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Measurement of the Surface Energies of Pharmaceutical Powders using a Novel Vapour Adsorption Method

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This paper presents a novel method for determining the surface energy of powders by measuring the adsorption isotherm of organic vapours using an automated gravimetric vapour sorption analyser. This approach avoids the limitations inherent in many of the currently available methods.

Introduction

The measurement of the surface properties of powders is of increasing importance to many industries, which depend upon powder processing or powder technology. If known, the surface energy of a powder may be used to predict a wide range of properties such as processing stability, adhesion, colloid stability, toughness, powder flow and product performance. In practice the measurement of the surface energy of powders is non-trivial and prone to potentially large errors or uncertainties despite a wide range of techniques being available.

Current methods for surface energy characterisation of powders include a number derived from classical wetting approaches for studying monolithic samples such as films and fibres. Additionally, various liquid penetration methods are used.

Liquid penetration methods determine the rate of liquid flow through a packed powder bed of the material of interest and rely on a Washburn Equation analysis of the liquid phase's capillary flow. A number of workers have reported data using this approach but it is generally found to be unsatisfactory due to difficulties in estimating the effective pore radius as well as a number of other complicating effects such as non-liquid penetration, non uniform flow and powder bed packing problems [1].

A number of wetting force approaches involving powders have also been reported. By coating a microscope glass slide with the powders using an adhesive, [2] used a classical Wilhelmy Plate wetting force technique for determining the advancing and receding contact angle for various liquids. A similar wetting force analysis may be undertaken by pressing the powder together to form a small compact monolithic sample. In this case the wetting force is measured as the porous sample pulled through an appropriate wetting liquid. However, both of these techniques are subject to a range of factors, including surface roughness, liquid penetration, powder contamination by the adhesive and mechanical induced changes during compact formation, which can make the unambiguous analysis of the data difficult.

More recently vapour adsorption based approaches such as inverse gas chromatography (IGC) have been shown to be a very sensitive way of characterising particulate surface properties [3]. Work published thus far on IGC of pharmaceutical powders has focused on infinite

dilution methods, which involve studying adsorption processes at very low surface solute concentrations. Invariably, these types of investigations highlight the higher energy surface sites on the sample surface. Consequently, IGC results reported have provided upper bound values of surface energy compared to other approaches such as traditional wetting studies, which characterise a surface at high surface solute concentrations. However, IGC is a highly versatile method and this technique can be used with higher concentrations of vapours to determine isotherms and surface chemical data more characteristic of the surface as a whole.

Duncan-Hewill and Nisman have reported on the surface energy of acetaminophen and adipic acid using a range of methods for surface energy analysis including Wilhelmy Plate, liquid penetration rate through powder compacts, sessile drops on compacts and sessile drops on single crystals. Not withstanding the experimental difficulties associated with some of these methods, the workers report good agreement in the contact angles determined for water using the various methods. Other workers whom have attempted similar method comparisons have reported much poorer agreement between the differing methods (Dove et al) due to the experimental difficulties previous indicated.

Theory

The interaction between a liquid and a solid surface may be described by Young's equation (1),

$$W_{S-L} = \gamma_{L-V} (1 + \cos \theta) + \pi_e \qquad (1)$$

where W_{S-L} is the work of adhesion between the solid and liquid phases, γ_{L-V} is the surface tension of the liquid phase, θ is the contact angle between a droplet of the liquid sitting and the surface and π_e is a term known as the equilibrium spreading pressure. The equilibrium spreading pressure is equal to the reduction in surface energy of the solid surface due to the surface adsorption of vapour onto the solid surface from the adjacent liquid phase. For

those cases in which the contact angle is greater than 10° it is presumed that π_e will be small in magnitude. In the case where the surface tension of the liquid is less than the energy of the exposed surface (eg. octane adsorbed on lactose) then the liquid will wet the surface. The resulting contact angle, θ, will be zero but π_e may be appreciable. In this case, Young's equation simplifies to equation (2).

$$W_{S-L} = 2\gamma_{L-V} + \pi_e \qquad (2)$$

The surface tension of the liquid phase γ_{L-V} is well quantified, hence if we can measure π_e then the solid liquid work of adhesion may be determined. From this quantity then the dispersive component of the surface energy of the solid γ^d_S may be determined using the semi-empirical relationship proposed by Fowkes shown below in Equation (3). In this relationship the work of adhesion, W_{S-L} is approximated to a geometric mean of the dispersive component of the surface energy of the liquid, γ^d_L and the dispersive component of the surface energy of the solid phase, γ^d_S.

$$W_{S-L} = 2 (\gamma^d_L . \gamma^d_S)^{1/2} \qquad (3)$$

Equation 3 is valid in the case in which the intermolecular forces for either the solid phase or the liquid phase are London van der Waals forces (dispersive) in origin. These types of intermolecular interactions are exhibited by non-polar materials such as polyethylene and hexane.

In the case of a non-polar wetting agent (eg. octane) W_{S-L} is a function of dispersive interactions only, whereas for a polar wetting agent (eg. isopropanol), it may be expressed as the sum of dispersive and polar components of the wetting interaction. Therefore if one measures W_{S-L} for both non-polar and polar wetting agents, both the polar and dispersive components of the surface energy may be calculated for a particular unknown material. This analysis is possible using a popular extension of the Fowkes' equation given below:

$$W_{S-L} = 2 (\gamma^d_S\gamma^d_L)^{1/2} + 2 (\gamma^p_S\gamma^p_L)^{1/2} \qquad (4)$$

The equilibrium spreading pressure π_e is defined as the net change in surface energy of a

surface due to the adsorption of a vapour on the surface. From the Gibb's surface tension equation (4), we may write the change in surface energy $d\gamma$ as:

$$d\gamma = -RT\ \Gamma d\ln p \qquad (5)$$

where p is the partial pressure of adsorbate, T is the temperature, R is the universal gas constant and Γ □s the surface excess, defined as the amount of adsorbate per unit area. We may therefore derive an expression for calculating π_e from the total amount adsorbed (Θ) as a function of partial pressure, and the specific surface area (σ) as shown in equation (6).

$$\pi_e = \frac{RT}{\sigma} \int \Theta d\ln p \qquad (6)$$

Hence, if we measure the adsorption isotherm on a solid using a wetting vapour, together with knowledge of the specific surface area we may therefore calculate π_e. In turn we then estimate W_{S-L}, γ^d_S and γ^p_S. In the current study a numerical integration procedure was implemented for evaluating Equation (6) and thus determining π_e from the experimental adsorption isotherms.

A π_e based approach for determining the works of adhesion as described above should provide accurate estimates of the surface energies of powders subject to the following guidelines:

The probe vapour must have a surface tension lower than the surface energy of the solid of interest. (ie $\theta = 0$).

The mechanism of vapour uptake must be surface adsorption and not bulk absorption.

The surface of interest must be thermodynamically, or kinetically during the time constant of measurement, stable at all partial pressures of the chosen adsorbate.

Method

All the vapour sorption experiments were carried out on a DVS automated gravimetric vapour sorption analyser (Surface Measurement Systems Ltd., London). This instrument measures gravimetric uptake and loss of vapour on the substrate using a SMS Ultra-Balance with a resolution of $\pm 0.1\mu g$. The partial pressure of the vapour flowing around the sample is controlled by mixing saturated and dry carrier gas flows using mass flow controllers and the whole system is kept isothermal by enclosing in a temperature controlled cabinet. The exhaust gases from the system were vented to a fume extraction system for safety considerations. Isotherms were measured on samples of lactose monohydrate (G. Buckton, SOP) and caffeine (Sigma Chemicals) in the partial pressure P/P_0 range 0-1.0 using analytical grade n-octane and isopropyl alcohol (IPA) vapours at 25.0°C. Typical sample size was 100mg. Baseline instrument performance achieved was better than $2\mu g$ drift per day of instrument operation. Baseline instrument stability was especially important in these experiments, as the absolute levels of vapour uptake were low, typically less than 0.1% by mass at P/P_0 equal to 1.0.

The surface areas of the samples were determined using a Micromeretics model 2000 N_2 surface area analyser. The samples were degassed overnight and a 10-point isotherm was obtained. The BET equation was used to determine the surface areas. The results are summarised in Table 2.

Results

Figure 1 shows typical gravimetric data for two complete cycles of sorption and desorption of octane vapour on caffeine. The data shows the percentage change in mass from the dry sample mass, as a function of time and relative partial pressure. The very low absolute levels of vapour uptake (<0.1% for P/P_0 range 0-1.0) are especially significant, as these levels of experimental accuracy could not normally be obtained using traditional vacuum adsorption equipment due to significant levels of buoyancy forces. The symmetrical design of the flow gravimetric analysis system used in this work is subject to negligible buoyancy forces and its use

under ambient flow operation allows baseline balance stabilities of 1μg per adsorption experiment to be achieved. Due to the very low levels of uptake on organic powders with a surface area between 0.2 and 1.0m^2/gm microbalance performance is very important
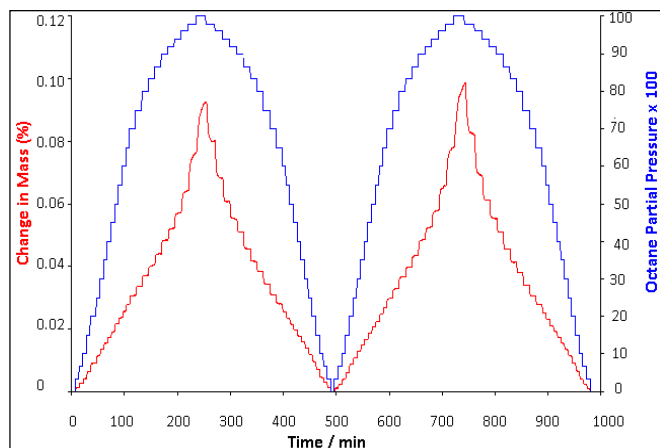

Figure 1 Octane sorption/desorption kinetics on caffeine

Figure 1 also demonstrates that the sorption and desorption kinetics are relatively fast and that for each step in partial pressure, equilibrium is rapidly established for two complete adsorption desorption cycles. Figure 2 shows the isotherm plots for the same data, demonstrating both the reproducibility and reversibility of the sorption/desorption processes in this case. Also important to note is the loss level of hysteresis which is consistent with surface adsorption via a physisorption mechanism. The isotherm shape shows a classic type II BET shape. Reproducible and fast sorption kinetics are further indicators that the vapour uptake is dominated by surface adsorption processes rather than bulk absorption. Adsorption of vapours exclusively on the substrate surface is a prerequisite to meaningful surface energy analysis using this gravimetric method. Absorption of vapours into the bulk for example can lead to morphological changes in the substrate and also invalidates the analysis which depends an accurate computation for Gibb's surface adsorption surface excess for a uniquely defined surface area.
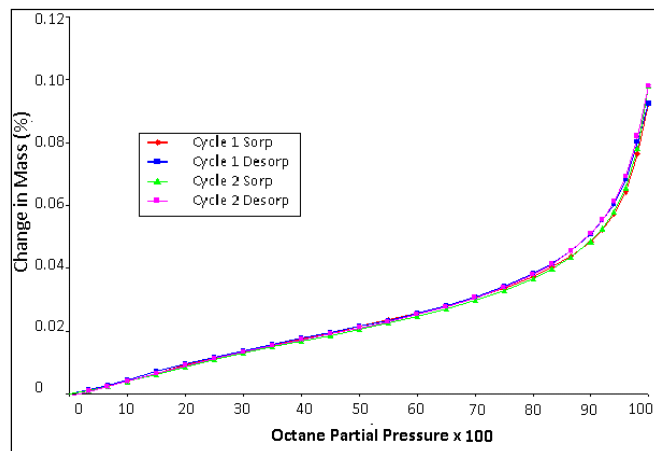

Figure 2 Sorption/desorption isotherms for octane on caffeine

The consequences of morphological changes due to adsorption/absorption of IPA molecules into amorphous regions of the caffeine substrate are demonstrated in Figure 3. In this case the uptake of the polar solvent into amorphous regions of the material during the first sorption cycle causes the T_g of the material to fall below 25°C at approximately 0.2 relative partial pressure. This leads to a collapse of the amorphous regions leading to a crystallisation event, concurrent with the expulsion of solvent from the sample. Therefore our surface energy analysis is not valid, however since the crystallisation process is an irreversible event, we may use the second sorption cycle data to calculate a lower estimate of the surface energy based upon the more stable crystalline form. This was undertaken in the current study.
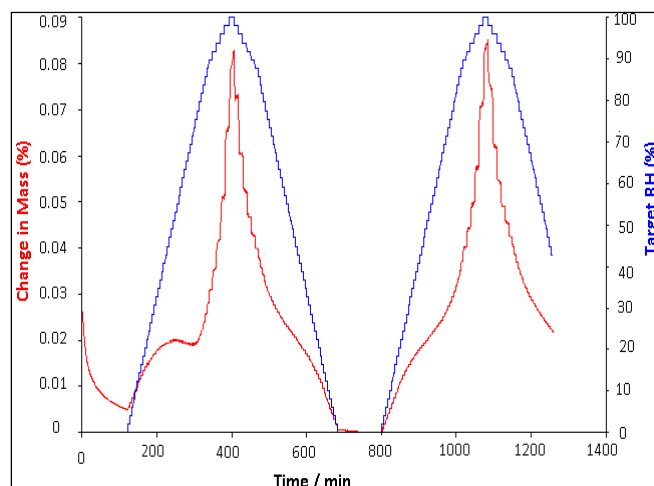

Figure 3 Kinetics of sorption/desorption for IPA on caffeine.

Table 1 shows a summary of the π_e and W_{S-L} data obtained for octane and IPA vapours on caffeine and lactose. It should be noted that a similar crystallisation event was observed for the lactose with IPA, and is consistent with the previously observed behaviour of amorphous lactose in the presence of water vapour, a highly polar solvent [4]. Therefore in the case of IPA for both lactose and caffeine adsorption studies, the surface energy analysis was carried out on the second cycle's adsorption data. Analysis of both adsorption and desorption cycles yielded π_e values which varied by less than 0.5mN/m. The adsorption cycles data that correspond most closely to advancing contact angles are reported in this study.

Table 1. Experimentally determined σ, π_ε and W_{S-L} data.

Sample	Vapour	σ / m^{2}g^{-1}	π_e/mN m^{-1}	W_{S-L}/mN m^1
Lactose	Octane	0.8051	8.7	52.3
	IPA	0.8051	12.7	56.1
Caffeine	Octane	1.16	10.7	54.3
	IPA	1.16	20.1	63.5

Table 2 includes data recently obtained for the components of the surface energy of IPA and octane based on Wilhelmy wetting experiments performed using a PTFE substrate of known surface energy. This data is necessary so that a full analysis of the surface energy may be undertaken.

Table 2. Literature values for γ^p_L , γ^d_L , and γ_L for octane and isopropyl alcohol (IPA).

Solute	γ^d_L / mN m^{-1}	γ^p_L /mN m^{-1}	γ_L / mN m^{-1}
Octane	21.8	0	21.8
IPA	19.3	2.4	21.7

Table 3 summarises the surface energy values obtained by the above methodology for samples of α-Lactose Monohydrate and Caffeine.

Table 3. Experimental values for γ^p_S, γ^d_S, and γ_S for lactose and caffeine.

Solute	γ^d_S/mNm^{-1}	γ^p_S/mNm^{-1}	γ_S. s/mN m^{-1}
Lactose	30.4	5.6	36.0
Caffeine	31.1	14.2	45.4

The γ^d_S values of 30.4 mN/m determined in the current work for α-lactose monohydrate are about 25% lower than the IGC estimates of [5]. The reasons for this difference are discussed later in this section. The IGC method employed in their study did not allow the polar component of the surface energy, and thus the total surface energy, to be estimated.

Buckton and his co-workers have estimated γ^d_S to be 39.9mN/m for caffeine using IGC, which is higher, but consistent, with our own estimate of 31.1mN/m. In both cases the wetting analysis yields estimates that are about 20% lower. This observation is completely consistent with the notion that IGC experiments at infinite dilution involve probing the higher energy surface sites at very low surface coverage (less than 0.1% typically). Our vapour adsorption method obtains average information based on complete surface coverage. Thus our vapour adsorption method is similar to traditional wetting experiments in which the solid surface is covered completely by either vapour or liquid species.

The total surface energy for caffeine was also determined by Dove et al [2] using two different Wilhelmy wetting balance approaches. Values of γ_S reported were 60.2mN/m using a porous powder compact and 47.9 mN/m using a powder coated microscope slide. Our own estimate of 45.4mN/m is in very good agreement with this coated slide data.

However, a more careful analysis of the components that make up the total surface energy reveals a more complex situation. The γ^d_S of 31.1mN/m for caffeine found by this study is much lower than the Doves coated slide estimate of 44.5mN/m. Interestingly a value of 33.1mN/m for γ^d_S may be deduced from Buckton's di-iodomethane wetting data for caffeine based on an experimental contact angle of 49° and a total

surface tension for di-iodomethane of 50.8mN/m. Also the estimates of γ^p_S for caffeine reported in thus study of 14.2mN/m are much lower than the Dove et al estimate of 3.4mN/m.

The results obtained for caffeine and lactose with IPA highlight potential reasons for some of the significant differences and discrepancies reported for surface energies of pharmaceutical materials. We have observed that the presence of polar vapour species can induce changes in powder morphology, presumable due to the transformation of small amounts of amorphous material into more stable crystalline form. In the case of the gravimetric technique used in the current study these transitions could be observed and the data rejected. Subsequent data obtained for a more stable sample could be thus analysed. In the case of other techniques such as wetting experiments this type of behaviour has not been reported and consequently wetting data has been analysed assuming the thermodynamic stability of the sample. We believe that this assumption may be unsafe for many pharmaceutical materials and result in potential errors in surface energy estimates.

Conclusion

Gravimetric flow gas techniques have been shown to be a highly sensitive method for obtaining adsorption/desorption isotherms for organic vapours on particulate pharmaceutical materials. These adsorption isotherms may be analysed to obtain the equilibrium spreading pressure and this has been successfully undertaken for octane and isopropanol on both caffeine and lactose monohydrate. From this data the dispersive, polar and total surface energies of these powders have been accurately estimated

using the classical semi-empirical model of Fowkes.

This new technique does not suffer from any of the problems often associated with liquid wetting based approaches and has the significant benefit of being able to monitor some aspects of the morphological stability of the powder during the experiment.

References

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