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The effect of the comminution technique on the surface energy of a powder

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Summary

Six samples of powdered aspirin were prepared from one crystalline source by use of ball, vibrating ball, hammer and fluid energy mills, either alone or in combination. These were compared with a sample of powdered aspirin obtained from Macarthy's. The surface energetics of the classified and milled samples were assessed with a vacuum microbalance and a microcalorimeter, to monitor water adsorption. Thermodynamic parameters and apparent rate constants for adsorption were obtained. Milling was shown to alter surface energetics in a manner related to the perceived energetics of the mill. Powders which were milled by two consecutive processes were found to retain the surface energetics imparted by the first process. Electron micrographs have been used to attempt an explanation of this phenomenon. The wetting process seems to be controlled by the availability of adsorption sites on the powder and the degree of order that is consequently imposed on adsorbed water; the entropy of adsorption is most directly related to wettability.

Introduction

There are many processes in which the surface energy of a powder is important. These include the preparation of pharmaceuticals (e.g. suspension formation and wet granulation in tableting processes) and the dissolution of pharmaceutical solid oral dosage forms to allow drug release.

It has long been recognised that the chemical nature of the powder and its physical pretreatment will both play a role in controlling surface

energetics. Unfortunately, there is very little published work to demonstrate how significant physical pretreatment can be in controlling this surface property. It would be interesting both fundamentally and industrially, to know the effects of standard treatment processes such as milling on the powder surface.

In this study, the interaction between 7 samples of a solid, which had been milled by a variety of techniques, and water has been measured.

The only similar work known to us (Cook, 1978) showed small differences between samples of griseofulvin, but used contact angles as the major research tool. The use of contact angles to assess the surface energy of powders can be undertaken by two methods, i.e. liquid penetration into

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powder beds, or measuring drops on powder compacts. Both these techniques have recently been criticised (Buckton and Newton, 1986a and b). The use of liquid penetration requires a hydrophilic powder if water is the solvent of interest. With hydrophobic powders, water does not penetrate and consequently most workers use alcohol/water mixtures; this produces many problems in terms of partition of the liquids and uncertainty about the composition of the vapour phase which prewets the powder (Buckton and Newton, 1986a). The use of compressed discs has the major disadvantage that the process of compression alters the surface energy that was to be measured (Buckton and Newton, 1986b).

In this work, interaction of the powder with water vapour has been studied. The use of vapour has been justified in a previous publication, where the experimental techniques of microcalorimetry and the vacuum microbalance have been described (Buckton and Beezer, 1987a). By using such techniques it is possible to measure the inter-

TABLE 1

The particle size of the milled and classified samples, obtained by use of the Coulter Counter TAI1 and the Malvern HSD2600 particle sizer

Sample	Coulter (μm)	Malvern (μm)
Vibrating ball	13.4	15.5
Fluid energy	6.7	7.6
Hammer/fluid energy	6.0	6.7
Hammer	14.5	18.7
Macarthy's	13.4	15.7
Ball/fluid energy	6.2	6.6
Ball	12.0	13.6

action between powder and water with greater confidence than before.

Materials and Methods

Crystalline aspirin was milled by a variety of techniques to produce the following 6 samples:

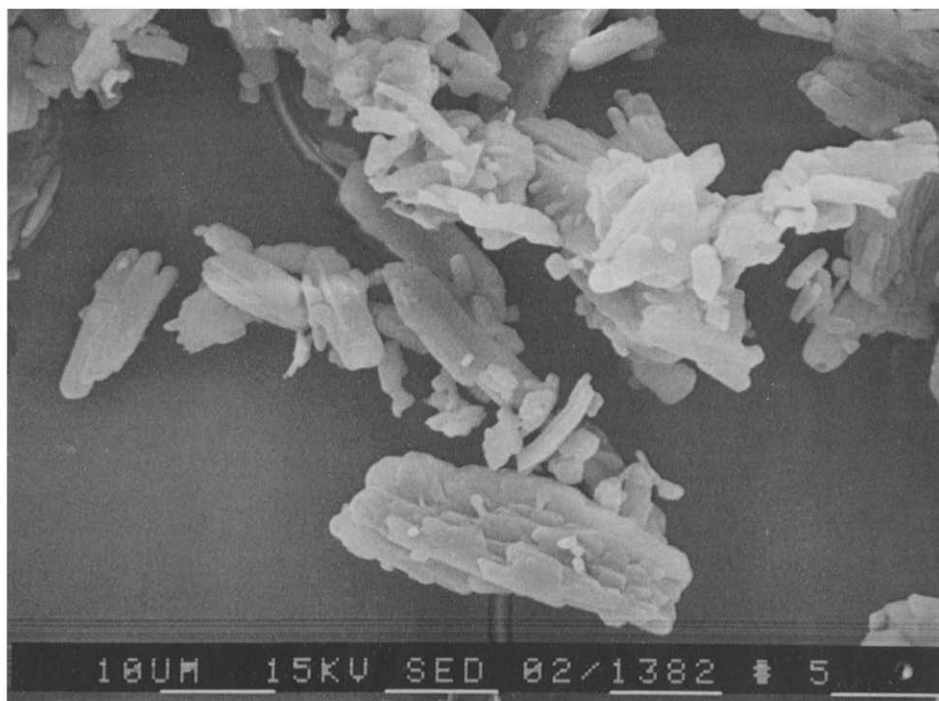


Fig. 1. Scanning electron micrograph of ball-milled sample.

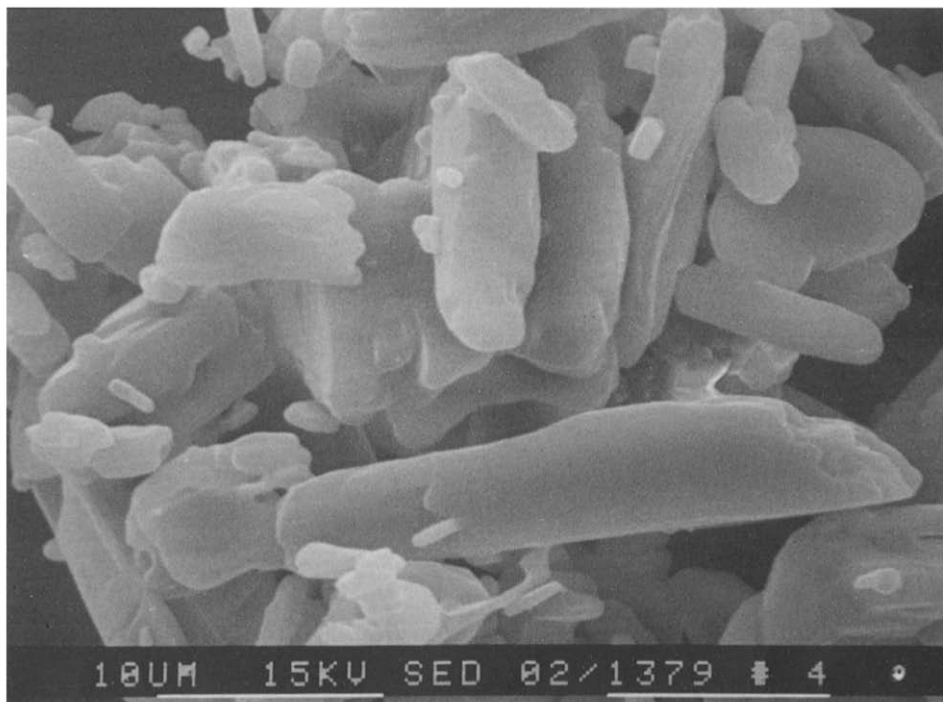


Fig. 2. Scanning electron micrograph of hammer-milled sample.

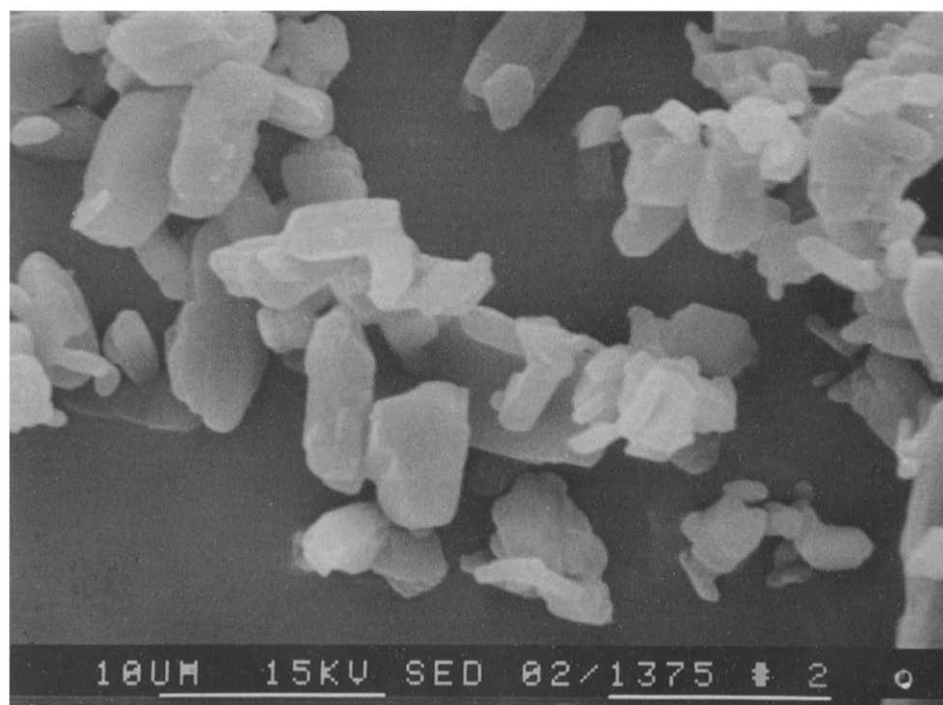


Fig. 3. Scanning electron micrograph of fluid energy-milled sample.

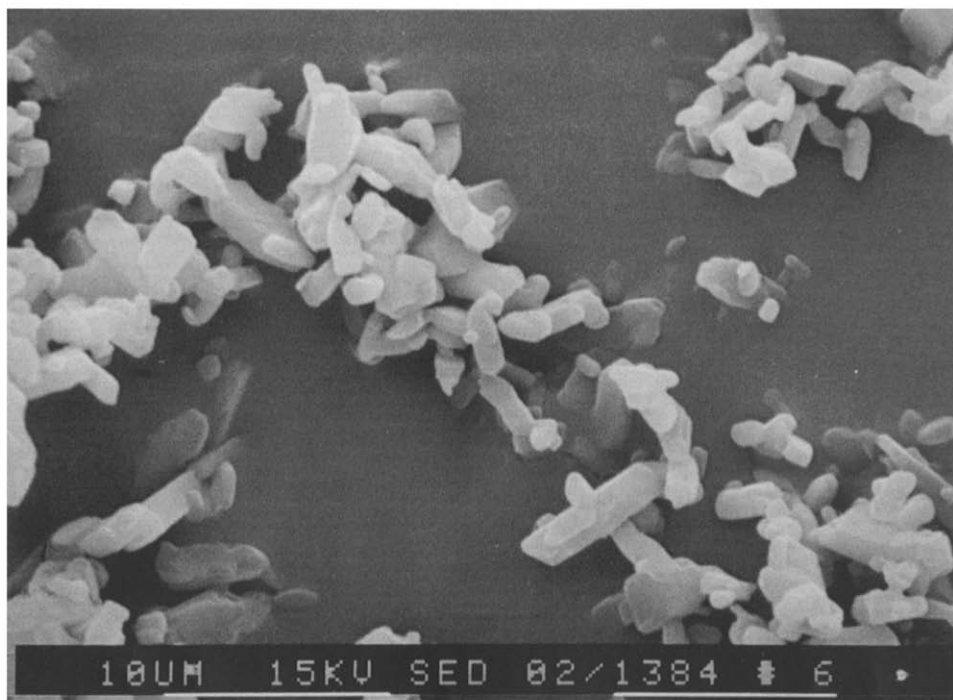


Fig. 4. Scanning electron micrograph of sample milled by hammer, then fluid energy mills.

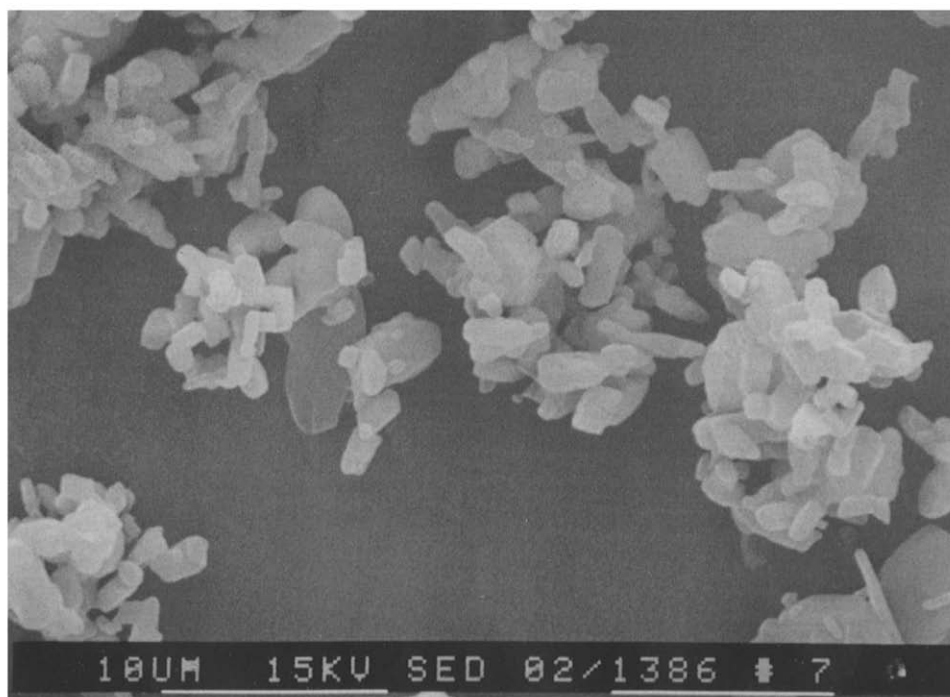


Fig. 5. Scanning electron micrograph of sample milled by ball, then fluid energy mills.

- (1) rotating ball-milled for 18 h
- (2) vibrating ball-milled (Fritsch, F.R.G., Type 502) (a high-energy process using an agate ball in an agate mortar which was agitated on a rotating sieve shaker)
- (3) hammer-milled (Alpine, Type C100)
- (4) fluid energy-milled (Gem, air jet mill)
- (5) ball-milled sample passed through fluid energy mill
- (6) hammer-milled sample passed through fluid energy mill.

Also a sample of powdered aspirin (Macarthy's), which had been milled previously by the manufacturer, was used.

The load for each mill was set at 10 g and all 7 samples were classified using a zig-zag classifier (Alpine, A 100 MZR) to produce a sub-20- μm cut. If necessary, more than one 10 g quantity was milled in order to produce sufficient sub-20- μm powder after mixing the batches. Particle size measurements were undertaken after dispersing the powder in a suitable non-solvent and treating with ultrasonics for 3 min, using a Coulter Counter (TAII) and by laser diffraction (Malvern, 2600HSD) (Table 1). Previous work (Buckton and Beezer, 1987b) suggests that variations in particle size over this range will not produce observable differences in surface energy.

Electron scanning micrographs were taken of each sample using a Philips EM501B and those for the ball, hammer, fluid energy, hammer and fluid energy, and ball and fluid energy milled samples are shown in Figs. 1–5.

The thermodynamics of adsorption were obtained using the vacuum microbalance and microcalorimetric techniques, with the method as previously reported (Buckton and Beezer, 1987a). The standard state was taken as the number of mol water adsorbed per gram of powder at 25.0°C. The enthalpy of adsorption (ΔH_{ads}) was obtained from the powder–time (p – t) output of the calorimeter corrected to the defined standard state, calibration was by electrical heat and as previously reported (Buckton and Beezer, 1987a). The Gibb's function for adsorption (ΔG_{ads}) was obtained by use of the vacuum microbalance, where an equilibrium constant (K) was defined as the number of mol water adsorbed per gram of powder

at the saturated vapour pressure (SVP) of water at 25.0°C, divided by the SVP of water at 25.0°C. Then Eqn. 1 is applied:

$$\Delta G_{\text{ads}} = -RT \ln(K) \quad (1)$$

(R , gas constant, T , absolute temperature). The entropy of adsorption (ΔS_{ads}) was obtained thus:

$$\Delta G_{\text{ads}} = \Delta H_{\text{ads}} - T\Delta S_{\text{ads}} \quad (2)$$

The surface energetics of the samples were measured ca. 1 week after milling in each case. Replicate determinations in 2-week periods subsequent to the first assessment of surface energy showed that the surface was not subject to measurable energetic alteration over this period.

Results and Discussion

The values obtained for the thermodynamic parameters show clear differences in energetics between the different samples. The nature of the interaction between the water vapour and aspirin is reflected by the fact that ΔH_{ads} values are negative (exothermic), ΔG_{ads} values are positive indicating a disfavoured process and ΔS_{ads} values are negative showing the disfavoured imposition of order into the system. The values of ΔH_{ads} are estimated to be accurate to ± 0.4 kJ/mol; this value has been obtained by working through the maximum and minimum values that could be calculated by the small variations in area under the power–time curve and sample to sample variations in weight of adsorption, it is clear that reproducibility is extremely good. The maximum projected error in ΔG_{ads} is such as to make the results virtually indistinguishable from one-another, whilst that for ΔS_{ads} is in the order of ± 4 J/mol/K. It should be stressed that the errors quoted above are in fact the total spread of results, rather than ± 1 S.D.; this has been done to demonstrate the very small level of variation observed in these measurements.

By comparison with the previous study on selected barbiturates (Buckton and Beezer, 1987a), the aspirin samples all adsorbed a much larger

quantity of water per unit weight of powder (Table 2), but the fact that values of ΔH_{ads} are much lower in this study shows that even though more water is bound the average binding force is considerably weaker. There are two possible explanations for the low enthalpy values; either the powder/water bonds are very weak or there are very few powder/water bonds and large numbers of weak water/water bonds. In our previous work (Buckton and Beezer, 1987a) we described a mechanism for wetting of hydrophobic powders in which water sat in 'droplets' anchored to only a few available binding sites on a solid surface, rather than spreading over the surface to form a monolayer. The mechanism can also be postulated in this case where entropic hindrance to wetting is observed and can be explained as being due to the production of water 'droplets' held together by weak binding forces, the 'droplets' being anchored to the powder surface by only a few powder/water bonds, producing a highly ordered system with low average bond strength. A consequence of this mechanism of adsorption is that entropy, rather than enthalpy, will be dominant in controlling the process; this is contrary to the previously held view which led some workers to quote only enthalpies of wetting.

The apparent first order rate constants for the decay of the $p-t$ curves have been calculated by the same method as before (Buckton and Beezer, 1987a) and are presented in Table 3. The method of calculation is not ideal, as was previously explained, but with small differences between blank and test curves it proves to be the only practical

TABLE 2

The thermodynamic functions for the adsorption of water vapour onto the milled samples

Sample	ΔH_{ads} (kJ/mol)	ΔG_{ads} (kJ/mol)	ΔS_{ads} (J/mol/K)
Vibrating ball	-1.8	21.5	-84.9
Fluid energy	-1.8	20.9	-76.2
Hammer/fluid energy	-5.6	20.4	-87.2
Hammer	-6.0	21.7	-92.9
Macarthy's	-6.0	21.5	-92.3
Ball/fluid energy	-7.4	20.2	-92.6
Ball	-8.9	21.0	-100.3

TABLE 3

Apparent first-order rate constants (correlation coefficients) for adsorption of water vapour onto the milled samples

Sample	k ($\times 100$)	half-life of $p-t$ curve (s)
Vibrating ball	0.6 (0.995)	115.5
Fluid energy	0.6 (0.989)	115.5
Hammer/fluid energy	1.2 (0.999)	57.8
Hammer	1.5 (0.999)	46.2
Macarthy's	1.3 (0.999)	53.3
Ball/fluid energy	1.1 (0.998)	63.0
Ball	1.4 (0.999)	49.5
Blank	1.8 (0.999)	38.5

option. The kinetics show that in all cases the ordering of water molecules takes longer when adsorbing to the powder than when entering/interacting with the empty cell. The samples prepared by fluid energy and vibrating ball mills show slow adsorption kinetics indicating that molecules have to orientate themselves to fit to very few binding sites on the powder followed by entropically hindered water/water binding. The other samples (hammer-, Macarthy's-, hammer/fluid energy-, ball/fluid energy-, and ball-milled) all show very similar adsorption kinetics intermediate between the blank response and that of the high-energy milled powders. Surprisingly, the entropies of adsorption of water onto the fluid energy and vibrating ball-milled samples are the smallest negative values (small entropic hindrance), even though the kinetics for adsorption onto these surfaces is slow.

It is possible to rank the samples of aspirin in terms of their entropy of adsorption, which seems to give the best indication of their interaction with water, as follows (going from high to low entropic hindrance): ball-milled, hammer-milled, ball- then fluid energy-milled, Macarthy's, hammer- then fluid energy-milled, vibrating ball-, and fluid energy-milled. This rank order is almost inversely proportional to the rank order of enthalpy of adsorption, the enthalpy of adsorption being directly proportional to the perceived energetic behaviour of the mills. It can be seen that low-energy milling processes result in powders with the

most entropically hindered and enthalpically favoured wetting, which based on past experience will result in the poorest wetting surface.

It would appear to be the total past history of the powder that controls its surface energy. This is demonstrated by those samples which have been milled twice. It is not unusual to mill a sample twice during production processes, either to produce a sufficiently fine material to allow suitable feed to a micronising mill or to remill a sample which has not achieved the required size. The sample that was milled by ball and then fluid energy mills and the sample produced by hammer and fluid energy mills behaved more like the powders that had been prepared by the first of the two treatment processes, even though the fluid energy mill had resulted in further size reduction in both samples (Table 1). This fact is of practical and fundamental interest although at present we are not able to offer an unequivocal explanation for this observation. One possible reason for the observation is that the scanning electron micrographs for the hammer-milled and ball-milled samples show rough edges and fracture lines in the crystals, it is possible that part of the subsequent size reduction produced by the fluid energy mill was initiated by the first milling process. This, if true, would mean that the mechanism of crystal fracture caused by the mill is responsible for the resulting surface energy of the powder. The scanning electron micrographs support this view, as the shape of the samples that have been milled by the ball as well as the fluid energy mill (Fig. 5) is more in line with the splintering effect seen on the ball-milled sample (Fig. 1) than the more regularly shaped particles produced by fluid energy milling alone (Fig. 3).

The general trend of size distributions is that all the samples showed little polydispersity, being tightly grouped around the mean. There are two size ranges, those which have been exposed to fluid energy processes ($\sim 7 \mu\text{m}$) and those which have not ($\sim 15 \mu\text{m}$). These differences in size are due to the efficiency of the comminution technique and as such are unavoidable, and are of an order of magnitude that is not likely to be the cause of any measurable change in surface energetics (Buckton and Beezer, 1987b). This state-

ment is supported as the rank order of surface energy is not the same as rank order of particle size.

The sample of Macarthy's aspirin produced values for the thermodynamic parameters that were in line with those for the hammer-milled sample. The possibility exists, therefore, that surfaces of unknown history can be characterised and defined retrospectively.

Conclusion

Physical treatment of powders, such as milling, causes large changes in powder surface energetics.

The change in a powder's surface properties are likely to be in proportion to the efficiency of the mill that is used; however, if two consecutive milling processes are used the powder will tend to have energetic properties more similar to powders treated by the first, rather than by the second, process used. It is probable that the second milling process used to reduce the size of a powder, achieves size reduction by means of disrupting flaws caused during the first milling process. There is a case for utilising the first milling process to which a powder is subjected as a means of obtaining the most desirable powder surface properties.

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