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The effect of moisture sorption on the strength and internal surface area of lactose tablets

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Summary

Tablets compacted from α-lactose monohydrate and from roller dried β-lactose both show time-dependent moisture uptake when exposed to an ambient humid atmosphere. Moisture sorption tends to reach a plateau within 10 min and is accompanied by a decrease in both crushing strength and specific BET-surface area of the tablets. Subsequent storage of the tablets in a dry atmosphere results in an increase in strength but no change in surface area. The tablets show no moisture uptake, nor any change in strength and surface area when transferred immediately after ejection from the die in a dry atmosphere. These changes in crushing strength endorse the need to standardize the time between tablet ejection and strength measurement. Concerning the BET-specific surface area, it is recommended to suppress blocking of small pores by transferring the tablets immediately after ejection from the die into a dry nitrogen atmosphere for transport to the gas-adsorption apparatus.

Introduction

The mechanical characteristics of tablets can vary significantly during storage under various conditions. Rees and Shotton (1970) reported that the strength of sodium chloride tablets stored at 25 and 100°C, respectively, raised approx. 100% within 1 h after compression. This strength increase was attributed to stress relief of the sodium chloride crystals and interparticulate bonds. Bolhuis et al. (1973) found that the crushing strength of sucrose tablets, compressed from granulations prepared with water as a binder, could be changed significantly by altering the storage humidity. Storage of dry compacts at high humidities resulted in a decrease in crushing strength. Compacts, previously weakened by 160 h storage at high relative humidity, recovered their high crushing strength on storage at low relative humidity. Sheikh-Salem and Fell (1981) observed no change in strength of tablets compressed from a fraction (125–150 μm) of lactose within 50 h after compaction. Nyström and Karehill (1986) showed that the surface area of sodium chloride tablets, measured by permeametry, remained practically constant, while the compact strength almost doubled within a few min. From these

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observations, it was concluded that the increase in bonding surface area during storage was either too small or was not detectable by permeametry. Karehill and Nyström (1990) reported that the strength of compacts compressed from Avicel PH 101, both coarse and fine sodium chloride and fine lactose, increased significantly during storage under vacuum. Tablets compressed from coarse lactose displayed only a minor increase in tensile strength. All compacts returned to their initial strength values when the tablets were exposed to air after being degassed at high vacuum. It was suggested the strength increase was primarily caused by increased surface interactions due to removal of adsorbed water vapour and surface contaminations which act as a filter, reducing bondings with intermolecular forces in the compact. Alderborn and Ahlneck (1991) reported an increase in strength for tablets of saccharose and sodium chloride during storage in a humid atmosphere. The (permeametry) surface area generally decreased with storage time. For tablets of dicalcium hydrogen phosphate dihydrate, the tablet strength varied with neither time nor storage conditions. It was suggested that the changes in tablet strength for the saccharose and sodium chloride tablets during storage were probably the result of a rearrangement of solid material within the tablet which is mediated or facilitated by water.

These changes in the mechanical characteristics of tablets with time have been well recognized and induced the use of time factors. Higuchi et al. (1953) measured tablet characteristics on the day of compaction. Lewis and Train (1965) determined the crushing strength of compacts immediately after their preparation, whereas Shotton et al. (1963) standardized a delay of 6 h after ejection. Alderborn and Nyström (1982) determined tablet strength after 1 week storage at 45% relative humidity (RH). Vromans et al. (1985) examined tablet strength within 15 min after compaction and the specific surface area of the compacts, using mercury porosimetry, within 48 h, without mentioning storage conditions. Nyström and Karehill (1986) compared the gas-adsorption surface area of tablets, measured after 2 days storage at 45% RH and 20°C, with the permeametry surface area of these tablets, measured within 1 h after compaction.

These completely empirical time factors complicate evaluation of results from different authors. The objective of the present work was to study the significance of the effect of short-term storage time and storage conditions on the strength and the specific surface area of tablets compacted from different powder fractions of α-lactose monohydrate and roller dried β-lactose.

Materials and Methods

The materials used were different sieve fractions of α-lactose monohydrate and of roller dried β-lactose, supplied by DMV, Veghel, The Netherlands. All handling was performed in a room of constant temperature (20 ± 1°C) and constant RH (45 ± 5%). The powders were stored in the same room for at least 1 week before compression.

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.

Grinding of α-lactose monohydrate and of roller dried β-lactose fractions (250–315 μm) was carried out in a mortar for 1 min using a hand-held pestle.

Tablets and powders were stored at the required relative humidity and temperature.

Tablet strengths were determined with a Schleuniger 4M tester (Dr Schleuniger Production AG, Solothurn, Switzerland). The data given are the means of at least five measurements.

Tablet dimensions were determined with an electronic micrometer (Mitutoyo, Tokyo, Japan).

Tablet porosities were calculated from the weight and the dimensions of the tablets, employing true densities of 1.54 g/cm^3 for α-lactose monohydrate and 1.59 g/cm^3 for roller dried β-lactose. The reported values are the means of three tablets.

Moisture sorption of tablets was measured by recording the increase in weight of 20 tablets (about 10 g) during storage at 45% (± 5%) RH.

To suppress water uptake during production of the 20 tablets, each tablet was transferred within 5 s after ejection from the die into a dry atmosphere (over silica gel); moisture sorption started from the moment the 20 tablets were brought into the 45% RH atmosphere.

BET-surface areas of both powders and tablets were measured with a Quantasorb gas-adsorption apparatus (Quantachrome Corp., Syosset, U.S.A.) in a single point determination using nitrogen as adsorbate. The samples were measured immediately or after storage for different time periods and under different humidity conditions. When measured 'immediately' the tablets were put within 5 s after ejection from the die in a nitrogen atmosphere for transfer to the gas-adsorption apparatus in order to suppress moisture sorption. No outgassing procedure was performed. The data given are the means of four tablets.

Tablet permeametry surface areas were determined with a Blaine apparatus equipped with a tablet holder. The specific surface areas were calculated according to Alderborn et al. (1985). The reported values are the means of three tablets.

Results and Discussion

Effect of moisture sorption on the crushing strength of crystalline lactose tablets

Fig. 1 shows the strength of tablets compressed at 20 kN from a sieve fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose, respectively, vs the storage time at 45% RH. As shown, tablet strength decreases rapidly and tends to reach a plateau within 10 min after compaction. To distinguish any influence of the specific surface area of the tablets on the compact strength, tablets were compressed from different sieve fractions of α-lactose monohydrate and roller dried β-lactose, respectively, and stored at low humidity (over silica gel), and at ambient (45% RH) and high (70% RH) humidity, respectively. The 'initial' tablet strength was measured as soon as possible (within 10 s); additional tablets were tested after a time interval of 30 min. The results, depicted in Table 1, demonstrate no significant change in crushing strength of the tablets when stored over silica gel, but for all tablets a decrease in strength when exposed to 45 or 70% RH. This result indicates that atmospheric moisture affects the strength of crystalline lactose tablets.

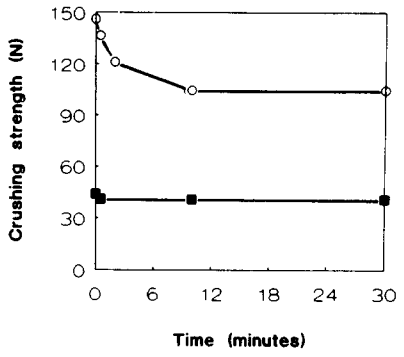

Fig. 1. Crushing strength of tablets compacted from a sieve fraction (250–315 μm) of α-lactose monohydrate (■) and roller dried β-lactose (○), respectively, vs storage time at 45% RH. Fractions were compacted at 20 kN into 500 mg, 13 mm tablets.

The effect of atmospheric humidity on the moisture sorption by crystalline lactose tablets is illustrated in Fig. 2. As expected, the tablets stored over silica gel did not increase in weight, whereas the weight of the tablets stored at 45% RH increased on sorption of moisture, and tended to reach a plateau within 15 min. Moreover, the

TABLE 1

Effect of humidity on the strength of tablets compacted at 20 kN from sieve fractions of α-lactose monohydrate and roller dried β-lactose, respectively

Fraction (μm)	Tablet strength (N) [a]			
	A	B	C	D
α-Lactose monohydrate				
250–315	44 (2)	45 (1)	41 (1)	40 (1)
63– 90	73 (4)	75 (2)	64 (5)	59 (3)
Roller dried β-lactose				
250–315	144 (8)	134 (7)	104 (6)	100 (5)
63– 90	154 (5)	140 (6)	100 (7)	99 (7)

A, within 10 s after compaction; B, stored for 30 min over silica gel; C, stored for 30 min at 45% RH; D, stored for 30 min at 70% RH.

[a] Standard deviations are given between parentheses.

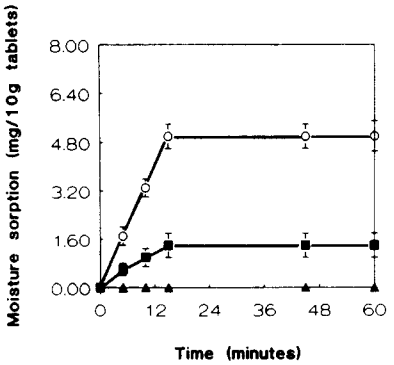

Fig. 2. Moisture sorption of tablets compacted from a sieve fraction (250–315 μm) of α-lactose monohydrate (■) and roller dried β-lactose (○), respectively, vs storage time at 45% RH. Fractions were compacted at 20 kN into 500 mg, 13 mm tablets. (▲) Stored over silica gel.

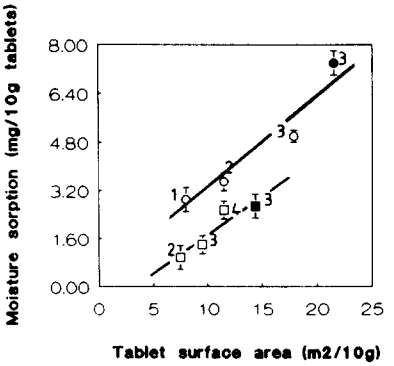

Fig. 3. Moisture sorption of tablets compacted from sieve fractions (250–315 and 32–45 μm) of α-lactose monohydrate (■) and roller dried β-lactose (○), respectively, vs tablet surface area. Fractions were compacted at 5 kN (1); 10 kN (2); 20 kN (3) and 30 kN (4), dependent on the required surface area, into 500 mg, 13 mm tablets. Open symbols: 250–315 μm fraction; closed symbols: 32–45 μm fraction.

amount of moisture sorbed in 24 h by both the α-lactose monohydrate and β-lactose tablets appears to be linearly related to the initial (BET)-surface area of the tablets determined immediately after ejection from the die (Fig. 3). This result indicates moisture uptake by adsorption of water vapour on the internal surface area of the lactose tablets. However, it is interesting to note that the sorption profiles were found to be different for the two different crystalline lactose types, α-lactose monohydrate and roller-dried β-lactose. It was therefore expected that changes in crushing strength on storage would be different for the two types of lactose tablets tested. The results presented in Table 2 indeed demonstrate smaller decreases in crushing strength of the α-lactose monohydrate tablets on storage for 30 min at 45% RH, as compared with the corresponding roller-dried β-lactose tablets. Moreover, the decrease in crushing strength was found to increase with compaction force and appeared to be greater for the tablets compacted from the smaller particle size fractions.

According to Leuenberger et al. (1989), the strength of crystalline lactose tablets originates from adhesion forces, acting at the coordination points between neighbouring lactose particles. The packing arrangement of the particles determines tablet porosity and consequently tablet strength. It is known from the literature that tablet porosity may increase after compaction due to time-dependent stress relaxation within the compact (Armstrong and Haines-Nutt, 1972; Hiestand et al., 1977).

TABLE 2

Effect of ambient storage humidity (45% RH) on the strength of tablets compacted from fractions of α-lactose monohydrate and roller dried β-lactose, respectively

Fraction (μm)	Cf (kN)	Tablet strength (N) [a]		(B–A)/A
		A	B	
α-Lactose monohydrate				
24– 32	5	15 (2)	14 (3)	−0.07
	20	88 (3)	75 (4)	−0.15
63– 90	20	73 (4)	64 (5)	−0.12
100–125	20	60 (3)	55 (1)	−0.08
180–200	20	48 (2)	46 (4)	−0.04
250–315	20	44 (2)	41 (1)	−0.07
Roller dried β-lactose				
32– 45	10	76 (3)	61 (4)	−0.20
63– 90	10	61 (2)	51 (6)	−0.16
	20	154 (5)	100 (7)	−0.35
90–125	20	134 (10)	99 (5)	−0.26
250–315	5	20 (1)	19 (2)	−0.05
	10	62 (3)	51 (1)	−0.18
	20	144 (8)	104 (6)	−0.28

Cf, compression force; A, within 10 s after compaction; B, stored for 30 min at 45% RH; (B–A)/A, relative change in tablet strength.

[a] Standard deviations are given between parentheses.

To evaluate dimensional stability, the porosity of tablets compressed from α-lactose monohydrate and roller dried β-lactose, respectively, was determined within 10 s after compression, after storage for 30 min over silica gel or at 45% RH, after storage for 30 min over silica gel before transfer to 45% RH, and after storage for 30 min at 45% RH before transfer to silica gel again for 30 min, respectively. The results listed in Table 3 show for both the α-lactose monohydrate and the roller-dried β-lactose tablets very small increases in porosity when stored at ambient humidity and no measurable change in dimensions when stored at low humidity. Moreover, it should be noted that the tablets retain their increased porosity when transferred from a humid to a dry condition. This observation is consistent with the work of Aulton et al. (1973) who showed that storage under humid conditions increased the expansion of compacts prepared from a paracetamol and an ibuprofen granulation, whilst storage over phosphorus pentoxide reduced recovery. Moisture obviously promotes relaxation of stress within a tablet. The porosity increases for the lactose tablets tested are, however, too small to explain the observed strength decreases.

Since sorbed moisture affected tablet strength, drying of lactose compacts was expected to result in a strength increase. Therefore, the effect of moisture sorption with subsequent drying, and vice versa, was examined for tablets compressed from a powder fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose, respectively. As seen from Table 4, final storage at ambient humidity (45% RH) generally weakened the compacts, whereas final drying of the compacts over silica gel at 50°C for one night yielded stronger tablets. A possible mechanism of the observed dependency of tablet strength on storage humidity might be dissolution of contact points between the lactose particles within the tablets, resulting in weaker tablets and recrystallization of dissolved lactose during drying, forming new contact points between the lactose particles and hence stronger tablets.

In conclusion, tablets compacted from α-lactose monohydrate and from roller dried β-lactose both sorb moisture when exposed to an ambient humid atmosphere (45% RH). Moisture uptake tends to reach a plateau within 10 min. The amount of moisture sorbed is linearly related with the initial (BET) internal surface area of the tablets, but differs for the two types of crystalline

TABLE 3

Effect of humidity on the porosity of tablets compacted at 20 kN from a fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose, respectively

Storage condition	Porosity [a]	
	α-Lactose monohydrate	Roller dried β-lactose
A	0.124 (0.001)	0.162 (0.002)
B	0.124 (0.001)	0.162 (0.002)
C	0.126 (0.001)	0.164 (0.001)
D	0.126 (0.001)	0.164 (0.001)
E	0.126 (0.001)	0.164 (0.001)

A, within 10 s after ejection from the die; B, stored for 30 min over silica gel; C, stored for 30 min at 45% RH; D, stored for 30 min over silica gel before transfer to 45% RH again for 30 min; E, stored for 30 min at 45% RH before transfer to silica gel again for 30 min.

[a] Standard deviations are given between parentheses.

TABLE 4

The effect of storage conditions on the strength of tablets compacted at 20 kN from a sieve fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose, respectively

Storage condition	Tablet strength (N) [a]	
	α-Lactose monohydrate	Roller dried β-lactose
A	44 (2)	144 (8)
B	45 (1)	140 (6)
C	41 (1)	100 (7)
D	42 (2)	100 (4)
E	53 (4)	138 (6)
F	50 (3)	129 (5)
G	45 (3)	120 (4)

A, within 10 s after ejection from the die; B, stored for 30 min over silica gel; C, stored for 30 min at 45% RH; D, stored for 30 min over silica gel followed by 30 min storage at 45% RH; E, stored for 30 min at 45% RH followed by one night at 50°C over silica gel; F, stored for 30 min over silica gel, followed by 30 min at 45% RH and afterwards one night at 50°C over silica gel; G, stored for 30 min at 45% RH followed by one night at 50°C over silica gel and afterwards 30 min at 45% RH.

[a] Standard deviations are given between parentheses.

TABLE 5

Effect of storage humidity on the BET-surface area of tablets compacted from fractions of α-lactose monohydrate and roller dried β-lactose, respectively

Fraction (μm)	Cf (kN)	Surface area (m^2/g)		(B–A)/A
		A	B	
Storage over silica gel				
α-Lactose monohydrate				
250–315	20	0.95	0.94	−0.01
Roller dried β-lactose				
250–315	10	1.15	1.16	0.01
Storage at 45% RH				
α-Lactose monohydrate				
24– 32	20	1.59	1.16	−0.27
63– 90	20	1.22	0.94	−0.23
100–125	20	1.14	0.92	−0.19
180–200	20	1.02	0.79	−0.23
250–315	20	0.95	0.69	−0.27
Roller dried β-lactose				
32– 45	10	1.46	1.04	−0.29
63– 90	10	1.36	0.93	−0.32
90–125	20	1.95	1.28	−0.34
250–315	5	0.80	0.57	−0.29
	10	1.15	0.84	−0.27
	20	1.78	1.27	−0.29

A, within 5 s after compaction, stored in a nitrogen atmosphere and transferred to BET apparatus; B, upper part of the table: after 30 min storage over silica gel; lower part of the table: after 30 min storage at about 45% RH; (B–A)/A, relative change in tablet surface area (standard deviations for all tablets were lower than 0.05 m^2/g).

lactose. Moisture uptake is accompanied by decreasing tablet strength which may be caused by dissolution of contact points between the individual lactose particles in the compact. Conversely, drying of lactose tablets shows increasing crushing strength which may be attributed to interparticulate crystallization within the compact.

Effect of moisture sorption on the BET-surface area of crystalline lactose tablets

Fig. 4 shows the BET-surface area of tablets compressed at 20 kN from a fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose, respectively, vs the storage time at 45% RH. As seen, tablets compressed from both materials show a considerable decrease in surface area, reaching a plateau within 10 min after compaction. To compare the effect of an ambient humidity with a dry humidity, the specific surface area of tablets, compacted from different powder fractions of α-lactose monohydrate and roller-dried β-lactose, respectively, were measured both immediately and after storage for 30 min over silica gel and at 45% RH, respectively. The results (Table 5) demonstrate no change in the internal surface area of the tablets when exposed to a dry atmosphere but considerably reduced values when stored for 30 min at an ambient humidity. In analogy with the decreases in crushing strength, discussed earlier (Table 2), the roller dried β-lactose tablets exhibited larger decreases in specific surface area than those of the α-lactose monohydrate tablets. Comparison of the corresponding results from Table 2 with those from Table 5 shows only slight conformity. This means that although the strength and specific surface area of crystalline lactose tablets are both changed by sorbed moisture, the decrease in strength is not directly related to the decrease in tablet surface area.

This observation is endorsed by examination of the moisture sorption and desorption, and changes in strength and internal surface area of the tablets on transfer from an ambient into a dry humidity. Table 6 presents the moisture sorption and desorption, tablet strengths and BET-surface areas of tablets compressed from a fraction (250–315 μm) of α-lactose monohydrate and roller

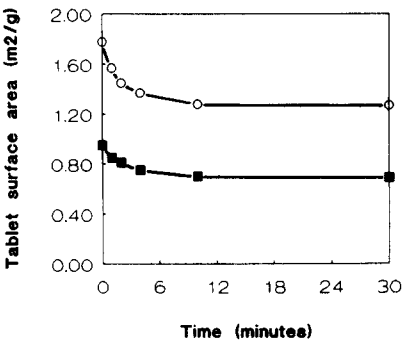

Fig. 4. Specific BET-surface area of tablets compacted from a fraction (250–315 μm) of α-lactose monohydrate (■) and roller dried β-lactose (○), respectively, vs storage time at 45% RH. Tablets were compacted at 20 kN into 500 mg, 13 mm tablets.

dried β-lactose, respectively. Crushing strength and specific surface area of the tablets were measured immediately after ejection from the die, after storage for 30 min at 45% RH, and after storage for 30 min at 45% RH with subsequent drying overnight at 50°C over silica gel, respectively. More rigorous outgassing procedures, as recommended by Gregg and Sing (1982), cannot be applied to lactose without disturbing the structure of the lactose crystals. As seen from the presented data, the drying procedure employed for the lactose tablets does not result in an increase in BET-surface area, in contrast to the observed reversibility of tablet strength.

It is well recognized that the BET-surface area depends on the type of treatment undergone by the material prior to determination. Gammage et al. (1969) showed for thorium oxide that surface water can affect the apparent specific area of the open surface and, in addition, can block or hinder the access of nitrogen and argon molecules to a system of fine pores. Lovell (1975) reported that preadsorption of oleate on appatite, magnesite and barite reduced the surface area, as determined by nitrogen and krypton adsorption, to between 90 and 50% of the value obtained for the pure mineral. These decreases could have resulted from the blockage of very narrow pores or surface cracks by chemisorbed material, preventing the entry of molecules of adsorbate into these pores, or from inadequacies in the basic adsorption theory used in the calculation of the surface area.

The applicability of the BET-surface area measurement for crystalline lactose tablets using nitrogen as adsorbate has been evaluated by calculating the BET constant C. This BET constant C is determined by the affinity of the adsorbate for the lactose surface area (Gregg and Sing, 1982; Lowell and Shields, 1984). A rough estimation of the BET constant from a multipoint nitrogen adsorption measurement performed on α-lactose monohydrate tablets resulted in a C value of about 100, for both the tablets transferred immediately after ejection into a nitrogen atmosphere and those stored for 24 h at about 45% RH. This value is considered to be acceptable for the usefulness of the BET method and indicates that the observed decreases in BET-surface area as found for the tablets of the crystalline lactoses cannot be ascribed to inadequacies in the surface area determination using nitrogen adsorption.

To distinguish whether the observed decrease in tablet surface area was a material or a tablet property, BET measurements were performed on a ground sample of both roller dried β-lactose and α-lactose monohydrate, stored after grinding at a very low and an ambient humidity, respectively (Table 7). The results presented demonstrate no change in surface area in the case of storage for 30 min over silica gel, whereas a decreased surface area is shown for storage at 45% RH. This observation is consistent with the work of Kontny et al. (1987), who reported a marked decrease in water vapour sorption for ground samples of water-soluble substances at ambient to high relative humidities. They concluded that water-soluble solids which are subjected to mechanical processing, such as grinding and compaction, can exhibit changes in their re-

TABLE 6

Effect of storage humidity on the moisture (de)sorption, the strength and the specific surface area of tablets compressed at 20 kN from a fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose, respectively

Material	Moisture sorption (mg/10 g tablets) [a]	Moisture (de)sorption (mg/10 g tablets) [a]	Specific tablet surface area (m^2/g) [a]			Tablet strength (N) [a]		
			A	B	C	A	B	C
α-Lactose monohydrate	1.4 (0.4)	−2.1 (0.4)	0.95	0.69	0.68	44 (2)	41 (1)	53 (4)
Roller dried β-lactose	5.0 (0.5)	−6.2 (0.5)	1.78	1.27	1.28	144 (8)	100 (7)	138 (6)

A, immediately after compaction; B, stored for 30 min at 45% RH; C, stored for 30 min at 45% RH followed by one night over silica gel at 50°C.

[a] Standard deviations are given between parentheses.

TABLE 7

The effect of storage conditions on the specific surface area of a fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose before grinding, after grinding and after 30 min storage over silica gel or at 45% RH

Treatment	Surface area (m^2/g) [a]	
	α-Lactose monohydrate	Roller dried β-lactose
A	0.07 (0.02)	0.17 (0.03)
B	0.57 (0.04)	0.62 (0.02)
C	0.56 (0.02)	0.62 (0.01)
D	0.42 (0.03)	0.50 (0.02)

A, before grinding; B, immediately after grinding; C, stored for 30 min over silica gel; D, stored for 30 min at 45% RH.
[a] Standard deviations are given between parentheses.

activity towards water vapour, and can give rise to surface area changes, apparently caused by 'surface dissolution'.

Finally, Table 8 lists the results on the permeametry specific surface area of tablets compacted from a sieve fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose, respectively, measured both immediately after compaction, without ejection from the die, and after 30 min storage at 45% RH. As seen, the data show no decrease in permeametry tablet surface area on storage, indicating that the diameter of the macropores of the lactose tablets has not changed. This implies that the observed changes

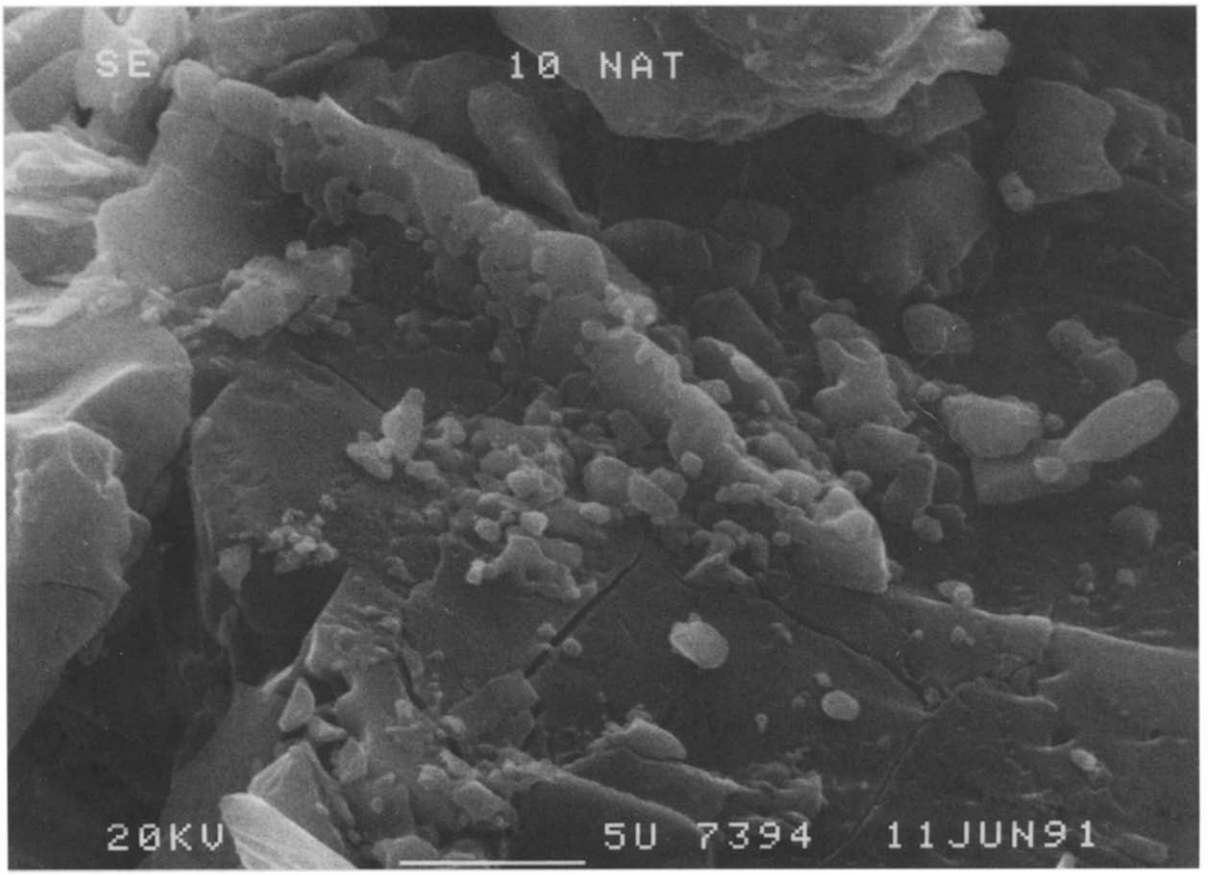

Fig. 5. Scanning electron micrograph of a fracture of a tablet compressed at 10 kN from a fraction (250–315 μm) of α-lactose monohydrate. Bar, 5 μm.

TABLE 8

Effect of storage humidity on the permeametry-surface area of tablets compacted at 10 kN from a fraction (250–315 μm) of α-lactose monohydrate and roller dried β-lactose, respectively

Fraction	Surface area (m^2/g) [a]	
	A	B
α-Lactose monohydrate	0.34 (0.04)	0.34 (0.04)
Roller dried β-lactose	0.74 (0.05)	0.74 (0.05)

A, immediately after compaction; B, after 30 min storage at 45% RH.

[a] Standard deviations are given between parentheses.

in BET-surface area of tablets when stored under ambient humid conditions, must be caused by changes in the smaller pores of the tablets.

Different mechanisms might be responsible for the observed decreases in BET-surface area. It is known from the literature that mechanical operations such as grinding and tabletting result in an increase in surface energy being stored as lattice defects. The surface becomes more amorphous and reactive (Hüttenrauch and Keiner, 1976; Hüttenrauch et al., 1976). Hydrophilic solids might react by the enhanced sorption of water vapour used as a medium for the rearrangement of the highly energetic sites, as was concluded for tablets compacted from sodium chloride (Down and McMullen, 1985) and for ground samples of sodium salicylate and sodium chloride (Kontny et al., 1987). Recrystallization and blocking of pores decreases the area available for nitrogen adsorption. Next to dissolution of surface structures capillary condensation of water vapour may fill mesopores (2 nm < pore diameter < 50 nm) and cracks which are generated during mechanical treatment, thereby reducing surface area as determined through gas adsorption. Fig. 5 illustrates a scanning electron micrograph of a fracture of an α-lactose monohydrate tablet. The micrograph clearly shows a rough structure containing many irregularities and pores which could be sensitive to moisture sorption.

In conclusion, both tablets and ground samples of crystalline lactose powders show no change in the apparent BET-surface area when stored in a nitrogen atmosphere or at low humidity (over silica gel), whilst decreased surface areas are exhibited for those exposed to ambient humidities (45% RH). The decreases in BET-surface area are irreversible and do not increase on drying. Air permeametric measurements show, however, no changes in surface area of the crystalline lactose tablets on storage under conditions of ambient humidities. This indicates that the observed changes in BET-surface area are not accompanied by a change in the structure of the macropores in the lactose tablets but might be caused primarily by blocking of the pores by sorbed water.

General Conclusion

Tablets compacted from α-lactose monohydrate and from roller dried β-lactose both show time-dependent moisture uptake when exposed to an ambient humid atmosphere (45% RH). Moisture sorption tends to reach a plateau within 10 min and is accompanied by a decrease in both crushing strength and specific BET-surface area of the tablets. Subsequent storage of the tablets in a dry atmosphere results in an increase in strength but no change in specific surface area. The tablets display neither moisture sorption nor change in crushing strength and specific surface area when transferred immediately after ejection from the die into a dry atmosphere. These results are indicative of dissolution of contact points between lactose particles in a tablet when exposed to a humid atmosphere and recrystallization of dissolved lactose when transferred from a humid into a dry atmosphere. The irreversible decrease in specific surface area of the tablets on exposure to humid conditions is suggested to be caused by blocking of the very narrow pores in the tablets by sorbed moisture. These observations raise doubts concerning the use of a time factor for the characterization of the physical properties such as crushing strength and specific surface area of lactose tablets. The significance of different time factors is illustrated in Fig. 6 by plotting the data of crushing strength from Table 2 vs specific BET-surface area from Table 5 of both the α-lactose monohydrate and the roller

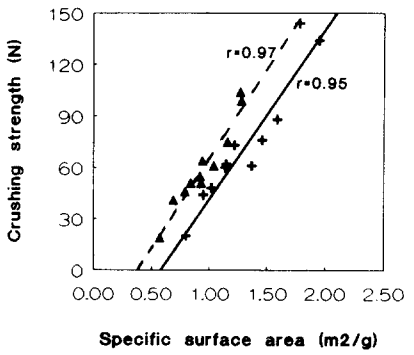

Fig. 6. Crushing strength of lactose tablets from Table 2 vs specific surface area of these tablets listed in Table 5. Solid line and + represent the relationship for the tablets immediately after compaction; the broken line and ▲ refer to the relationship after 30 min storage at 45% RH.

dried β-lactose tablets. Consistent with previous studies (Riepma et al., 1991), the results show linear relationships between strength and surface area, when measured both immediately after compression and after 30 min exposure to an atmospheric humidity of 45%. Moreover, it should be noted that the linear relationship referring to determinations performed after 30 min storage under atmospheric conditions exhibits a higher correlation coefficient (0.97) as compared with immediate measurement of the tablet characteristics (0.95), as was expected from the observations reported.

From a practical point of view, it is evident to use a time factor, of for instance 30 min, for the characterization of the mechanical properties such as crushing strength of lactose tablets. Concerning the BET-specific surface area of the tablets, however, it should be borne in mind that exposure to atmospheric conditions causes blockage of very narrow pores by sorbed moisture within the porous structure. The access of nitrogen to the internal surface area of the tablet is consequently hindered, resulting in decreasing and thus non-representative BET-surface areas. It is therefore recommended to suppress moisture sorption by transferring the lactose tablets immediately after ejection from the die into a dry (nitrogen) atmosphere for transport to the gas-adsorption apparatus.

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