle contact angle. Kossen and Heertjes (1965) proposed a method whereby the compact is pre-saturated with the test liquid before the drop is placed on the surface, thus reducing liquid penetration. This is a necessary procedure if the contact angle is to be measured after an extended time period. One question that remains unanswered is whether an equilibrium contact angle can be measured within a short time frame (i.e. $t < 1$ s) and if so, is there a need to pre-saturate the powder compact with the test liquid? Few published studies have detailed time-dependent droplet interactions with pharmaceutical compacts over the time scale 10 ms to 10 min (Buckton, 1993).

The present study aims to define the criteria needed to produce both accurate and reproducible sessile drop contact angles, which are representative of a pharmaceutical powder's surface energy. In addition, to determine the influence of powder characteristics (i.e. particle size, particle shape and crystalline form) and experimental conditions (humidity and powder compaction pressure) on the determined contact angles. In particular, the roles that physical and chemical heterogeneities (e.g. face specific surface chemistry (Muster and Prestidge, 2001) play on droplet wetting of pharmaceuticals are differentiated. The pore density and surface roughness of powder compacts were determined by atomic force microscopy (AFM) imaging. Sulfathiazole (an anti-bacterial drug) was used as a model pharmaceutical powder in this study and its well-documented polymorphism (Grove and Keenan, 1941; Kruger and Gafner, 1972; Bladgen et al., 1998; Apperley et al., 1999; Patel et al., 2001) enabled the influence of polymorphic form on compact wettability to be explored.

2. Experimental

2.1. Materials

Sulfathiazole (4-amino-*N*-2-thiazolylbenzenesulfonamide) powder was obtained from SIGMA® and further recrystallised into its polymorphic forms following the method reported by Bladgen et al. (1998). Form I was crystallised by cooling a warm (45 °C) saturated isopropanol solution to 25 °C and formed as needle-like hexagonal prisms. Hexagonal plate shaped crystals of Form III were prepared by cooling a saturated 10% ammonia in water solution from 70 to 25 °C. After crystallisation the suspensions were filtered, washed with saturated water, and then dried and stored in a vacuum dessicator for ~ 24 h prior to compaction and wetting investigations. Melting point studies have confirmed the different crystalline forms of sulfathiazole and powder X-ray diffraction (XRD) has confirmed the purity of each form to be > 98%.

A sample of each form was also ground in an agate motar and pestle. The particle size and surface area of the sulfathiazole samples were determined by laser diffraction (Malvern Mastersizer) and BET gas adsorption (Coulter Omnisorb 100), respectively, and are given in Table 1. Ultra high quality water ($\gamma_{\mathrm{lv}} = 72.8$ mN m^{-1} at 25 °C) from a Milli-Q system was used in all procedures. All other reagents used were analytical grade unless stated otherwise. All experimental studies were undertaken at 25 °C unless stated otherwise. Saturated solutions of sulfathiazole in water were used as probe liquids in the wetting studies, a surface tension of 71.3 ± 0.5 mN m^{-1} was deter-

Table 1
Particle characteristics of sulfathiazole powders

Form (and treatment)	BET surface area (m^2 g^{-1})	Mean particle diameter (equivalent spherical) (μm)
I (as prepared)	0.36 ± 0.07	11.0 ± 1.3
I (ground)	2.70 ± 0.14	2.5 ± 0.3
III (as prepared)	0.22 ± 0.04	17.2 ± 1.9
III (ground)	2.98 ± 0.15	1.7 ± 0.3

mined by the drop weight method (Adamson, 1990).

Compacted powder discs (13 mm diameter) were prepared using a stainless steel punch and die set. A ring press was used to compress 120 mg of powder for 1 min at pressures ranging from 70 to 700 MPa. Prior to wetting studies the compacts were then stored for ~ 12 h at a relative humidity of either 45 or 85% using saturated salt solutions of KNO_3 and KCl, respectively, (Greenspan, 1977). For some investigations sulfathiazole compacts were pre-saturated by placing ~ 1 ml of the wetting solution in contact with the base of the compact and allowing it to penetrate for up to 1 h.

We acknowledge that recent studies (e.g. Apperley et al., 1999; Patel et al., 2001) have shown that polymorphic transformations for sulfathiazole are highly complex and that compression and humidity treatment may influence the polymorphic stability. However, in the context of the present investigation, optical microscopy, powder XRD and melting point studies have confirmed that the samples of Form I and Form III under investigation are not significantly altered by the treatments undertaken.

2.2. Methods

2.2.1. Dynamic sessile drop contact angles

An adjustable pipette (Eppendorf) was used to attach a 6 μl drop ($d \sim 1.1$ mm) to a vertically suspended wire applicator. Powder compacts were then raised into contact with the droplet using a motorised platform assembly at an approach velocity of less than 10 $\mu m\ s^{-1}$. The momentum of the droplet on approach to the compact surface was negligible compared with the momentum caused by the droplet wetting step. The droplet spreading kinetics was shown to be highly reproducible and independent of the droplet approach velocity. Images of droplets were observed through a stereo microscope (Olympus OM) and CCD camera (Sony) and recorded on a 40 ms temporal resolution VCR. Video images were transferred to a PC and the drop shape (contact angle and wetting radius) characterised using an on-screen protractor provided by an image analysis package (Galai™). The error in contact angle determination was estimated to be ± 0.4° over six measurements of six different drops on a single compact.

2.2.2. Liquid penetration contact angles

Liquid penetration particle contact angles (θ_p) were determined from capillary penetration rate studies (Washburn, 1921). The Washburn method determines the penetration of a liquid through a consistently packed powder bed exhibiting an effective pore radius, r. A known weight of powder was transferred into a capillary tube (internal diameter ~ 2 mm) plugged at one end with a section of glass wool to retain particles. The tube was then vibrated to produce a powder volume fraction of 0.66. The length, L, travelled (determined visually) by a liquid of viscosity, η, in time, t, is given by:

$$L^2 = \frac{r\gamma_{lv} \cos \theta_p t}{2\eta} \tag{3}$$

To avoid the requirement for direct determination of r, the rates of liquid penetration through packed powder beds were measured using both water and a perfectly wetting liquid, i.e. $\cos \theta_p = 1$. Cyclohexane was used as a perfectly wetting liquid due to its low γ_{lv} (25.0 $mN\ m^{-1}$) and proven wetting of pharmaceuticals (Parsons et al., 1992; Prestidge and Tsatouhas, 2000). Eq. (4) was used to evaluate the contact angle for a partially wetting liquid (water), where $_p$ and $_w$ denote partially wetting and perfectly wetting liquids, respectively.

$$\cos \theta_p = \frac{(L^2/t)_p \eta_p \gamma_w}{(L^2/t)_w \eta_w \gamma_p} \tag{4}$$

2.2.3. Gravimetric determination of powder compact porosity

Powder compact porosities were estimated by gravimetric measurement of liquid uptake. Powder compacts were weighed and their geometric size characterised using a micrometer. A saturated solution of sulfathiazole ($\rho = 1.021\ g\ cm^{-3}$) was then allowed to penetrate the compact. After 20 min the excess liquid was removed using a syringe, prior to reweighing of the compact (additional water uptake after 20 min was shown to be negligible). Care was taken to minimise evaporation losses. Compact porosities were determined in vol.%; the errors quoted correspond to the spread of data over five separate measurements on different compacts.

2.2.4. Atomic force microscopy

A Nanoscope III (Digital Instruments, USA) atomic force microscope (AFM) was used for imaging the surfaces of sulfathiazole compacts, which were mounted on steel stubs using double-sided adhesive tape. To ensure that only representative features are presented, images were taken at several positions over the sample surface whilst routinely modifying the scanning frequency and scanning direction. The applied force between sample and cantilever was minimised where possible to avoid any physical arrangement of surfaces. The root-mean-square surface roughness was determined over different areas using the instrument's software.

3. Results and discussion

3.1. Wetting of sulfathiazole compacts

3.1.1. Unsaturated (dry) compacts

Sessile water droplets at the surfaces of dry sulfathiazole compacts (i.e. not pre-saturated with water) were imaged over the contact time range 0.04–120 s. Droplets were found to spread in a reproducible manner and were characterised in terms of their wetting radius, ω, droplet height, h, and contact angle, θ (Fig. 1). For a given droplet volume, a readily wetted surface is indicated by low values of θ. Fig. 2 demonstrates the apparent θ of a droplet spreading over the surface of a dry compact of sulfathiazole Form I. The apparent contact angle decreases from ~53 to ~33° in a 120 s period; this is due to the combined effect of droplet spreading over the surface as controlled by Eq. (1) and imbibition (penetration) of the droplet into the compact, as described by Eq. (3). The spherical cap volume of the droplet (V_{cap}) is described geometrically by:

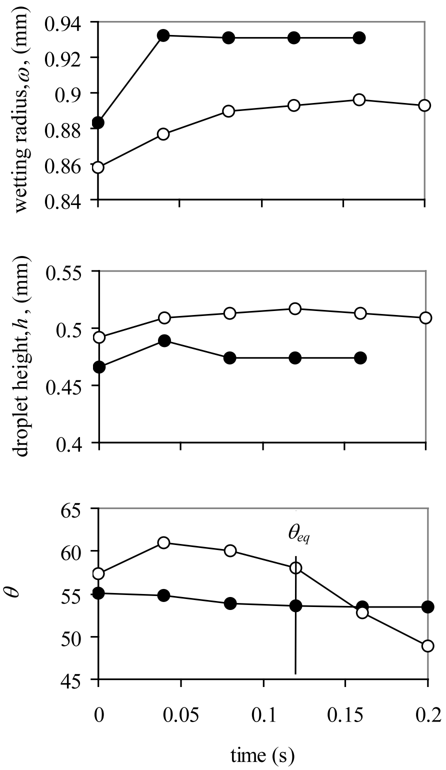

Fig. 1. Time dependent values of ω, h and θ for a sessile drop spreading over an unsaturated (○) and pre-saturated (●) sulfathiazole Form I powder compacts compressed at 210 MPa.

$$V_{\mathrm{cap}} = \frac{1}{6}\pi h(3\omega^2 + h^2) \tag{5}$$

This enables the volume of the droplet imbibed into the compact to be determined and is plotted as a function of time in Fig. 2. After 120 s, over half of the original droplet volume (6 μl) was reduced due to imbibition. Reliable equilibrium contact angle measurement is unachievable on the time scale presented due to the dynamic nature of dry compact wetting.

For all wetting experiments on unsaturated compacts, the time taken for a droplet to reach its maximum spreading radius was 0.12 ±0.04 s, as exemplified in Fig. 1. (In comparison, Mao et al. (1997) reported that water droplets impacting onto the surface of paraffin wax (non-porous) reached equilibrium within 0.08 s.) After this time, the spreading radius decreased slowly and by less than 2%, before becoming essentially constant for the majority of compacts investigated. The substantial decreases in the three-phase contact angle after ~ 0.12 s are not strictly determined by energy balance considerations, but are governed by loss of droplet volume due to liquid imbibition. The precise time-scale of imbibition is controlled by the pore structure and pore wettability. Given that droplet spreading is considered complete after ~ 0.12 s, any contact angle measurement taken after this time will represent a receding rather than an advancing or equilibrium angle. Assuming that the surface energy of the compact alone controls the droplet shape within the first 0.12 s, an equilibrium contact angle may be estimated. The validity of this assumption is revisited and further discussed in the following sections.

3.1.2. Compacts pre-saturated with water

The initial droplet interaction kinetics for a pre-saturated sulfathiazole compact is exemplified in Fig. 1. The maximum wetting radius was reached in ~ 0.08 s, a similar period to that required for unsaturated compacts. After achieving a maximum value, ω showed negligible change over several minutes, indicating that the compacts were sufficiently pre-saturated with water to prevent droplet imbibition. The stability of the three-phase contact line after 0.08 s is further evident from the constant values of droplet height and contact angle. An estimate of the equilibrium contact angle is achievable. Over significantly longer periods of time (e.g. Fig. 3), droplets on pre-saturated powder compacts are considerably more stable than on unsaturated compacts. However, even for saturated compacts, contact angles can be observed to decrease by up to 5° for contact times in excess of 100 min. This is considered a result of the advancing angle changing into a receding angle upon a decrease in droplet volume and is due to imbibition and evaporation. Gravimetric studies of weight loss for the present system revealed droplet volume loss to be < 5% after 100 min.

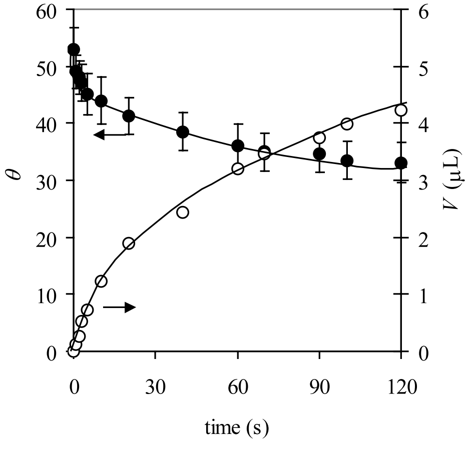

Fig. 2. Time dependent characteristics of a sessile drop spreading over an unsaturated sulfathiazole Form I powder compacts: contact angle (●) and droplet volume loss V (○) that equals the initial droplet volume (6 μl)$- V_{\mathrm{cap}}$ (calculated using Eq. (5)).

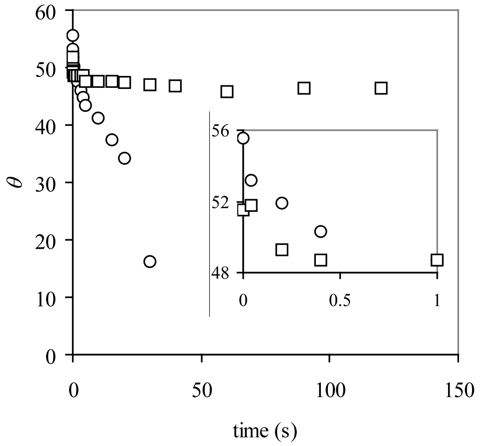

Fig. 3. Contact angle as a function of time for (○) unsaturated and (□) pre-saturated (15 min pre-saturation) sulfathiazole Form III powders compressed at 210 MPa and stored at 45% relative humidity.

Powder compact pre-saturation time has been shown to be an important factor in the determination of an equilibrium contact angle, see Fig. 4. VCR playback ensured that when ω did not decrease after reaching its maximum value, the reproducibility of sessile drop contact angle measurement was improved. For sulfathiazole Form I (compressed at 210 MPa) a pre-saturation time of 15 min gave a stable droplet and reproducible contact angle.

3.2. Factors affecting water droplet spreading on sulfathiazole compacts

3.2.1. The influence of humidity

The insert within Fig. 3 shows that for times less than 0.5 s, pre-saturated compacts display lower contact angles than unsaturated compacts. It may be hypothesised that the presence of moisture in the pores of the compact gives rise to a decrease in the initial contact angle. Here, we note that the surface energy of a dry solid, γ_s, is greater than a partially wet solid, γ_{sv}, since the spreading pressure, π_e, is always positive (Good, 1979):

$$\pi_e = \gamma_s - \gamma_{sv} \tag{6}$$

Though there is a larger driving force for water to spread across the solid, the physical movement of the wetting front may be retarded by the presence of air-filled pores. Both liquid–solid interactions and liquid–pore interactions will influence liquid movement over the surface of a pharmaceutical powder compact. If the pore density is high, the spreading of water across the surface will be restricted due to energetically unfavourable interactions between water and air contained within the pores.

The advancing contact angle of a heterogeneous surface characterises the low-energy sites, whilst the receding angle probes the high-energy sites (Good, 1979). Therefore the advancing contact angle observed for a dry compact is expected to be greater than on an identical but partially saturated compact. This suggests that both humidity and the surface pore density may influence the spreading of sessile drops over pharmaceutical powder compacts.

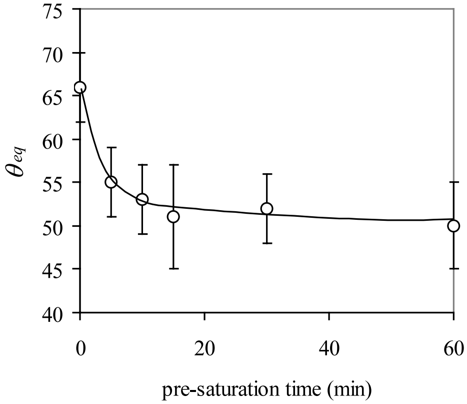

Fig. 4. θ_{eq} (determined 0.12 s after droplet contact) for compacts of sulfathiazole Form I powder (compressed at 210 MPa) as a function of pre-saturation time.

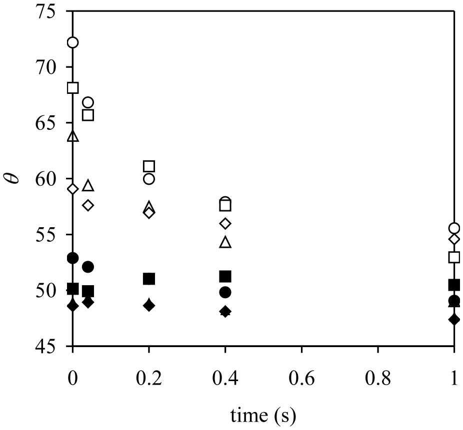

Fig. 5. The influence of compression, primary particle size and humidity on dynamic sessile drop contact angles of unsaturated sulfathiazole Form I powder compacts. Compaction pressures of 210 MPa (open symbols) and 350 MPa (filled symbols). Powders stored at 45% RH, no size reduction (○ and ●) and reduced particle size (△and ▲). Powders stored at 85% RH, no size reduction (□ and ■) and reduced particle size (◇ and ◆).

For a series of sulfathiazole compacts stored at relative humidities of 45 and 85%, the time-dependent sessile drop contact angles are reported in Fig. 5. The observed trends highlight differences in droplet spreading, which resulted from the preparation history and hence physical properties of the compacts, and differences in the rate and extent of imbibition (for times >0.12 s). Powder compacts stored at higher humidity resulted in increased wetting rates, as indicated by lower initial contact angles. Blake (1993) detailed the existence of precursor films, which move ahead of the main droplet volume in systems where strong solid–liquid intermolecular attractions create positive spreading coefficients. For large spreading coefficient and low viscosities, the precursor film has been cited as moving at speeds of up to 0.1 ms^{-1} (Blake, 1993). Samples stored at higher humidites may be more susceptible to enhanced spreading due to the formation of a precursor film (De Gennes, 1985).

Interestingly, the initial rate of wetting and spreading was found to play a major role in dictating the magnitude of the contact angle at longer time periods, i.e. the equilibrium contact angle value may not be readily determined. This implies that for unsaturated compacts, sessile drop contact angle measurements for assessment of surface energy may be misleading. However, the reproducible manner in which droplet spreading occurs may allow itself to be used as a method for probing the physical nature (porosity and surface roughness) of powder compacts.

3.2.2. The influence of surface roughness and porosity

The effects of compaction pressure and primary particle size on the time-dependent wetting of sulfathiazole Form I compacts are shown in Fig. 5. For droplet contact times <1 s, the contact angles for compacts compressed at 210 MPa were consistently greater than those compressed at 350 MPa; this trend is irrespective of the humidity and particle size. It is apparent that droplets spread at a greater rate and reach their equilibrium-contact angles more rapidly on compacts prepared at a greater compression pressure. The primary particle size is shown to have little influence on the equilibrium contact angle, but droplet spreading is faster for compacts prepared from finer powders.

The surface roughness and porosity of sulfathiazole compacts were characterised using AFM, see Table 2. Increased compression generally gives rise to a denser compact with both decreased pore size and pore density, as well as reduced surface roughness. Correlations between the magnitude of surface roughness and the initial contact angle are dependent on the crystalline form, the extent of grinding and the compression pressure. Previous experimental studies (Bascom et al., 1964; Cazabat and Cohen-Stuart, 1987) have shown that surface roughness can inhibit the rate of droplet spreading. Bascom et al. (1964) suggested that roughness perpendicular to the direction of flow restricts fluid movement, whilst roughness parallel to the direction of flow can enhance the spreading rate due to capillary forces. Variations in surface roughness may be responsible for differences in the initial dynamic contact angle, however, one must keep in mind that increased surface roughness also leads to a decreased equilibrium contact angle when $\theta < 90°$ (Onda et al., 1996).

The crystalline properties of a pharmaceutical powder also influence its compressibility (Ferrari et al., 1996; Garekani et al., 1999) and hence the surface roughness of its compacts. With this in mind, sulfathiazole Form I compacts exhibit smoother surfaces and show better compression properties (higher strength, higher density) than Form III compacts, which show signs of flaking and peeling. Differences in compression density have been identified by gravimetric water porosity

Table 2
Surface roughness evaluations of sulfathiazole compacts. The influence of roughness on droplet spreading as indicated by initial contact angles

Form (compression pressure, (MPa)	Initial θ (°)	Root mean square roughness (nm) over area		
		2×2 μm	5×5 μm	100×100 μm
I (210)	68 ± 4	11.4	13.2	59.5
I (210)[a]	64 ± 3	6.5	6.5	78.9
I (350)	52 ± 4	7.5	8.4	87.5
III (70)	62 ± 2	149	220	-
III (210)	50 ± 4	4.8	10.5	94.6
III (350)	49 ± 3	7.7	9.4	-
III (700)	47 ± 2	7.2	8.5	-

[a] Ground sulfathiazole sample.

Table 3
Porosity of sulfathiazole compacts estimated by gravimetric water imbibition

Compression pressure (MPa)	Porosity (% v/v)	
	Form I	Form III
70	29 ± 1	27 ± 4
210	15 ± 3, 7 ± 1[a]	21 ± 1, 15 ± 2[a]
350	14 ± 1	17 ± 3
700	6 ± 1	13 ± 1

[a] Ground sulfathiazole sample.

investigations as presented Table 3. The increased compact density for sulfathiazole Form I is considered to be aided by the fracturing of needle-shaped crystals, whereas Form III crystals are less likely to fracture due to their lower aspect ratio. Compression at greater than 210 MPa is considered to result in plastic deformation and/or fracturing of crystals, and is responsible for pore filling, hence the resultant increase in compact density. The strength of compacts is improved by decreased porosity, however it is also highly dependent upon attractive interactions between particles in the solid-state (Brittain and Fiese, 1999).

Compacts prepared from the different crystalline forms of sulfathiazole and compressed at an equivalent pressure (210 MPa), exhibit different topographical features, as shown in the AFM images in Fig. 6 and as inferred from the microscopic and macroscopic roughness values detailed in Table 2. These observations also result in time-dependent contact angles (Fig. 7) that are strongly, crystalline-form dependent. Under identical conditions, the rate of change of contact angle over compacts of sulfathiazole Form III was greater than for compacts of Form I. It is proposed that the large number of microscopic undulations on the surface of sulfathiazole I compacts may restrict the movement of the wetting front to a greater extent than the macroscopically rough Form III surface, resulting in larger contact angles at short time. Neumann et al. (1971) reported that a roughness less than 100 nm has little effect on the movement of fluid over a surface, however, high-energy surfaces have a much lower critical size (Neumann, 1978). Data from this study indicates that microscopic roughness is equally as important as larger asperities for controlling liquid spreading rates.

Compacts with lower levels of surface roughness, such as those prepared with higher compression or made from finer powders, give lower initial contact angles yet provide a more stable droplet with respect to imbibition. The rate of liquid imbibition through a network of capillaries is controlled by the magnitude of the Laplace pressure and is limited by the bulk flow achievable through the pores present (Marmur, 1992). In the presence of few pores the restriction in bulk liquid flow stabilised the sessile drop despite an increase

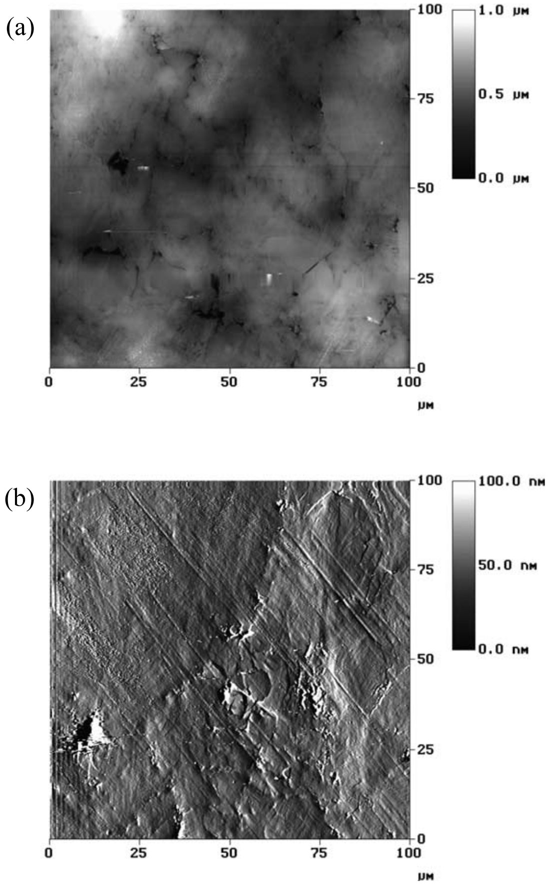

Fig. 6. Contact mode AFM height images of sulfathiazole powder compacts stored at 45% RH and compressed at 210 MPa: (a) Form I and (b) Form III.

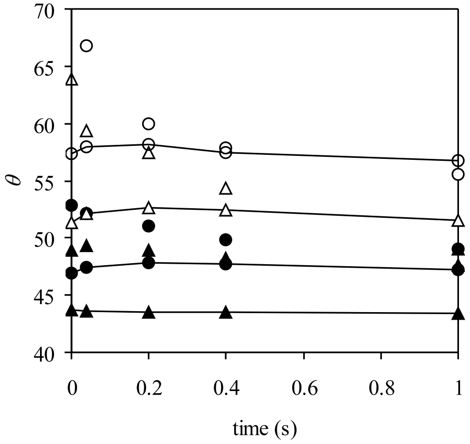

Fig. 7. Dynamic sessile drop contact angles on sulfathiazole powder compacts stored at 45% RH: Form I (symbols only) and Form III (symbols and lines): ○ no size reduction, 210 MPa; ●no size reduction, 350 MPa; △size reduction, 210 MPa and ◆size reduction, 350 MPa.

in the Laplace pressure. In contrast to our observations for sulfathiazole compacts, Buckton and Newton (1986) reported that more highly compressed tablets of barbiturate powder resulted in greater water uptake. It is evident that liquid imbibition into a pharmaceutical powder is dependent upon the chemical and physical nature of the powder as well as the extent of compression.

3.3. Considerations for the determination of contact angles on sulfathiazole compacts

3.3.1. The combined use of unsaturated and pre-saturated wetting

For both saturated and dry compacts of sulfathiazole Form I, compressed at 210 MPa (see Fig. 1), droplet spreading is effectively complete within 0.12 s (this has also been verified for Form III). The dynamic nature of the spreading transforms the contact angle from advancing to receding, i.e. dynamic contact angles deviate from their equilibrium values due to the velocity dependence and the presence of chemical/physical heterogeneities (Blake, 1993). Equilibrium contact angles on compressed powders are therefore likely to exhibit a dependence on the direction of droplet momentum (i.e. whether advancing or receding). The contact angle at 0.12 s, which we assign θ_{eq}, (an estimated- or pseudo equilibrium- contact angle) is considered to be indicative of both the chemical and physical nature of the surface. Therefore, to increase the accuracy of contact angle estimations from sessile drops on compressed powders, the effect of physical heterogeneities should be minimised. Here, we demonstrate the advantages of using a combination of both pre-saturated and unsaturated compacts for the evaluation of surface heterogeneities. For dry compacts, the contact angle is greatly controlled by the magnitude of the compression. The influence of compression on pre-saturated compacts is now further investigated.

Fig. 8 shows the droplet spreading kinetics for pre-saturated compacts prepared at various powder compaction pressures. A lower compression pressure resulted in an increased spreading rate, as indicated by a more pronounced decrease of contact angle. This is due to the high density of pores that are filled with water. In agreement with this observation, Young et al. (1998) reported that sessile drop contact angles on artificial skin decreased upon increasing the surface porosity. Greater liquid presence on or near the surface resulted in accelerated spreading rates due to ei-

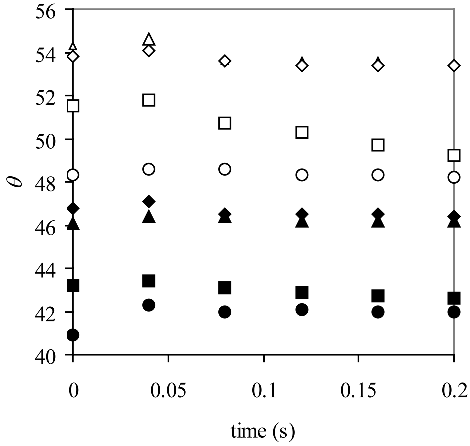

Fig. 8. The influence of compression on sessile drop contact angles determined on pre-saturated sulfathiazole powder compacts as a function of time. Form I: (○) 70 MPa, (□) 210 MPa, (△) 350 MPa and (◇) 700 MPa. Form III: (●) 70 MPa, (■) 210 MPa, (▲) 350 MPa and (◆) 700 MPa.

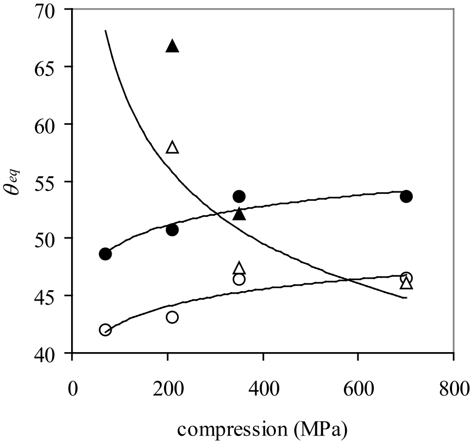

Fig. 9. The effect of compaction pressure on the θ_{eq} of sulfathiazole powder compacts: (▲) unsaturated Form I, (●) pre-saturated Form I, (△) unsaturated Form III and (○) pre-saturated Form III.

ther, a thin precursor liquid film, or liquid filled pores.

Fig. 9 shows that an increase in compaction pressure decreases the θ_{eq} of unsaturated compacts, yet increases θ_{eq} of pre-saturated samples. The increased compression decreases the extent of physical heterogeneities and, therefore, reduces the effect of surface moisture or air in pores on the spreading rate. Increased compression will, therefore, lead to a more representative determination of the equilibrium contact angle, providing that the surface energy of the powder remains unaltered.

3.3.2. The influence of crystalline form and crystal habit

The equilibrium contact angles for compacts prepared from powders of sulfathiazole Form I and III were 53 ± 2 and 46 ± 2°, respectively. Table 4 compares these values with contact angles determined by sessile drop on sulfathiazole single crystals and liquid penetration through particle-packed capillaries. The surface energy of sulfathiazole Form I was in all cases, lower than Form III; this reflects the arrangement of molecules within the crystals and exposure of different faces in the polymorphic forms (Muster, 2001).

Dynamic and static contact angles determined for the specific faces of sulfathiazole Form I were in the range of 60 ± 3°. The face of lowest surface area [010] was predicted (from crystallographic data) to exhibit the greatest wettability. Sessile drop contact angles determined on single crystals of Form I were in excellent agreement with those obtained for compacted Form I powders. This suggests that compression-induced aspect ratio changes, which increase the exposure of the [010] face with reference to the lower energy [102] and [001] crystal faces, are not significant. The individual faces of sulfathiazole Form III have contact angles of 40, 48 and 53°, with an average value of ~47°, which is in good agreement with that estimated from sessile drops on compacts (i.e. 46°). Single crystals of Form III lack a cleavage plane and, therefore, size reduction through compression is unlikely to significantly change the aspect ratio (Bladgen et al., 1998) hence surface energy. The contact angle values determined through liquid penetration are invariably greater than the equilibrium values determined with sessile drop and may be reflective of advancing wetting. The qualitative agreement between sessile drop and liquid penetration is, however, encouraging.

The semi-quantitative agreement between sessile drop contact angles on both powder compacts and single crystals confirms the value of these techniques for probing the chemical and physical surface properties of pharmaceutical particles. In particular, the contact angle values obtained may be used for predicting and/or controlling the processing performance of pharmaceutical powders.

Table 4
Contact angles of sulfathiazole particles, compacts and single crystal faces

Form	θ_p	θ_{eq} (compact)	θ_{eq} (single crystal)
I	71 ± 1	53 ± 2	54 ± 3[a]
III	68 ± 1	46 ± 2	40 ± 3 [102] 48 ± 4 [100] 53 ± 4 [110]

[a] Sample of Form I converted to Form III (Muster and Prestidge, 2001).

4. Conclusions

Sessile drop contact angles on sulfathiazole compacts are time-dependent and influenced by pre-saturation with water, humidity, surface roughness and the polymorphic form. Compact surface roughness was controlled predominantly by the compression force and to some extent by particle size and particle shape. Microscopic heterogeneities, as well as macroscopic roughness, are shown to influence droplet-spreading kinetics. The presence of air within sulfathiazole compacts reduced the droplet spreading rate across the surface, increased the time required for the droplet to reach equilibrium and increased the rate and extent of liquid imbibition. Pre-saturation of powder compacts enabled a stable sessile drop for contact angle measurement and lowered the magnitude of the contact angle with respect to the solid surface energy. Contact angles determined on compacts of sulfathiazole Form I were greater than for polymorphic Form III, which is in agreement with contact angles of the individual crystal faces. This provides evidence that sulfathiazole powders retain both their original polymorphic structure and surface chemical properties upon compression. If used with care, sessile drop investigations on compacts are effective at characterising the surface energetics of sulfathiazole powders.

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