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Rapid Communication

The effect of storage at ambient humidity on the BET-specific surface area of tablets compacted from different materials

K.A. Riepma [a], B.G. Dekker [b], R.S. Jager [a], P.A. Elberse [b] and C.F. Lerk [a]

[a] *Department of Pharmaceutical Technology and Biopharmacy, University of Groningen, Groningen (The Netherlands) and* [b] *Department of Inorganic Chemistry, Heterogeneous Catalysis Division, University of Utrecht, Utrecht (The Netherlands)*

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Summary

Tablets compacted from both water soluble and water insoluble particulate solids showed no change in BET-specific surface area when transferred immediately after ejection from the die in a dry atmosphere. Storage at ambient humidity resulted in an irreversible decrease in surface area, caused by capillary condensation of moisture and blocking of pores in the tablet. Nitrogen physisorption isotherms performed on crystalline β-lactose tablets demonstrated diminution of the mesopore surface area.

A previous paper reported the effect of moisture sorption on the strength and BET-internal surface area of lactose tablets (Riepma et al., 1992). The results showed for both α-lactose monohydrate and roller dried β-lactose tablets neither moisture uptake nor any change in crushing strength and specific surface area when transferred immediately after ejection from the die in a dry atmosphere. The tablets demonstrated, however, time-dependent moisture uptake when exposed to an ambient humid atmosphere. Moisture sorption reached a plateau within 10 min and was accompanied by a decrease in both crushing strength and BET-specific surface area of the tablets. Subsequent storage of the tablets in a dry atmosphere resulted in an increase in strength but no change in surface area. The irreversible decrease in specific surface area was suggested to be caused by blocking of pores in the tablets by sorbed moisture, which cannot be removed without applying a rigorous outgassing procedure. The present study was performed to prove the general significance of moisture sorption in tablets by extending the surface area determinations to excipients with different water solubilities.

The materials used were α-lactose monohydrate, crystalline β-lactose and roller dried β-lactose, supplied by DMV (Veghel, The Netherlands). Calcium sulphate and barium sulphate were obtained from Fluka Chemie AG (Buchs, Germany) and dicalcium phosphate dihydrate from E. Mendell Co. (U.S.A.). All handling was

Correspondence to: C.F. Lerk, Dept of Pharmaceutical Technology and Biopharmacy, University of Groningen, Ant. Deusinglaan 1, 9713 AV Groningen, The Netherlands.

performed in a room with constant temperature (20 ± 1°C) and constant relative humidity (45 ± 5%). The powders were stored in the same room for at least 1 week before use.

Compaction of 500 mg flat-faced tablets with a diameter of 13 mm was carried out using a programmable hydraulic press (ESH Testing, Brierley Hill, U.K.). The die was prelubricated with magnesium stearate.

The BET-surface area of tablets was measured with a Quantasorp gas-adsorption apparatus (Quantachrome Corp., Syosset, U.S.A.) in a single point determination. The samples were measured 'immediately' or after storage for different time periods and different humidity conditions. When measured immediately the tablets were put in a nitrogen atmosphere for transfer to the gas-adsorption apparatus in order to suppress moisture sorption. No outgassing procedure was performed. The data are the means of four tablets.

The general significance of the effect of storage conditions on the BET-specific surface area of tablets is demonstrated by the results as obtained for a series of materials with different solubilities (Table 1). Different compaction forces were used for the different materials in order to obtain tablets with sufficient strength and a measurable BET-surface area. The data in column A represent the specific surface area of the tablets as obtained by immediate transfer of the tablets from the die into a nitrogen atmosphere. The data in columns B and C demonstrate the effect of storage of the tablets for 30 min and 24 h, respectively, over silica gel. As expected from the previous study (Riepma et al., 1992), the tablets exhibited no significant change in surface area when stored in a dry atmosphere. Columns D and E present the specific surface area of the tablets when stored for 30 min and 24 h, respectively, at 45% RH. These results demonstrate decreased surface areas, caused by moisture sorption. Subsequent drying of the compacts for one night at 50°C over silica gel showed no or only an insignificant increase in surface area, except for dicalcium phosphate dihydrate tablets. The latter tablets demonstrated both a dramatic increase in surface in surface area and a considerable loss in weight, evidently caused by loss of water of crystallization at the increased temperature of 50°C.

In conclusion, all tablets compacted from excipients with different water solubilities showed no change in BET-specific surface area when stored in a dry (silica gel) atmosphere, but an irreversible decrease in surface area when exposed to an ambient humid atmosphere.

The effect of water sorption on BET-surface area determinations by nitrogen physisorption was studied more closely for tablets of crystalline β-lactose. This lactose type was chosen because of the absence of water of crystallization which al-

TABLE 1

The effect of storage conditions on the BET-specific surface area of tablets compacted from different materials with different water solubilities

Materials		Water solubility (g/100 ml)	Cf (kN)	Specific tablet surface area (m^2/g)					
				A	B	C	D	E	F
α-Lactose monohydrate	(250–315 μm)	20 [b]	20	0.95	0.94	0.96	0.69	0.53	0.50
Crystalline β-lactose	(250–315 μm)	20 [b]	20	0.75	0.80	0.70	0.53	0.41	0.46
Roller dried β-lactose	(250–315 μm)	20 [b]	20	1.78	1.81	1.72	1.27	0.80	0.85
Barium sulphate	(< 300 μm)	0.02 [a]	50	4.53	4.50	4.76	4.36	4.06	3.95
Calcium sulphate	(< 300 μm)	< 0.2 [a]	80	6.48	6.52	6.45	5.77	4.04	4.28
Dicalcium phosphate dihydrate	(< 300 μm)	< 0.1 [a]	30	1.46	1.44	1.42	1.24	1.03	5.02

Cf, compression force; A, 'immediately' after compaction; B, after storage for 30 min over silica gel; C, after storage for 24 h over silica gel; D, after storage for 30 min at 45% RH; E, after storage for 24 h at 45% RH; F, after storage for 24 h at 45% RH followed by one night over silica gel at 50°C. Sources: [a] Handbook of Chemistry and Physics, 60th Edn. (1980); [b] Martindale, The Extra Pharmacopoeia, 29th Edn. (1989).

lows more rigorous drying. For two tablets of crystalline β-lactose the complete nitrogen adsorption isotherm (77 K) was measured using a Gemini 2360 Analyzer (Micromeritics Instrument Corp., Norcross, U.S.A.). The single isotherm was measured immediately after compaction and the other was measured after storage of the tablet for 5 days at room temperature under atmospheric conditions. Before measurement of the isotherms the tablets were evacuated for 3 min at 10^{-3} Torr. This drying procedure proved to be adequate as evacuation of the tablets under more rigorous conditions (10^{-4} Torr at 80°C for 18 h) did not result in significantly different BET-surface areas. The isotherms are represented in Fig. 1. The multipoint BET-surface areas were calculated for the range $0.08 < p/p_0 < 0.35$. It was found that the BET-surface area decreased from 0.61 to 0.42 m^2/g when the tablet was stored under atmospheric conditions. The isotherms were analysed on pore distribution. The tablets were shown to contain no micropores (pore widths < 2 nm) and only a small number of macropores (pore widths > 50 nm). The mesopore area distribution was calculated from the

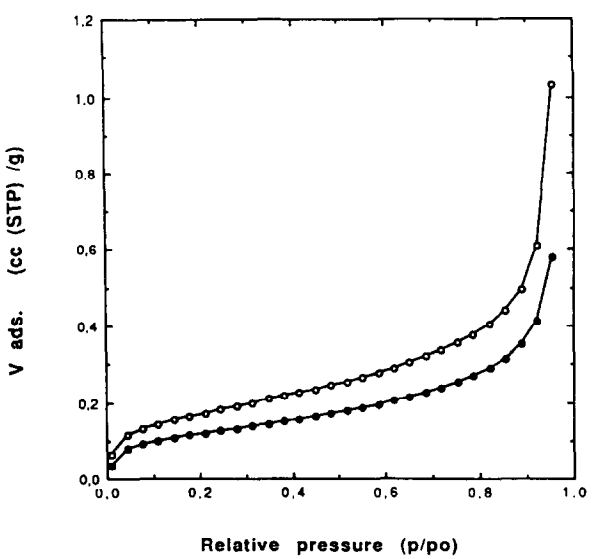

Fig. 1. Nitrogen adsorption isotherms at 77 K performed on tablets compacted at 20 kN from a sieve fraction (250–315 μm) of crystalline β-lactose. Open symbols, immediately after compaction; closed symbols, after 5 days storage under atmospheric conditions.

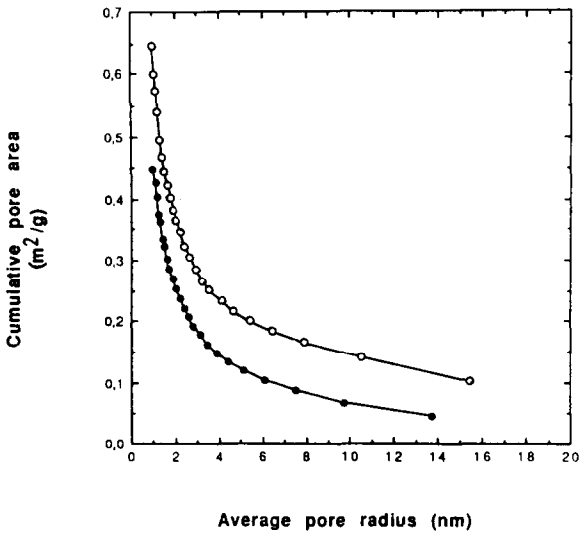

Fig. 2. Cumulative mesopore area vs average pore radius for tablets compacted from a sieve fraction (250–315 μm) of crystalline β-lactose. Open symbols, immediately after compaction; closed symbols, after 5 days storage under atmospheric conditions.

adsorption isotherm. For both samples it was found that the surface area is concentrated for the greater part in pores with radii in the range from 1 to 10 nm (see Fig. 2). From the data presented it can be concluded that the adsorption of water leads to a diminution of the mesopore surface area. Obviously, the uptake of water vapour results in pores ($r < 6$ nm). Desorption of water is hindered by pore-blocking effects (Everett, 1979) resulting in reduced surface areas as determined by nitrogen physisorption.

In summary, all tablets compacted from excipients with different water solubilities showed no change in BET-specific surface area when transferred immediately after ejection from the die in a dry atmosphere (silica gel). However, exposure to an ambient humid atmosphere resulted in an irreversible decrease in surface area, caused by capillary condensation of moisture and blocking of pores. This conclusion is supported by nitrogen physisorption isotherms performed on tablets compacted from crystalline β-lactose. Uptake of water in the mesopores diminished the accessible surface in the tablets. Removal of adsorbed water resulted in a small increase of the BET-surface area only.

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