Quantitative Characterization of Sorption through Isothermal Microcalorimetry

Introduction

When a problem is encountered in the production or storage of solid dosage forms, invariably the problem is somehow connected to the sorption of water. In the presence of water, the physical properties of solids may be altered causing changes in flow properties, free volume, and compressibility; or there may be an accelerated interconversion between polymorphic forms seriously affecting bioavailability. Very often, shelf life or chemical stability is markedly compromised by high humidity[1]. Further, with regard to chemical stability, the reactivity of solids in their amorphous state is usually greater than in their crystalline state[2]. The availability of high sensitivity microcalorimeters and the computer software necessary to analyze the calorimetric data has resulted in the increased application of this technique in pharmaceutical systems[3,4,5,6]. This application note presents the results of a calorimetric investigation of the adsorption of water vapor on a crystalline solid and introduces a model to quantitate calorimetric adsorption isotherms. It further demonstrates how this model can be applied to characterize the interaction of water with an amorphous material; a freeze-dried decapeptide.

Background

The relationship between the volume (or mass) of an adsorbed gas at a particular temperature on a solid material as a function of the partial pressure of the gas is described by the BET equation. An analogous equation (Equation 1) relates the total heat evolved upon adsorption of a gas on a solid and the partial pressure of the gas[7].

$$Q_{int} = \frac{CV_m\left[H_1 x + (H_L - H_1)x^2\right]}{(1-x)(1-x+Cx)}$$

Equation 1

Q_{int}, is the total heat evolved per gram of solid at any partial pressure x and V_m is the number of moles of the gas required to form a monolayer on the solid. The constant C is equal to $\exp[(H_1-H_L)/RT]$ as in the BET equation. H_1 and H_L are the heats of adsorption in the first and the subsequent layers respectively. The heat of adsorption in the second layer (and the subsequent layers) is assumed to equal the heat of condensation of the gas (H_L). Buckton and Beezer[8] invoked a similar mechanism involving a monolayer and condensed layers to explain the calorimetric adsorption data. If the heat of condensation of the adsorbate is known, *e.g.* 44 kJ/mol of water

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Fields of application
Material Sciences-Pharmaceuticals

Instrument configuration

2277	Thermal Activity Monitor (TAM)
5510	Prethermostat
2277-201	4 ml Ampoule Microcalorimetric Unit
2277-131	Digitam Software
2255-010	Stainless Steel RH Perfusion Ampoule
640-01/02	Mass Flow Controller

Note: A set of two Matheson Mass Flow Controllers 0-10.00 SCCM, Model 8270-0441 in conjunction with 2 Matheson Flow Transducers, Montgomeryville, PA, USA and two Stainless Steel RH Perfusion Ampoules (2255-010), Thermometric, were used in the original work.

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at 25 °C, the number of unknown parameters in the above equation reduces to two, H_1 and V_m. In a manner comparable to the BET model calorimetric data provides an estimate of V_m and hence an apparent surface area of the sample, if the cross sectional area of the adsorbate is known.

Experimental

Microcalorimetry

A 100-300 mg sample of sodium benzoate (Baker, 30/45 sieve fraction) or 14 mg of a freeze dried decapeptide (Smithkline Beecham, (amorphous) contained in a small glass boat is placed in the ampoule. The relative humidity (±0.1 %) above the solid sample was controlled by mixing dry nitrogen and nitrogen presaturated with water vapor[5]. Most experiments were conducted using a total flow rate of 2 mL/min controlled by two mass flow controllers. The calorimeter was calibrated using internal electrical calibration heaters.

Adsorption and Desorption experiments

Adsorption experiments were conducted at 25°C. After insertion into the calorimeter, the sample was dried overnight under dry nitrogen flow. After a sufficient drying of the sample, a defined relative humidity was created in the sample cell and the heat flow was recorded. At each relative humidity a blank experiment was conducted in an identical manner with no sample in the sample cell. The experiment was performed at several relative humidities and a calorimetric adsorption isotherm was obtained. The water sorption

properties of a lyophilized decapeptide peptide were also studied. The material is amorphous in nature. Figure 4 shows the results obtained using 14 mg of material at 25°C, and a total gas flow rate of 5 mL/min. Blank corrections are a little higher at this flow rate compared to 2 mL/min. Least squares parameters that are generated using Equation 1 are C = 8.66 and $V_m = 277 \times 10^{-5}$ mol water/gram decapeptide.

Desorption experiments were performed at the end of the adsorption experiments by changing the gasflow to dry nitrogen.

Results and Discussion

A typical calorimetric response to the adsorption of water vapor on a sample of sodium benzoate is shown in Figure 1. Areas under the adsorption peaks were equal in magnitude but opposite in sign to the area under the corresponding desorption peak, as shown in Figure 2, indicating the reversibility of adsorption.

The amount of water associated with solid material before and after exposure to water vapor was determined by Karl Fischer Titrimetry. Considering the amount of water involved in the sorption and desorption processes as indicated in Figure 3 it is evident that the sensitivity achievable via microcalorimetry is quite good.

Isotherms for the adsorption of water on sodium benzoate are obtained from the area under the heat flow time curve at several relative humidites after correcting using the appropriate blank.

Figure 3 shows the calorimetrically derived adsorption isotherm of water on sodium benzoate at 25°C. The symbols are experimental values (average of three replicates) and the line is least squares generated using Equation 1 with fit parameters C = 7.296 and $V_m = 4.276 \cdot 10^{-5}$ moles water/gram sodium benzoate.

Conclusions

Heat conduction microcalorimetry can be a very sensitive and convenient means of obtaining adsorption isotherms. An equation is presented that describes the adsorption isotherm and provides a means of obtaining water vapor sorption surface area from the calorimetric data. This method is more sensitive than some of the conventional methods. Because the entire isotherm can be recorded using very small samples (as low as 10 mg), the method may be extremely valuable in a pharmaceutical setting where drug compounds are available in limited quantities. Furthermore, the method is not limited to the use of water alone, valuable information about the surface may be obtained by using different adsorbates. The calorimetric method can be easily adapted for such measurements by simply replacing the water in the humidifying chambers with appropriate solvents.

Although it may not be proper to refer to a "monolayer" using a lyophilized/amorphous solid[9,] the mathematics associated with BET adsorption can be used to characterize the relationship between water sorbed and relative humidity even for

amorphous materials. The value of this is that there is a link between the amount of water present and the glass transition temperature of the solid. The plasticizing effects of water, potentially lowering glass transition to near ambient temperatures, and the resultant increased susceptibility of amorphous materials to physical and chemical changes in the rubbery state makes knowing the amount of water important.
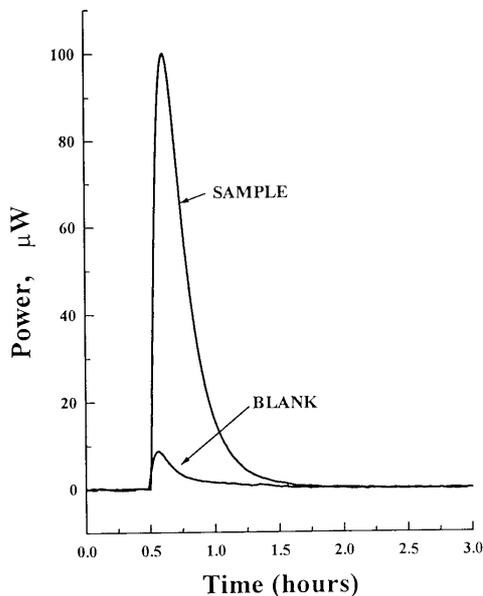

Figure 1. *A typical calorimetric response to the adsorption of water vapor on sodium benzoate at 25°C. Sample size 100 mg, relative humidity 10%, total flow rate 2.0 mL/min (0.2 mL/min water saturated nitrogen and 1.8 mL/min dry gas).*
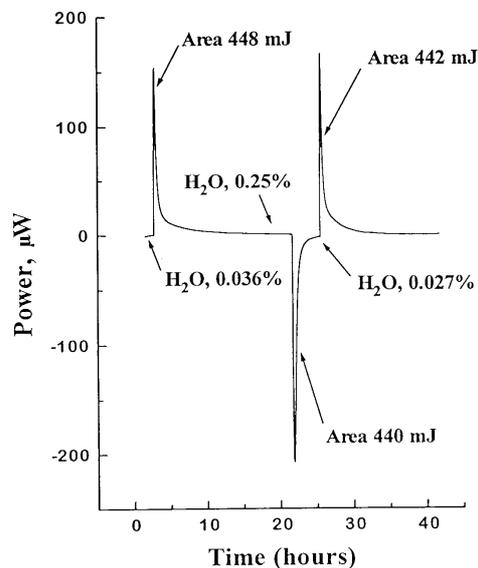
Figure 2. *Adsorption-Desorption cycles of water on sodium benzoate at 25°C and 40% relative humidity. The water content at the beginning and the end of the experiment are also shown.*
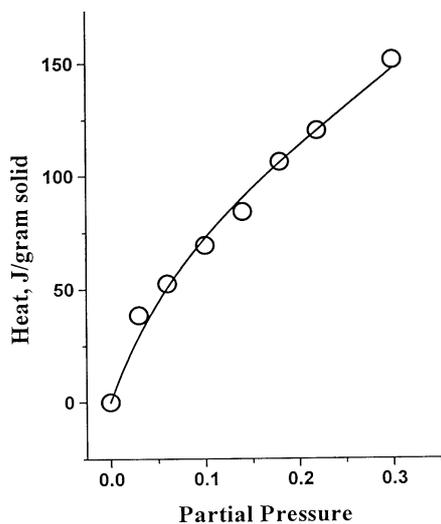
Figure 3. *The calorimetric adsorption isotherm of water vapor on sodium benzoate at 25°C . Each point represents an average of three replicates. The curve is the least squares generated using Equation l.*
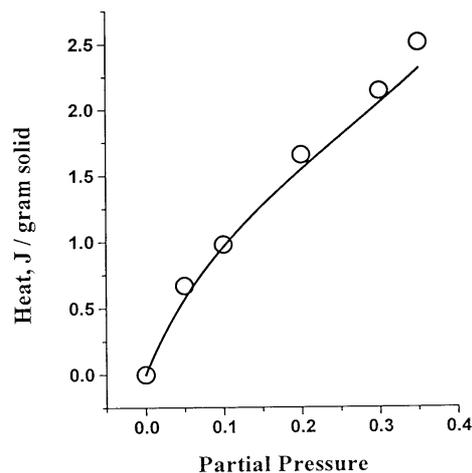
Figure 4. *Water sorption isotherm derived calorimetrically for an amorphous solid decapeptide at 25°C. The symbols are experimental points and the line least squares generated using Equation l.*