DRUG DEVELOPMENT AND INDUSTRIAL PHARMACY, 9(1&2), 215-222 (1983)

THE USE OF A FLOW MICROCALORIMETER TO CHARACTERISE POWDER SURFACES

B. BHATT AND M.H. RUBINSTEIN, School of Pharmacy,
Liverpool Polytechnic, Byrom Street, Liverpool L3 3AF, U.K.

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/20/12
For personal use only.

INTRODUCTION

When a material is exposed to air at a definite temperature and humidity, it will gain or lose moisture until on equilibrium moisture content is attained. This value depends on the chemical and physical properties of the material and is generally lower for non-porous solids and higher but more variable for fibrous or colloidal organic substances[1]. In pharmaceutical powders the sorption of moisture poses many problems for the formulator. Moisture uptake can have a profound effect on both the physical and chemical stability of the powder. The presence of a film of moisture can provide a medium where chemical reactions such as hydrolysis can take place. This in turn affects the powder properties such as the potency of the drug or may result in the formation of insoluble products on the surface thus affecting drug availability. It can also lead to changes in coloration of the drug. From a manufacturing point of view, moisture uptake has an added adverse effect in terms of the handling properties of the material. This is because an increase in moisture content generally causes a free-flowing powder to cohere, thus causing inefficient mixing with other powders, blocking of machinery and

Copyright © 1983 by Marcel Dekker, Inc.

0363-9045/83/0901-0215$3.50/0

RIGHTSLINK

resultant non-uniformity of the product. On the other hand a very fine dry powder may become easier to handle when a little moisture is present and may also reduce the dustiness of the powder and increase the powder's capacity to consolidate.

Moisture usually condenses on the surface of the substance exposed to the atmosphere. However in porous powders, it may penetrate the depth of the powder bed. At a given temperature condensation increases with an increase in the partial pressure of water vapour in the atmosphere. Powder surfaces in general are very reactive and the amount of moisture adsorbed increases as the surface area of a powder increases, because moisture uptake is essentially a surface phenomenon (Sprowls[2]). For the measurement of adsorption at liquid/solid interfaces, Groszek[3] developed the flow microcalorimeter. This instrument has been used to measure the lubricating action of solid lubricants such as graphite[4,5] and more recently for the study of dental enamel surfaces[6]. In addition the instrument has been used for the measurement of specific surface area[7,8]. The flow microcalorimeter has been modified and adapted for use in the present work in order to evaluate heats of adsorption and desorption of moist air at various powder surfaces.

EXPERIMENTAL

The flow microcalorimeter (Microscal Ltd., London) is shown in Fig.1. It consists of a metal block (A) surrounding a cylindrical cavity in which the calorimeter cell (B) made from P.T.F.E. is situated. The bottom of the cell is closed by a fine stainless steel gauze (C) attached to a metel outlet tube (D) which can support the adsorbent (E). The top end of the cell adheres tightly to the bottom walls of a central channel in the metal block forming a continuation of the cell cavity. The interior of the cell is thus accessible either from the top of

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/20/12
For personal use only.

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/20/12
For personal use only.

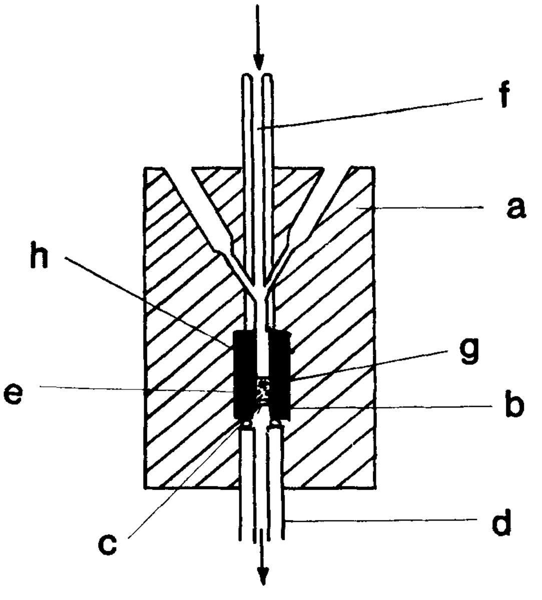

Fig. 1. The Flow Microcalorimeter

a. Metal block
b. Calorimeter cell
c. Gauze
d. Outlet tube
e. Adsorbent
f. Central channel
g. Thermistors
h. Reference thermistors

the metal block or from the bottom of the block after removal of the outlet tube. Liquids (or gases) can percolate freely through the cell, after flowing along the walls of the central channel (F). The temperature of the adsorbent is measured by two thermistors (G) protruding from the walls of the cell. The thermistors are connected in a Wheatstone bridge circuit and are opposed by two reference thermistors (H) embedded in the metal block. The four thermistors constitute the arms of the bridge, its output being fed to a potentiometric recorder. The maximum sensitivity of the instrument is 5 μJ and temperature changes down to 10^{-5} °C can be detected. The calorimeter is

RIGHTSLINK

principally designed for use with liquid adsorption systems. Normally, when adsorption is complete, the temperature of the bed returns to the original value and the recorder pen returns to the base line; indicating that adsorption is complete and the bed is in equilibrium with the fluid. The area under the adsorption curve can be related to the total heat evolved during the interaction. The apparatus is basically designed for use with liquid adsorbates. The calorimeter was therefore modified and adapted so that heats of adsorption and desorption of moist air could be determined. The modifications involved blocking off the two liquid inlet ports to prevent any air escaping from the cell. Further modifications were necessary so that dry air or air at known humidities could be passed through the calorimeter cell. The flow rate of air was maintained constant using a calibrated kerosene filled manometer. Prior to entry to the calorimeter, air was dried through a column of silica gel. The air was then diverted to humidifying flasks containing saturated salt solutions or through a column of calcium chloride for further drying, before the conditioned air was passed through the cell. It was found that the rate of air flow was very critical, since the shape of the curve depended largely on the rate of air flow; a higher flow rate resulted in sharper peaks. The following saturated solutions, maintained at 30°C, were employed:

(a)	Lithium chloride	11% R.H.
(b)	Potassium acetate	22% R.H.
(c)	Magnesium chloride	33% R.H.
(d)	Sodium chloride	75% R.H.

Various crystalline and amorphous powders were investigated with the modified apparatus together with granular materials and pure materials artificially contaminated with a small amount of an antibiotic.

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/20/12
For personal use only.

RIGHTSLINK

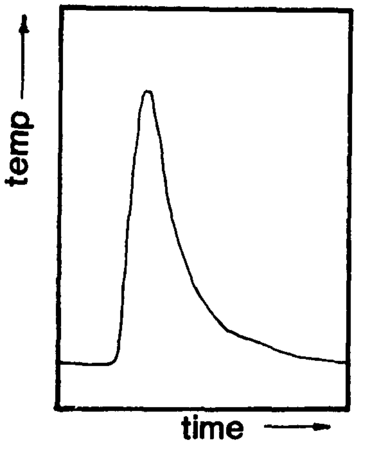

Fig. 2. Adsorption curve for calcium hydrogen orthophosphate crystals

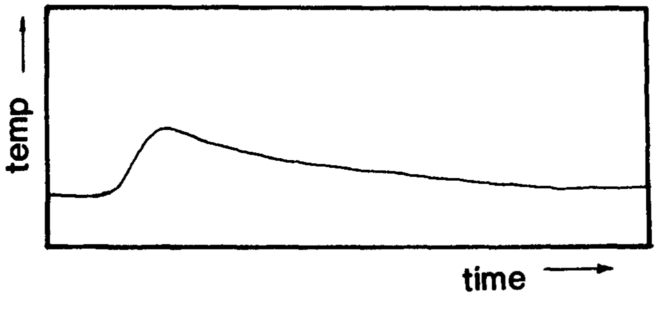

Fig. 3. Adsorption profile for amorphous calcium hydrogen orthophosphate

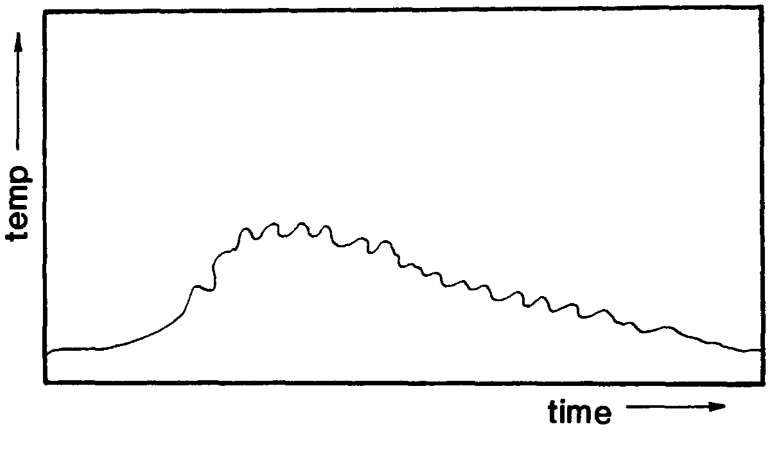

Fig. 4. Curve for calcium hydrogen orthophosphate granules

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/20/12
For personal use only.

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/20/12
For personal use only.

RESULTS AND DISCUSSION

It was generally found that the shape of the adsorption/desorption profiles appeared to characterise the surface nature of the material under test. Crystals such as calcium hydrogen phosphate ($CaHPO_4$) were found to exhibit a sharp smooth peak with the chart pen returning rapidly to the base line (Fig.2). The profiles were found to be very reproducible. Crystals such as $CaHPO_4$ are normally smooth with very few indentations and therefore build up of the moisture monolayer is rapid and a sharp adsorption peak is obtained. For amorphous powders with smooth surfaces and no indentations, e.g. amorphous $CaHPO_4$ (Fig.3), a smooth but broad peak is produced for the build-up of the monolayer. The broadness is due to the continuing release of heat as the humid air slowly penetrates the amorphous mass. For amorphous particles having indentations, a peak is obtained which

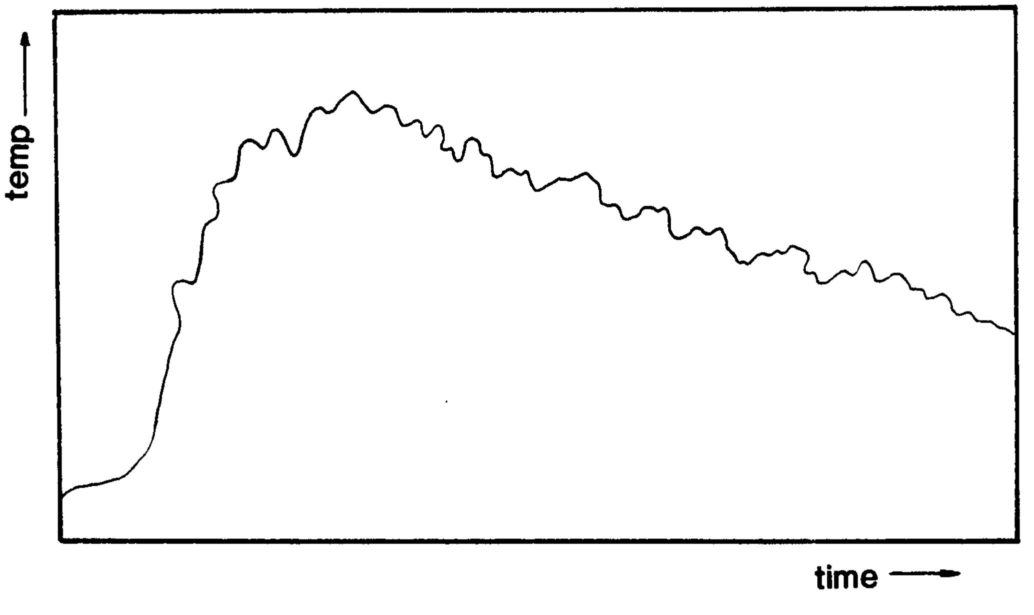

Fig. 5. Spray dried lactose

RIGHTSLINK

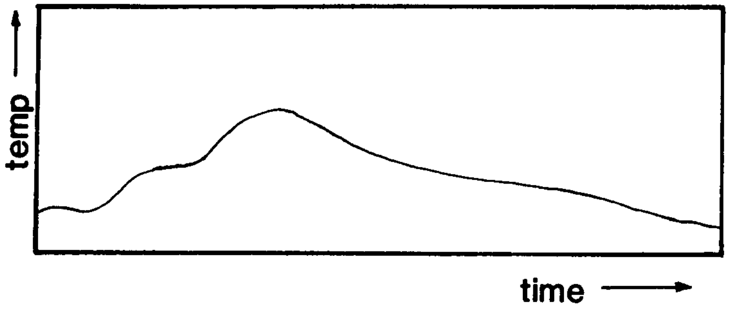

Fig. 6. Calcium hydrogen orthophosphate crystals with contaminant.

is broad and serrated. This is because penetration of the humid air is slow and as it reaches into the crevices it generates transient heat which leads to a transient rise in temperature to produce a serrated profile. Granules such as $CaHPO_4$ granules, produce similar curves for similar reasons (Fig.4). However curves for hollow granules, such as spray dried lactose (Fig.5), are much broader compared to solid granules, as it takes much longer for the water vapour to penetrate the inner orifices. For a given powder, the general shape of the curve is always the same, provided that the surface is not contaminated. If a contaminant is introduced, e.g. $CaHPO_4$ with a small quantity (0.01% w/w) of an antibiotic (Fig.6), then the adsorption profile exhibits more than one broad peak; being the combined profiles of the $CaHPO_4$ and the antibiotic. Thus the calorimetric technique described is a simple and powerful method for examining the surface structure and surface poisoning of drug and powder samples.

REFERENCES

1. Theory and Practice of Industrial Pharmacy. Lea and Febiger, Philadelphia (1970).
2. Sprowl. In: Sprowl's American Pharmacy, 7th Ed., J.B. Lippincott Co., Toronto (1974).
3. A.J. Groszek. Proc. Roy. Soc., 314, 473 (1970).

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/20/12
For personal use only.

RIGHTSLINK

4. A.J. Groszek. Proc. of ASLE/ASME International Solid Lubrication Symposium, Tokyo., 22 (1975).

5. R.M. Matveevsky, A.B. Vipper, A.M. Markov, I.A. Buyanovsky and V.L. Lashkhy. Wear, 45, 143 (1977).

6. M.V. Stack and R.P. Fletcher. Symposium on Thermal Analysis and Calorimetry, Plymouth Polytechnic, Plymouth, U.K., September 1977.

7. T. Allen and R.M. Patel. Particle Size Analysis Conference, Bradford (1970).

8. A.H. Collins, G.R. Heal, I.J. McEwan., British Rail, Derby. Particle Size Analysis Conference, September 1977.

Drug Development and Industrial Pharmacy Downloaded from informahealthcare.com by Biblioteca Alberto Malliani on 01/20/12
For personal use only.