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A microcalorimetric study of powder surface energetics

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Summary

The enthalpies of adsorption (ΔH_{cal}) of water vapour onto powdered drug surfaces (amylobarbitone, butobarbitone, pentobarbitone and phenobarbitone) have been measured in a modified commercial microcalorimeter. These data are compared with the thermodynamic parameters (including ΔH_{iso}, the isosteric enthalpy of adsorption) obtained previously from vacuum microbalance studies. The results are used to discuss the relative values of ΔH_{cal} and ΔH_{iso} with respect to the mechanism of interaction and the relative hydrophobicity of the surfaces. The calorimetric studies also allow calculation of kinetic parameters which further describe the adsorption process.

Introduction

The surface energetics of a powder will play a potentially vital role in the ease of preparation, stability and bioavailability of pharmaceutical products. A recent series of publications (including Buckton and Newton, 1985; Buckton and Newton, 1986a and b) has demonstrated a number of important factors, such as: (1) the surface properties of a powder are, at least in part, a measure of its past history; and (2) the energetics will be dependent upon the prevalance of crystal defects. However, the most important conclusion was that existing techniques for assessing surface energetics of powders (i.e. liquid penetration and measurements of contact angles on sessile drops on compressed discs) suffered from practical and/or theoretical limitations. Consequently, the opinion has been developed that meaningful data on small systematic chemical/physical changes of the individual powders will not be obtained from such techniques. Subsequently, two alternative approaches to the problem of understanding powder/water interactions have been proposed (Buckton et al., 1986; Buckton et al., 1987) which concentrate on the vapour phase interaction. The approach of Brunauer et al. (1938) works on the principle of assuming that the initial binding of water vapour to the powder will provide the most important component of the total interaction, with subsequent vapour wetting being analogous to condensation; immersion being the ultimate extension of this theory. The rationale for study of the vapour phase is that, at least in theory, a powder must first be wetted by a vapour and then by a liquid. The powders that were used in the work reported in the original papers (Buckton and Newton, 1985; Buckton and Newton, 1986a and

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b) (the barbiturates) and in the vapour phase studies carried out to date (vacuum microbalance (Buckton et al., 1986) and dielectric spectroscopy (Buckton et al., 1987)) have been used once again in this study, for the simple reason that such a large body of data now exists for these samples. Each powder was a 63–90 μm sieved size fraction of the original. Later in this paper the case will be made for studies on more logically selected powders.

The data obtained from the vacuum microbalance (Buckton et al., 1986) demonstrated that the enthalpy (ΔH_{iso}), entropy (ΔS_{iso}) and Gibb's function (ΔG_{iso}) of the adsorption process could be obtained by use of a van't Hoff approach (the subscript "iso" referring to the traditional notation of these values as being isosteric). The problem of propagation of errors in the van't Hoff analysis was discussed and it was concluded that the differences observed in ΔH_{iso} were not distinguishable within the limits of experimental error. Consequently, it was decided that a more suitable approach would be to attempt to combine the data for surface coverage obtained from the microbalance with that obtained by direct measurement of the enthalpy of adsorption in a microcalorimeter (ΔH_{cal}) at one fixed temperature.

In the design of both experiments (microbalance and calorimetry) it was important that the surface was standarised prior to adsorption of water vapour. To achieve this the powders were vacuum-treated until a reproducibly desorbed surface was obtained; this was regarded as "clean".

Whilst calorimetric determinations of vapour adsorption have been undertaken before no reference can be found relating to any published study where one adsorbate (in this case water) has been adsorbed onto a range of adsorbents (in this case powder surfaces). The fact that no similar studies exist leads to certain problems, and the need to make decisions on the choice of such factors as suitable standard states. The reasons for the choices made and the problems that were encountered will be discussed in the appropriate sections.

Commercial calorimeters are classified as batch or flow instruments. Depending upon which type of instrument is being used, the theoretical basis for data treatment will be different. In this work it is not absolutely clear as to whether the instrument should properly be regarded as a batch or flow system; from the data which are to be presented, onset of action is apparently instantaneous, implying that water vapour access is not rate limiting, and consequently the process is best considered as a batch experiment.

Materials and Methods

Measurements of the enthalpy of adsorption (ΔH_{cal}) were undertaken using an LKB 10700 microcalorimeter. The signal output, a power–time (p–t) curve, was recorded on a chart recorder, via an amplifier operated at 100 μV sensitivity, such that an electrical calibration peak of 0.02 W when applied for 10 s produced a peak height equivalent to an 81% deflection on the recorder with a decay half life of 84.1 s. The experimental design (Fig. 1) consisted of a vacuum pump connected by stainless steel tube and a glass tap system to the calorimeter cell, via a temperature equilibration coil. The glass tap allowed the calorimeter cell to be open to vacuum or to a water reservoir. The vacuum pump and water reservoir were postioned just outside of the calorimeter's air thermostat box and were controlled at 25.0 ± 0.1° C, this coil was sufficient to present water vapour to the cell at the required temperature (as determined by blank, powder-free, experiments). The calorimeter cell was specially engineered from stainless steel and was connected to the vacuum/vapour line via a PTFE tap fitting (standard high-pressure chromatography system adaptor). The inner surfaces of the stainless steel cell were coated with di-

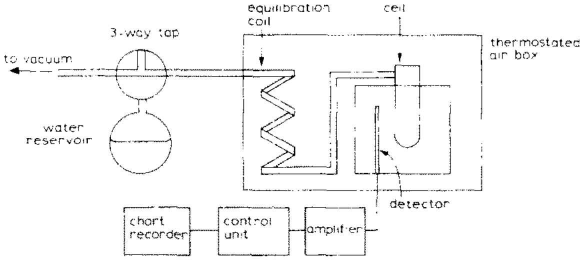

Fig. 1. Diagrammatic representation of calorimetric system.

chlorodimethylsilane to reduce the interaction with the water vapour. A quantity of powder (about 10 mg) was transferred to the cell, outgassed and then quickly weighed to allow minimal adsorption from the atmosphere. By measurements on a range of weights of powder, it was ascertained that a linear response was obtained for area under the *p–t* curve as a function of weight up to approximately 20 mg. The cell was equilibrated overnight (under vacuum) and then vapour adsorption and desorption cycles were undertaken. Total adsorption response was normally complete in 20–30 min, as was the vacuum desorption. Four replicates of each were undertaken.

Calibration of the system was by means of electrical energy provided by an LKB 2107 microcalorimeter control unit. It is generally accepted that calibration via this technique will be equivalent to heat generated from within the cell, despite the fact that the heater for calibration is positioned in a physically different position. Reputable workers will routinely undertake a standard reaction of the type under study in order to prove the validity of the electrical calibration. This is not possible in this case, simply because the adsorption onto surfaces is open to so many variables, e.g. the previous treatment of the surface, the presence of defects, etc. Rouquerol et al. (1986) have addressed this problem and have suggested the imposition of a bronze sample as a standard surface by which different laboratories can calibrate their results *. Until a suitable standard is agreed upon other workers in this field may apply for a sample of the powder used in this work if direct comparisons are required.

All the *p–t* curves that were obtained were studied by two methods: firstly, the areas under the curve were measured (Apple microcomputer graphics package) and the average of 4 replicates taken. The blank (no powder) response was then subtracted from the area and the enthalpy calculated by reference to the electrical calibration. The enthalpy values were calculated per mole of water adsorbed. The quantity of adsorbed water was obtained from the vacuum microbalance data for the same powders (Buckton et al., 1986) at the same temperature, as the experimental conditions can reasonably be assumed to be the same in both cases. Secondly, the kinetics of the adsorption and desorption processes were examined by measuring the rate of decay of the response of the *p–t* curves obtained for the powder system, in relation to the blank determinations and electrically generated responses. Published procedures, which will be discussed later, were employed.

Results

Enthalpy of adsorption

The enthalpy of adsorption was calculated in the following manner. The area under the curve for the blank determination was subtracted from the area under the curve for the actual response. By reference to the electrical calibration the area due to adsorption onto the powder was converted into joules (J). This value was then converted into J/mol of adsorption water onto that weight of powder. The quantity of adsorbed water at 25 °C was previously determined using the vacuum microbalance (Table 1). The reason for standardising to moles of adsorbed water was to remove the variable of surface area of the different powders.

Gibb's function and entropy of adsorption

The Gibb's function for adsorption was calculated directly from a single point determination using the vacuum microbalance (Buckton et al., 1986). It has been commonplace in previous attempts to obtain the thermodynamic functions of adsorption to link one adsorption isotherm with calorimetric determinations (Schroder, 1984). The standard state assumed is the number of moles of water adsorbed (b) per gram of powder at the saturated vapour pressure (p) of water at the temperature of the experiment. The equilibrium constant is thus defined as:

$$K_{\mathrm{ad}} = \frac{[b]}{[p]} \qquad (1)$$

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* We are not entirely confident that electrical calibration under different experimental conditions will lead to the same calibration constant. However, for the system as described here *all* conditions have been maintained constant from experiment to experiment.

TABLE 1

The thermodynamic functions of adsorption at 25.0°C

Powder	Quantity of adsorbed water (mg/10,000 mg)	ΔH_{cal} (kJ · mol^{-1})	ΔG * (kJ · mol^{-1})	ΔS_{cal} (J · mol^{-1} · K^{-1})	ΔH^{*}_{iso} (kJ · mol^{-1})	ΔS^{*}_{iso} (J · mol^{-1} · K^{-1})
Amylobarbitone	0.080	-25.5	+38.4	-214.4	-66.8	-353.0
Pentobarbitone	0.080	-12.7	+38.4	-171.5	-67.5	-355.4
Phenobarbitone	0.074	-8.1	+38.6	-156.7	-65.2	-348.3
Butobarbitone	0.080	-4.5	+38.4	-144.0	-61.4	-334.9

* Recalculated for revised standard state from the data previously published (Buckton, et al., 1986).

ΔG is obtained by:

$$\Delta G = -RT \cdot \ln(K_{ad}) \tag{2}$$

It is then possible to calculate a value for the entropy of adsorption from:

$$\Delta G = \Delta H - T\Delta S \tag{3}$$

The values obtained for the thermodynamic functions are presented in Table 1.

Kinetics of adsorption

If it is accepted that this experiment is to be regarded as a batch experiment, then the method by which the kinetic analysis should be made is to determine the excess heat output decay as a function of time compared with the decay from an electrical calibration peak (Hunt et al., 1972). The differences observed were fairly small, and measurement of the enclosed area became unrealistic when compared with the experimental error involved in making the measurement. It was clear, however, that the rates observed for the different samples varied from each other and from the blank, and consequently half-lives for the decay, and apparent first-order rate constants have been calculated by a method which theoretically relates to flow microcalorimetry (Beezer and Tyrrell, 1972). The natural logarithm of the power (q) is plotted as a function of time. The gradient being the apparent first-order rate constant. Fig. 2 shows how the blank determination was subtracted from the results obtained for the powdered samples. It should be stressed that this approach shows the real differences that exist between the rates for individual samples, but the arithmetic value ascribed should not be regarded as being of absolute significance.

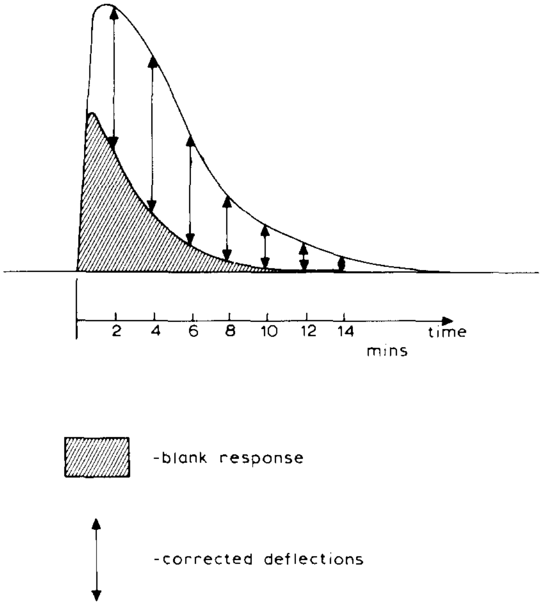

Fig. 2. The method by which kinetic data was obtained, allowing correction for blank response.

Discussion

From previous studies (Buckton and Newton, 1985; Buckton and Newton, 1986a and b) it has become clear that the use of contact angles in order to obtain values of ΔG for wetting processes is not advisable due to the uncertainty about the meaning of measured or derived contact angle values. This is the major limitation in previous attempts to obtain a thermodynamic assessment of surface energetics of powders (e.g. Storey, 1985). However, it is clear that obtaining values of ΔG, ΔH and ΔS is particularly useful as these parameters provide sufficient data by which the process cannot only be quantified, but can also be potentially explained.

In this work a value of ΔH has been obtained by direct calorimetric measurement (ΔH_{cal}) for the adsorption process, and ΔG has been obtained from a single adsorption isotherm, rather than by use of a dubious contact angle. This technique of combining microcalorimetric and vacuum microbalance data provides a method by which small changes in powder surfaces can be examined without the need to rely on contact angle measurements. The results can, therefore, be regarded as thermodynamically valid; this is not the case if contact angles are used where it becomes necessary to employ the much criticised Young equation

$$\cos\theta = \frac{\gamma_{\text{SV}} - \gamma_{\text{SL}}}{\gamma_{\text{LV}}} \tag{4}$$

where θ is the contact angle, γ refers to the interfacial tensions between the solid (S), liquid (L) and vapour (V) coupled with interpretations of wetting, such as that described by Parfitt (1973), to obtain a value for the Gibb's function. In a recent review (Schroder, 1984) typical values for adsorption at 20°C were reported for isosteric (differential) and calorimetric (integral) functions. These were ΔH_{cal} -10 to -60 $\text{kJ} \cdot \text{mol}^{-1}$, ΔH_{iso} -30 to -200 $\text{kJ} \cdot \text{mol}^{-1}$, ΔS_{cal} 0 to -200 $\text{J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$, ΔS_{iso} -100 to -700 $\text{J} \cdot \text{mol}^{-1} \cdot \text{K}^{-1}$ and ΔG -2 to -14 $\text{kJ} \cdot \text{mol}^{-1}$ at 25°C. The orders of magnitude of our results are clearly in keeping with published data. It should be stressed that values obtained for ΔG and ΔS will be altered numerically by changes in the choice of standard state (hence the difference between this work and previously published data on these powders (Buckton et al., 1986)); consequently, the values for these functions cannot be regarded as absolute, but rather as a relative indication of variations between powders.

The values of ΔG obtained are very similar for all 4 powders (Table 1). This is entirely due to the fact that the total amount of water vapour adsorbed onto the standard weight of each powder at equilibrium is almost identical. This shows that the Gibbs energy change in the adsorption process is virtually identical for each powder. When the values of ΔH and ΔS are calculated directly from the adsorption isotherm data, it follows that it will be impossible to differentiate between the types of adsorption that occur at each surface, and the numerical values will therefore not be significantly different. These isosteric functions will only give a valid representation of the adsorption process if it is assumed that the adsorption progresses by the same mechanism for each powder surface, ideally by monolayer and then multilayer formation. This was assumed in our previous publication (Buckton et al., 1986) where ΔH_{iso} was split into two terms, one relating to monolayer formation and the other to condensation (multilayer formation). From the calorimetric data it is clear that although the total amount of water adsorbed onto the powder is very similar, the enthalpy change (ΔH_{cal}) varies significantly from powder to powder (Table 1). If the liquid penetration data (Buckton and Newton, 1985; Buckton and Newton, 1986a) is taken as an empirical indication of wettability for these powders, the rank order from most hydrophobic to most hydrophilic would be: amylobarbitone/pentobarbitone, phenobarbitone and then butobarbitone. From the data obtained for ΔH_{cal} (and to a lesser extent ΔH_{iso}) it is clear that the reverse of this rank order is observed, amylobarbitone having the largest negative value suggesting the process to be, enthalpically, the most favoured. The entropy term (ΔS_{cal}) clearly shows that the adsorption process involves the imposition of a more ordered system (and is thus less favoured) for the more hydrophobic powders, than for the more hydrophilic powders. Summarising this information it can be seen that the overall process of adsorption for each powder is similar in terms of Gibbs energy change, and the positive value shows that the wetting is not favoured. Enthalpically the wetting of the more hydrophobic powders is most favoured; however, the entropic hindrance is largest with the most hydrophobic surfaces and this is the dominant component. This clear com-

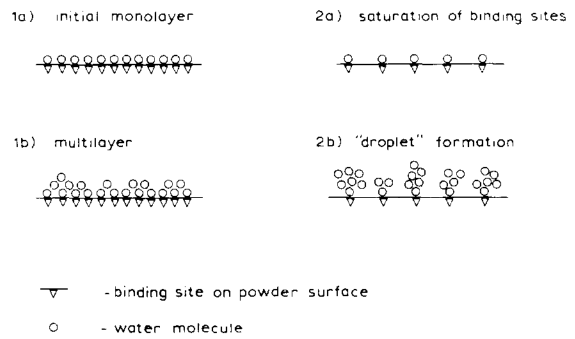

Fig. 3. Schematic representation of two possible methods of vapour adsorption: (1) BET theory; (2) mechanism proposed as explanation of results published here.

petition between an enthalpicaly favoured and entropically hindered process suggests that authors who have only reported values for the enthalpy of wetting processes may have misleading conclusions to their work.

In an attempt to explain the results obtained in this work the following mechanism is proposed. If it is assumed that the availability of surface adsorption sites (their prevalance and/or their ease of access) is a major factor controlling wettability, then two extremes can occur (Fig. 3). It is clear that the total adsorption (and Gibbs energy change) may be very similar in 1b and 2b of Fig. 3 and also that the total enthalpy change involved in 2b (small powder/water interactions plus many water/water interactions) may be as large, or indeed larger, than that in 1b. Equally it is clear that the entropy associated with the formation of each wetted surface will be very different, with 2b being a much more ordered system. The hypothesis that is proposed is that increasing hydrophobicity can be related to decreased prevalance of, or access to, adsorption sites, thus preventing monolayer coverage and thus making wetting entropically unfavourable.

TABLE 2

Apparent first-order rate constants for adsorption and desorption (calculated by subtracting blank values; see text) and the half-life for the decay of the adsorption power–time curve ($t_{1/2}$).

Powder	Rate constants ($\times 10^3$)		$t_{1/2}$ (s)
	Adsorption	Desorption	
Amylobarbitone	6.67 (0.997)	7.17 (0.999)	103.9
Butobarbitone	9.94 (0.999)	14.00 (0.991)	69.7
Pentobarbitone	7.03 (0.999)	9.09 (0.984)	98.6
Phenobarbitone	6.67 (0.999)	8.77 (0.992)	103.9
Blank	9.83 (0.985)	4.46 (0.996)	70.5

Correlation coefficients (in brackets) are for plots of ln(power) vs t.

The kinetic data (Table 2) shows that amylobarbitone, pentobarbitone and phenobarbitone, all of which are classically described as hydrophobic (will not spontaneously immerse in water), have indistinguishable apparent rate constants that are significantly slower than the kinetics of adsorption onto butobarbitone (classically described as hydrophilic). The rate of adsorption onto butobarbitone is indistinguishable from the blank determination. This supports the aforementioned hypothesis if one assumes that a monolayer is formed on butobarbitone, which has many easily available adsorption sites, whilst "droplets" (Fig. 3) are formed on the other surfaces. The kinetics of monolayer formation are likely to be rapid, with the need for orientation of water molecules small, whilst orientation for the other powders will be critical, allowing the water molecules to bind to the few available sites.

A recent publication (Buckton et al., 1987) on the use of dielectric spectroscopy in the assessment of wettability showed that a hydrophilic powder (barbitone) had two adsorption processes, including one strongly favoured process which was not present for the hydrophobic powder (amylobarbitone). The single process for adsorption observed for amylobartitone was also present for barbitone. The dielectric study correlates well with the results from this work, and suggests that the easily accessible site described for the hydrophilic powder is monolayer adsorption, whilst the smaller response observed for the hydrophobic powder relates to binding to the few available sites. Further use of the dielectric technique alongside the vacuum microbalance and calorimeter should provide a clearer understanding of the mechanisms of wetting. It will then be possible to select and treat powder surface in such a way as to understand the importance of molecular structure and physical treatment, and hopefully suggest how both of these parameters can be controlled to produce optimum properties. This work is currently progressing towards the study of potential structure–activity relationships of wetting phenomena.

Conclusions

The combination of microcalorimetric and vacuum microbalance techniques for studies on water vapour adsorption onto powders permits a full set of thermodynamic parameters to be calculated, without the need to rely on a contact angle. The information obtained by this combination allows considerably more insight into the mechanism of wetting than was possible from any single technique.

The mechanisms of vapour phase adsorption suggested for these 4 powders are such that the one which is regarded as hydrophilic (contact angle less than 90°) appears to be wetted by a monolayer of adsorbed water vapour; whilst those that are regarded as hydrophobic exhibit a barrier to wetting which seems to be due to the lack of availability of binding sites.

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