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The effect of moisture content on the compression and bond-formation properties of amorphous lactose particles

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Abstract

A lactose solution was spray-dried and the particles obtained were stored at relative humidities of 0, 11, 22 and 33%. The moisture content (gravimetric analysis), crystallinity (microcalorimetry), particle density (air pycnometry) and glass transition temperature (differential scanning calorimetry) of the particles were determined and compacts were prepared (50–200 MPa). From porosity-applied pressure profiles, the yield pressure for the materials was calculated and the tensile strength and porosity of the compacts were determined. Compacts were also examined in an electron microscope.

The moisture content of the amorphous material varied between 0 and 6.2 wt.% and an increased moisture content related rectilinearly to a reduced particle density, a reduced glass transition temperature and a reduced yield pressure. An increased moisture content gave an increased tablet tensile strength and a reduced tablet porosity. Different relationships between tablet strength and porosity were obtained dependent on the moisture content of the particles, while a single relationship seemed to exist between tablet strength and a contact area coefficient.

To conclude, amorphous lactose powders reduced in volume due to particle deformation, and powder compression was facilitated by an increased moisture content due to an increased deformability of the particles in their glassy state. The particle deformability controlled the area of contact formed between the particles during compression, which controlled the tablet tensile strength. Particles seemed to bind by adsorption bonding and, at high compaction pressures, by solid bridges. © 1997 Elsevier Science B.V. All rights reserved

Keywords: Amorphous lactose; Bond type; Interparticulate contact area; Moisture content; Particle deformability; Tablet strength

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1. Introduction

Preparation by spray-drying is a possible approach to control chemical and physical proper-

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ties of particles used in tableting. Benefits thus gained are an increased solubility (Corrigan et al., 1984) and an improved compactability (Vromans et al., 1986; Sebhatu et al., 1994b) of the material. In fact, spray-dried lactose was the first excipient introduced which was specially designed for direct compaction (Bolhuis and Chowan, 1996). The improved compactability of spray-dried compared with crystallised lactose particles (Vromans et al., 1986; Sebhatu et al., 1994b) has been explained by the solid-state characteristic of the spray-dried material, i.e. spray-dried particles are partially or completely amorphous.

It has been suggested that a powder bed of spray-dried lactose particles compresses by particle fragmentation (McKenna and McCafferty, 1982). However, by studying fully amorphous lactose, it was concluded that an amorphous lactose powder compresses by particle deformation (Vromans et al., 1986). Moreover, a reduced tablet porosity and an increased tablet fracture resistance with increased moisture content of the particles was observed. It was suggested that absorbed moisture increased the deformability of the material due to a decrease in viscosity of the glassy amorphous material which increased the bonding area between particles in the compact. Similar results were also reported later (Sebhatu et al., 1994b), but here the authors speculated that absorbed moisture can affect the bond-formation process also by facilitating a transition of the amorphous material from a glassy to a rubbery state, occurring during the compression phase. Such transition of an amorphous material from a glassy to a rubbery state can facilitate local interfacial fusion of particles, i.e. formation of solid bridges, or increase the deformability of the particles with an increased interparticulate bonding area as a consequence.

Different mechanistic explanations for the effect of moisture content on the compaction behaviour of amorphous lactose have thus been proposed. Concerning the compression process, an increased amount of absorbed water can either cause a gradual change in deformability of the particles (i.e. plasticise the glassy amorphous material) or can facilitate a temporary transition of the amorphous material from a glassy to a rubbery state. Concerning the binding process, an improved particle deformability or a glass–rubber transition can affect either the type of bonds formed between the particles (i.e. bridges of fused material or bonds formed between particle surfaces in contact) or the area of bonding formed between the particles during compression.

To conclude, although it is well known that amorphous materials can exhibit comparatively good compaction properties, it is obvious that there is a lack of deeper mechanistic understanding of how these materials form compacts and how the moisture content of the material affects a volume reduction and compaction process. The aim of this work was thus to study the effect of moisture content on the compression behaviour and the bond-formation properties of amorphous lactose particles. A recently developed contact area coefficient (Eriksson and Alderborn, 1995) was used to mechanistically evaluate the results.

2. Materials and methods

2.1. Preparation of spray-dried lactose

Crystalline lactose α-monohydrate (Pharmatose, DMV, The Netherlands) was dissolved in water in the ratio 1:6 and the solution was dried in a counter-current spray drier (Niro Atomiser Minor, A/S Niro, Denmark) as described earlier (Elamin et al., 1995). The particles obtained were nearly spherical with a non-crystalline appearance and they seemed to form aggregates (Fig. 1). The size of the individual particles was roughly estimated as 5–30 μm.

The material was stored in dessicators with P_2O_5 at 60°C for 2 weeks. Samples were then transferred to room-temperatur dessicators with a series of relative humidities (0, 11, 22 and 33% relative humidity (RH), obtained by P_2O_5 or saturated salt solutions) and stored for at least 2 weeks until an equilibrium moisture content (MC) was reached. 33% RH is below the critical RH which can cause spontaneous crystallisation of lactose at room temperature (Elamin et al., 1995).

Fig. 1. SEM photomicrograph of spray-dried lactose particles, stored at 0% RH after spray-drying.

2.2. Determination of solid-state properties of powder

The degree of crystallinity of spray-dried lactose was determined by isothermal microcalorimetry (Thermal Activity Monitor model 2277, Thermometric AB, Sweden) as described earlier (Sebhatu et al., 1994a). Samples (16 mg, $n = 3$), prestored at 0% RH, were placed in a miniature humidity chamber with an RH of 57%. The sample was thereafter placed in the microcalorimeter and the heat flow signal caused by the crystallisation of amorphous lactose was monitored and analysed.

Moisture uptake was determined gravimetrically. Samples (approx. 1 g, $n = 2$), prestored at 0% RH, were weighed on an analytical balance and placed in room-temperature desiccators with 11, 22 and 33% RH. The samples were taken out periodically and weighed until a constant sample weight was obtained. The MC of the powder, defined as the amount of moisture taken up by the sample divided by the initial weight of the dry sample, was then calculated.

The apparent particle density (i.e. what is sometimes referred to as the true density of the material) was determined by air pycnometry (Air Comparison Pycnometer model 930, Beckman, USA). Samples (approx. 20 g, $n = 2$), prestored at the range of RHs, were transferred from the dessicator to the pycnometer and the volume which the material occupied was then directly determined without degassing the sam-ple. By this procedure, changes in MC of the material during the measurement procedure were minimised.

The apparent glass transition temperature (Elamin et al., 1995) was determined by differential scanning calorimetry (Mettler TA3000 system with a DSC 20 measuring cell and a TC 10A processor, Mettler, USA). Samples (4–5 mg, $n = 3$) prestored at the range of RHs, were transferred from the dessicator to aluminium sample pans which were directly sealed. The samples were scanned over a temperature range of 25–250°C at a rate of 10°C/min.

2.3. Determination of powder surface area

The surface area of the spray-dried lactose powder was determined by air permeametry. Samples (approx. 1 g, $n = 3$), prestored at 0% RH, were poured into the container and compressed by hand until a porosity of about 40% was reached. The permeability (Blaine apparatus) and porosity of the powder bed were determined and the surface area calculated with the permeability equation including a slip flow correction term (Alderborn et al., 1985).

2.4. Determination of apparent yield pressure during powder compression

Samples (approx. 500 mg, $n = 3$) prestored at the range of RHs, were compressed in an instrumented single punch tablet machine (Korsch EK 0, Germany, equipped with 1.13-cm flat-faced punches) at an applied pressure of 200 MPa. The distance between the punch faces at the lowest position of the upper punch was in all cases 3 mm at zero pressure. External lubrication with 1% (w/w) magnesium stearate suspension in ethanol was performed before each compression. The powder for each compact was individually weighed and manually poured into the die. The motor of the machine was started when the upper punch was in its highest position and the motor was stopped and the flywheel manually arrested directly after the compaction.

During the compression phase, the upper punch pressure and position were monitored each ms. By pressing the punches against each other under normal movement rate of the upper punch, the elastic deformation of the punch and punch holder was assessed. After correction for this deformation, the changes in in-die tablet porosity as a function of applied pressure were calculated. The porosity data were treated according to the Heckel expression (Duberg and Nyström, 1986), and the reciprocal of the slope in the linear part of the Heckel profile, i.e. in the range 25–150 MPa, was determined. This value is referred to as the yield pressure.

2.5. Preparation of tablets and determination of porosity, tensile strength and surface area of tablets

Tablets were prepared in the instrumented single punch tablet machine, as described above, at applied pressures of 50, 100, 150 and 200 MPa. Immediately after compaction ($t \approx 45$ s), the compacts were loaded diametrically at 0.5 mm/min in a material testing instrument (M30K, J.J. Lloyd Instruments, UK) until they fractured. From the fracture force, a tensile strength was derived (Fell and Newton, 1970) and the tablet porosity was derived from the weight and dimensions of the compacts and the apparent particle density of the materials. The results presented are the mean of five measurements.

Tablets were also prepared in the instrumented single punch tablet machine at an applied pressure of 75 MPa by compressing the powder in a special die, placed on the die table as described earlier (Alderborn et al., 1985). The air permeability of the tablets was measured with a Blaine apparatus immediately after compaction ($t \approx 45$ s) and the volume specific surface area of the compacts was calculated with the permeability equation, corrected for slip flow (Alderborn et al., 1985). The results presented are the mean of three measurements.

2.6. Imaging of particles and tablets

Photomicrographs of a powder sample and of upper and fracture surfaces of tablets were taken with a scanning electron microscope (JSM T330, Jeol, Japan) using secondary electron imaging at an accelerating voltage of 10 kV. The examined tablets were prepared at 60, 150 and 200 MPa from powders prestored at 0% and 33% RH. The compacts were stored at the same RHs before microscopy examination.

3. Results and discussion

3.1. Solid-state properties of particles

In an earlier paper (Sebhatu et al., 1994a), the

Table 1
Solid-state and compaction properties of amorphous lactose stored at different relative humidities

Storage RH (%)	Solid-state characteristics			Compaction properties		
	MC (%)	Density (g/cm^3)	T_g (°C)	TSA (cm^2/cm^3)	TPD (μm)	P_y (MPa)
0	0	1.513	104 (0.60)	4289 (172)	2.91 (0.04)	207 (1.34)
11	1.93	1.500	89.0 (0.46)	4016 (527)	2.87 (0.3)	185 (4.40)
22	4.30	1.488	61.5 (1.4)	4433 (208)	2.27 (0.07)	144 (2.83)
33	6.21	1.482	41.5 (0.72)	4878 (167)	1.39 (0.04)	109 (5.23)

The values in parentheses are the arithmetic S.D.
MC, moisture content; TSA, tablet surface area; TPD, tablet pore diameter; P_y, yield pressure.

specific heat of crystallisation for amorphous lactose was determined by calorimetry. By exposing the sample to a humid atmosphere (57% RH), crystallisation of the spray-dried lactose was initiated and monitored within a controlled time period, i.e. about 7 h. By comparing the specific heat of crystallisation of the spray-dried lactose used in this paper with the earlier determined value for the amorphous lactose, it was concluded that the spray-dried lactose used in this paper can be described as completely amorphous.

The amount of sorbed moisture increased in a rectilinear way with an increased RH (Table 1) and reached a level of 6.21 wt.% at 33% RH. This value compares favourably with earlier results (Elamin et al., 1995). Since only a few layers of molecules can probably be adsorbed at the range of RHs used, nearly all sorbed water is absorbed. The equilibrium MC of the material was reached after storage periods of up to 48 h. Thereafter, no marked drop in MC of the material was noticed, i.e. the material seemed not to crystallise during storage (Sebhatu et al., 1994a).

An increased MC of the material decreased the glass transition temperature (T_g) in a nearly rectilinear way (Table 1). The values compare favourably with earlier results (Elamin et al., 1995).

The apparent particle densities of the amorphous lactose were generally lower compared with an earlier reported value for crystalline lactose (Eriksson and Alderborn, 1995). An increased MC decreased the apparent particle density of the amorphous lactose in a nearly rectilinear way (Table 1). This is consistent with findings for microcrystalline cellulose (Khan et al., 1988), which is considered to be a partly amorphous material. It seems, therefore, that the absorption of water into the amorphous lactose particles caused the particles to swell.

3.2. Densification behaviour of powders

The surface area of compacts formed at 75 MPa seemed to be independent of the RH during prestorage of the powder (Table 1). A slightly higher tablet surface area compared with powder surface area was obtained. This increase is limited and similar to earlier findings on sodium chloride of a comparable particle size (Eriksson and Alderborn, 1995). It can thus be concluded that the amorphous lactose particles showed limited fragmentation during compression.

The low incidence of particle fragmentation during compression is supported by the absence of a marked initial curvature of the Heckel profiles (Duberg and Nyström, 1986), although a small curvature was observed at applied pressures up to 20 MPa. For the powder prestored at 0% RH, the Heckel profile was rectilinear in the pressure range above this level (Fig. 2a). For the moist powders, deviations from a straight line were obtained at the highest applied pressures and the curvature became more pronounced with an increased MC. A curvature of the Heckel profile at high applied pressures has been attributed to a limitation of the Heckel equation when the tablet porosity approaches zero (Roberts and Rowe, 1985).

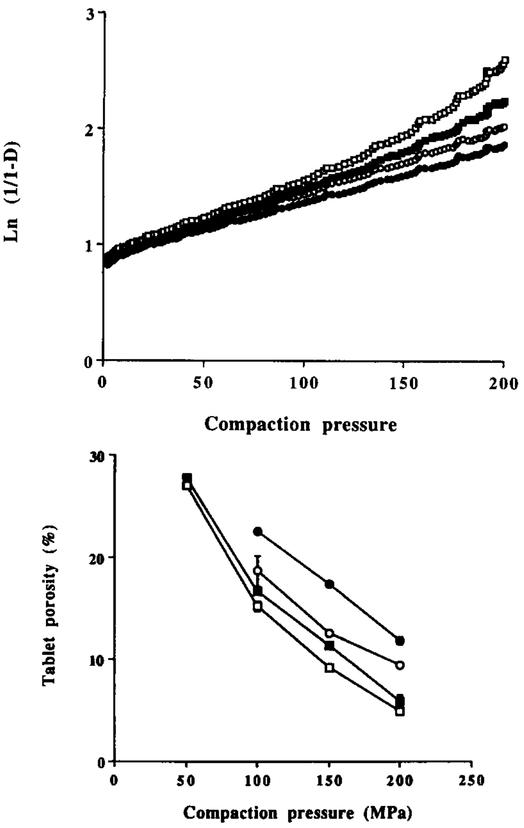


Fig. 2. (a) Tablet porosity–compaction pressure profiles (according to the Heckel function) for spray-dried lactose stored at different RHs before compression: (●) 0% RH; (○) 11% RH; (■) 22% RH; (□) 33% RH. Bars represent 95% confidence limits of the mean. (b) Tablet porosity as a function of compaction pressure for compacts of spray-dried lactose stored at different RHs before compaction. Symbols as in Fig. 2a. Bars represent 95% confidence limits of the mean.

An increased MC increased also the slope of the Heckel profile in the linear part of the profiles, i.e. about 25–150 MPa, which corresponds to a decreased apparent yield pressure for the material (Table 1). Thus, densification of the powder was facilitated by sorbed water. This is also illustrated by the fact that an increased MC of the material gave compacts of lower porosity within the entire pressure range used (Fig. 2b).

The traditional interpretation of the yield pressure is that it reflects the propensity of the particles to flow while stressed and is related to the hardness of the material (Rowe and Roberts, 1996). A reduced yield pressure corresponds, therefore, to an increased degree of deformation which the particles undergo when loaded to a certain extent. A possible interpretation of the effect of MC of the amorphous lactose on the yield pressure is thus that the deformability of the particles increases continuously with an increased MC. The absorbed water molecules act as a plasticiser or molecular mobility enhancer and increase the propensity of the molecules in the amorphous state to move relative to each other. Support for this explanation might be the fact that the density and T_g of the material decreased with an increased MC (Table 1). Moreover, the plasticisation of amorphous particles might also be facilitated by temperature increase during compression, due to particle–particle friction. A temperature increase during compaction has been reported earlier (Pilpel et al., 1991; Bechard and Down, 1992).

3.3. Microstructure of tablets

Compacts formed of amorphous lactose (Fig. 3a–h) can generally be described as consisting of cohering, individual particles, the sizes of which are similar to the original particles. Thus, the photomicrographs support the view that fragmentation of particles occurred only to a limited degree during compression. However, at the upper tablet surface, one can observe cracks in the particles which seem to originate at the particle

Fig. 3. SEM photomicrographs of tablets, formed at 150 or 200 MPa, of spray-dried lactose stored at 0% or 33% RH before compaction: (a) compaction pressure 150 MPa, powder storage RH 0%, fracture surface of tablet; (b) compaction pressure 150 MPa, powder storage RH 0%, upper surface of tablet; (c) compaction pressure 200 MPa, powder storage RH 0%, fracture surface of tablet; (d) compaction pressure 200 MPa, powder storage RH 0%, upper surface of tablet; (e) compaction pressure 150 MPa, powder storage RH 33%, fracture surface of tablet; (f) compaction pressure 150 MPa, powder storage RH 33%, upper surface of tablet; (g) compaction pressure 200 MPa, powder storage RH 33%, fracture surface of tablet; (h) compaction pressure 200 MPa, powder storage RH 33%, upper surface of tablet.

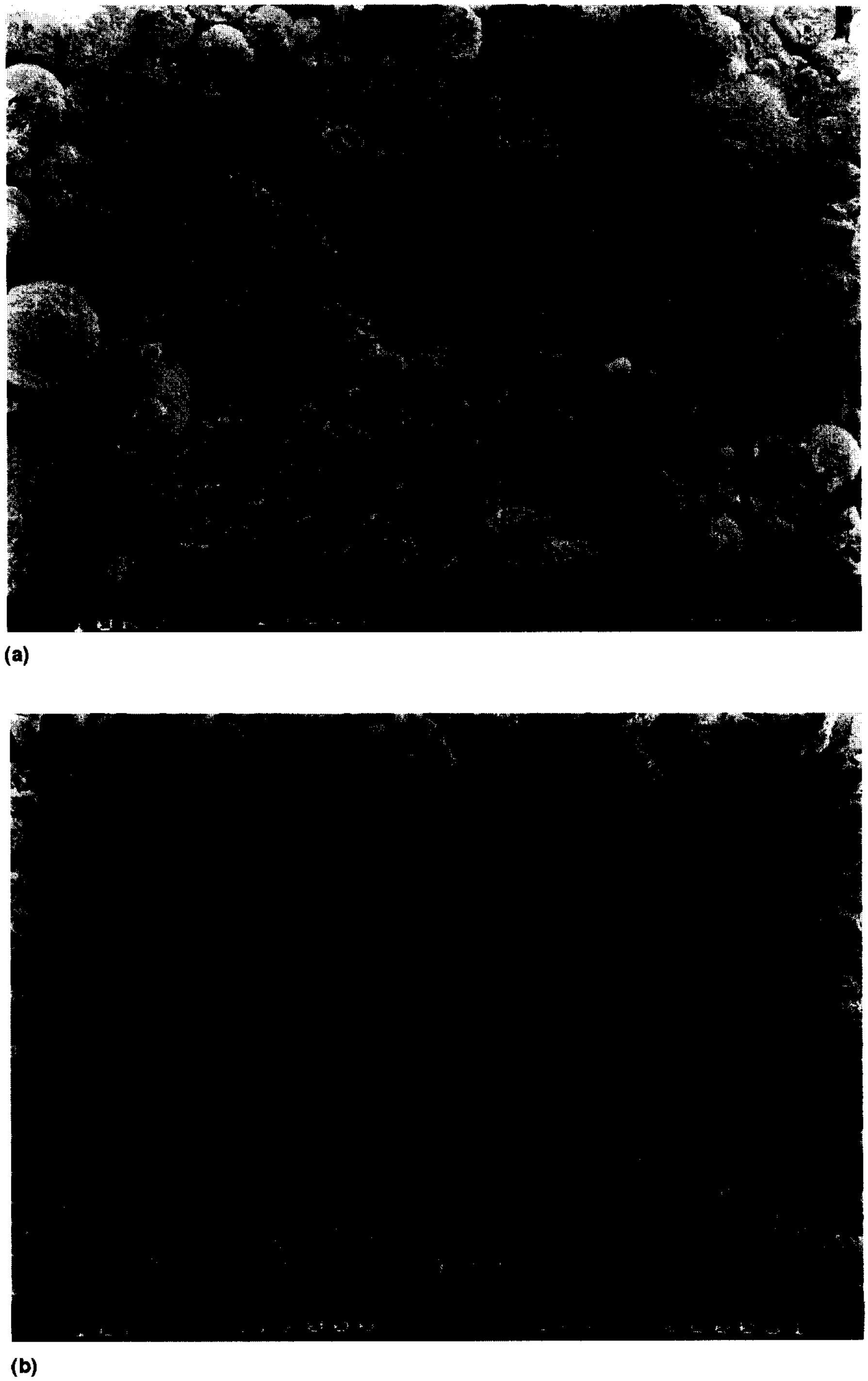
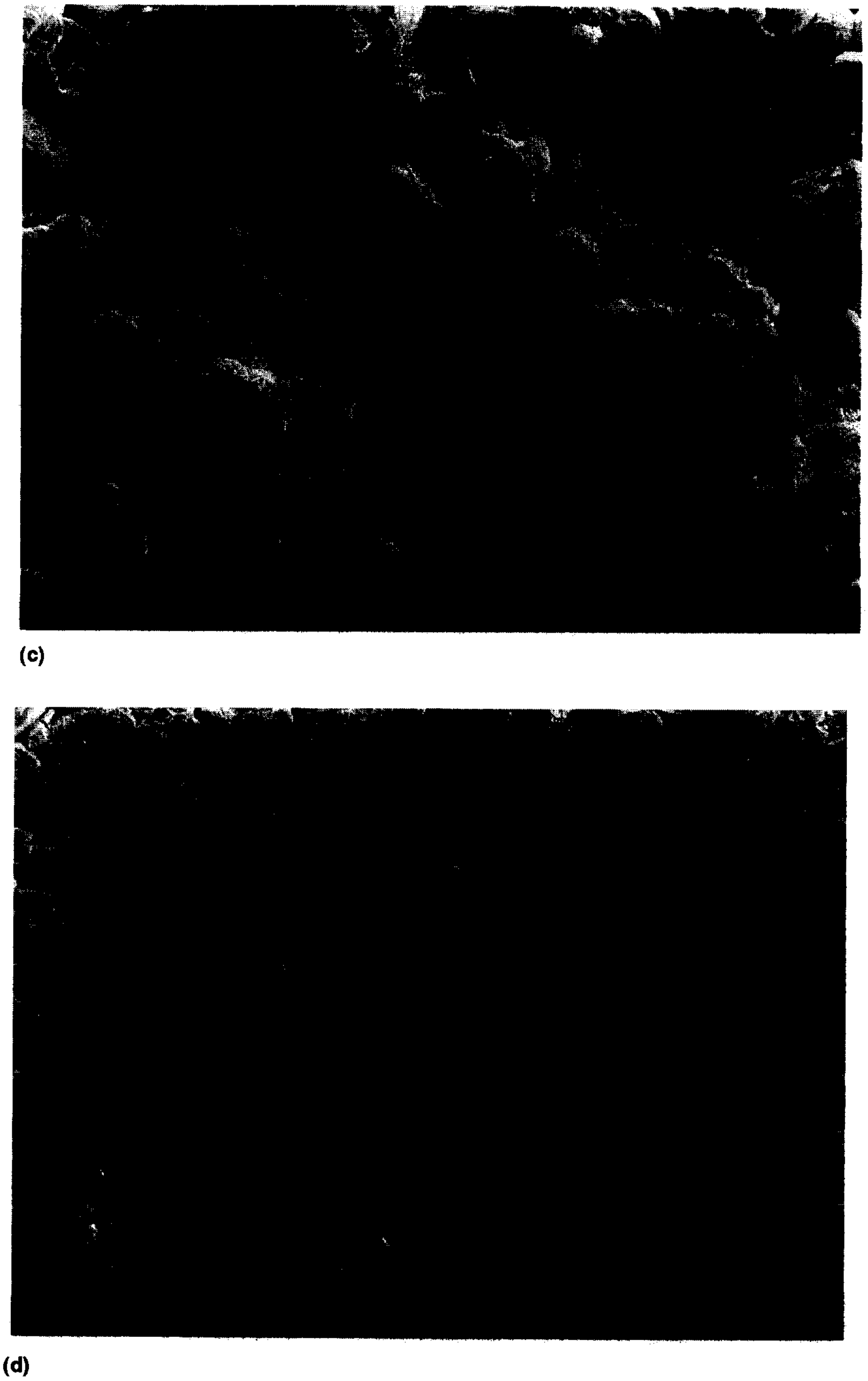


Fig. 3.



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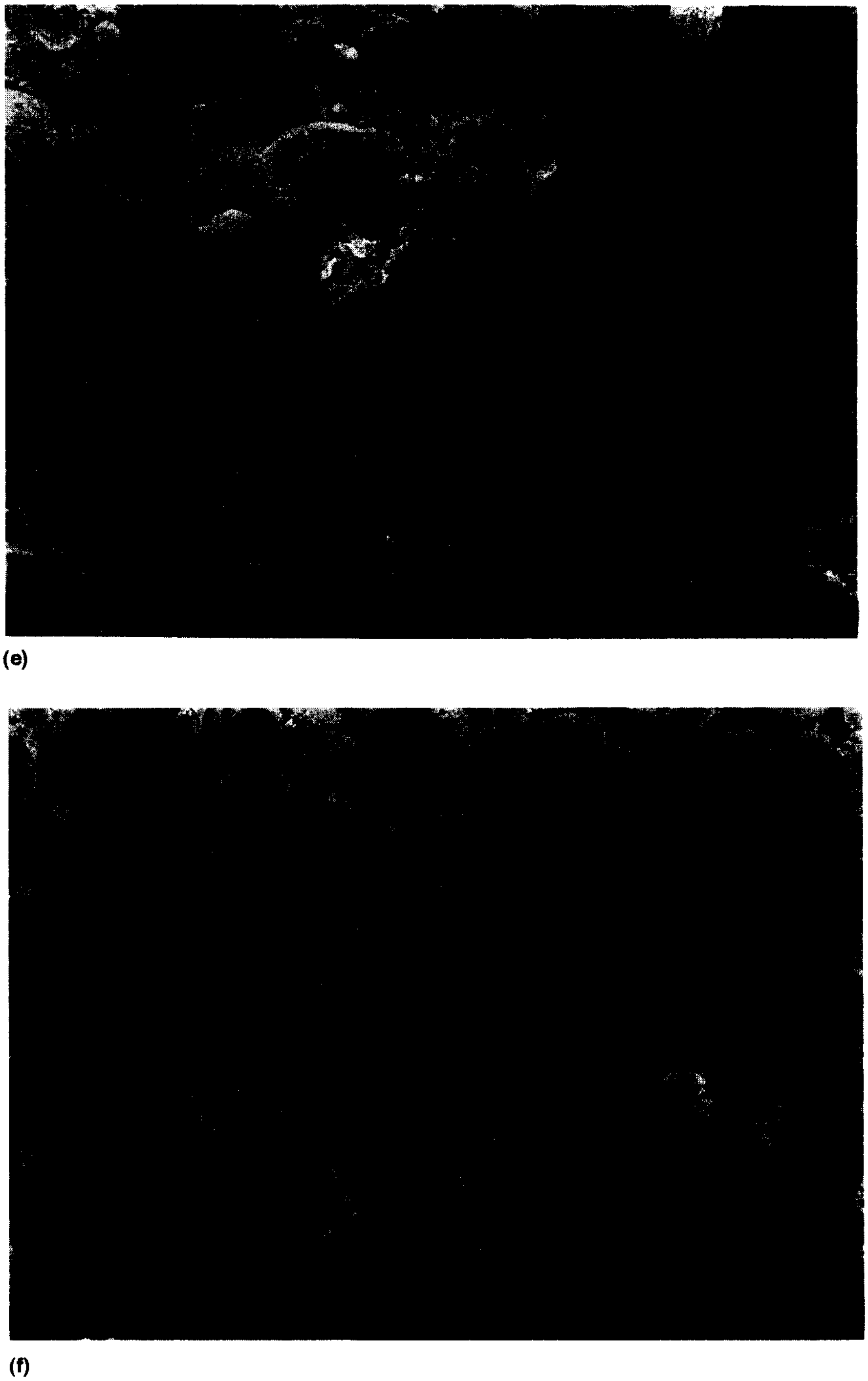

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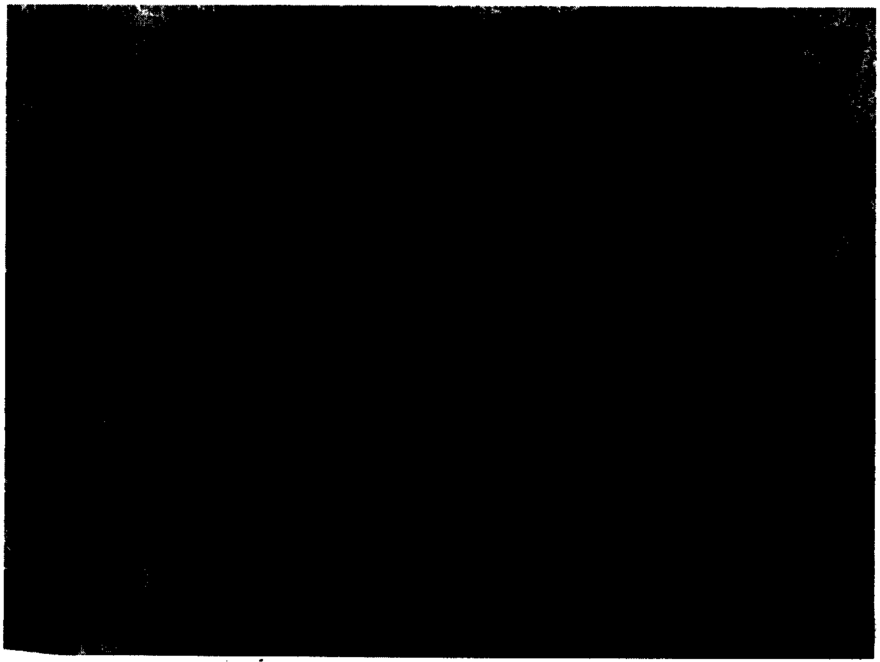

Fig. 3 continued.

surfaces and propagate towards the centres of the particles without causing complete failure of the particles. Also, the particles are often slightly deformed, especially at the contact points between particles.

For the material prestored at 0% RH, the particles became more closely packed and seemed more deformed with an increased applied pressure. For compacts prepared at the highest applied pressure, some of the particles have deformed extensively and seemed to have locally fused together during compression, i.e. although individual particles can be distinguished, the spaces between the particles are filled with material. For the material prestored at 33% RH, the same principal effects of compaction pressure on the physical structure of the formed compacts were valid. However, at a given pressure, the increased MC of the material seemed to give a closer packing of more deformed particles (which is supported by a reduced tablet mean pore diameter (Table 1)).

In adhesion science, the process whereby two solids are mixed at their interfaces and accordingly form a continuous phase is referred to as the diffusion theory of bonding, in contrast to the adsorption theory, where the surfaces of the two solids bind to each other due to intimate contact (Kinloch, 1987). The formation of diffusional bonds might require a very mobile phase of low viscosity to allow repositioning of molecules at the particle–particle interface in order to form a continuous phase of material. The photomicrographs (Fig. 3) indicate that both adsorption and diffusional bonds can be formed between the amorphous lactose particles during compaction. The incidence of diffusional bonds seems to be affected by the compaction pressure and the MC of the material. It can be speculated that a transition of glassy to rubbery amorphous material is required to obtain a phase of such low viscosity. Since individual particles can be distinguished, even though the gaps between them are filled with a solid, it can be argued that such a glass–rubber transition occurred initially at the surface of the particles, probably due to an increase in temperature in these regions of the particles due to interparticulate friction. However, at a high MC of the material and at a high applied pressure, it seems that more or less an entire particle can change to a rubbery state, deform markedly and locally fuse with another particle (Fig. 3h).

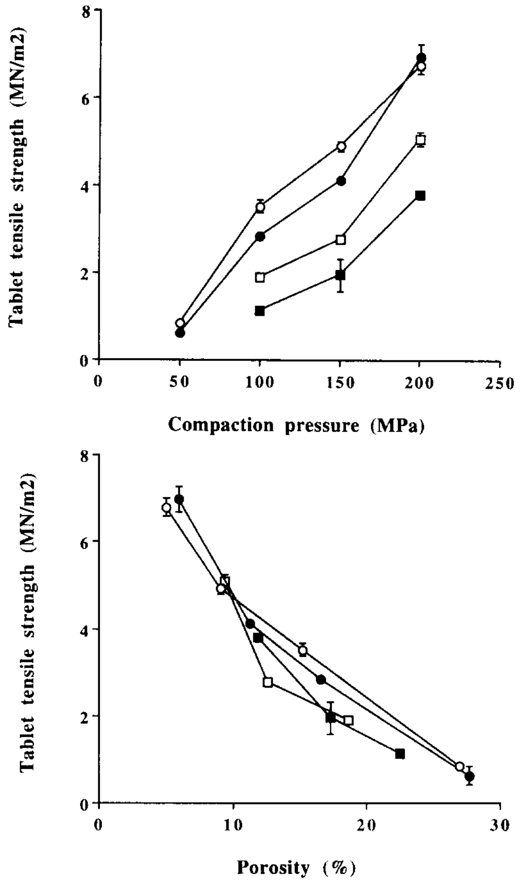

Fig. 4. (a) Tensile strength as a function of compaction pressure for tablets of spray-dried lactose stored at different RHs before compaction. Symbols as in Fig. 2a. Bars represent 95% confidence limits of the mean. (b) Tensile strength as a function of tablet porosity for tablets of spray-dried lactose stored at different RHs before compaction. Symbols as in Fig. 2a. Bars represent 95% confidence limits of the mean.

3.4. Tensile strength of tablets

Generally, the tensile strength of the tablets increased in a nearly rectilinear way with applied pressure and MC of the powders (Fig. 4a). However, the tablets formed at 290 MPa from lactose of the highest MC seemed to possess an unexpectedly low tensile strength (6.47 ± 0.24; not shown in figures). Capping of tablets of spray-dried lactose formed at high pressures has been reported earlier (McKenna and McCafferty, 1982). A possible reason for the low tensile strength of some of the tablets is thus a tendency for the tablets to cap or laminate.

The increased compactability of the amorphous lactose with an increased MC corresponded to an increased compressibility (Fig. 2b). However, an examination of the tablet strength–tablet porosity relationships indicates that the moisture-induced differences in compactability cannot be explained solely by differences in tablet porosities. At the lowest tablet porosities, i.e. below approximately 10% (tablets made at 200 MPa), it is difficult to distinguish a trend in the tablet strength–tablet porosity relationship (it can be speculated that incipient capping and viscous effects can affect the relationships at these porosities). However, above this porosity level, it seems that the materials can be rank-ordered in terms of the tensile strength of the compacts at a given porosity, i.e. for these porosity-normalised tablet strength values, the tablet strength increased with an increased MC (Fig. 4b).

The tensile strength of a tablet is sometimes discussed mechanistically by assuming a physical model of a tablet formed from pharmaceutical powders as an aggregate of more or less individual particles which, however, possess significant areas of interparticulate contact (Alderborn, 1996). The examination of the microstructure of the compacts discussed above supports this model for compacts of amorphous lactose. Ignoring the importance of a crack propagation process occurring during strength testing of the tablet, the tensile strength of the tablet equals the number of interparticulate bonds (contacts) per cross-sectional area of compact multiplied by the mean force needed to break an individual interparticulate bond. Since the MC of the material seemed to have a limited effect on the degree of fragmentation of the particles during compression, it is reasonable to assume that at a given tablet porosity, the number of contact points between lactose particles per compact cross-section is independent of the MC of the material. The increased porosity-normalised tablet strength ought then to be explained by an increased bonding force of the interparticulate bonds. The moisture-induced increase in particle deformability, as assessed by the yield pressure, will thus control differences in tablet porosity, but will also affect the bonding force between particles in the compact more than can be expected from the differences in tablet porosity. This effect of MC on the bonding force can be due to either an effect on the contact area formed between particles during compression or to an effect on the relative fractions of adsorption and diffusional bonds in the tablet.

Another interpretation of the porosity-normalised difference in tensile strength between tablets formed of amorphous lactose of different MC is that the difference is related to the fracture event during strength testing. It cannot be excluded that the bond structure within the compact is similar at a given tablet porosity, but the increased MC will change the mechanical properties of the material in such a way that the crack propagation process becomes more difficult.

Assuming the physical model of a tablet described above, a dimensionless measure (σ_a/P_y, where σ_a is the applied compaction pressure and P_y is the yield pressure for the material) which was derived earlier (Eriksson and Alderborn, 1995) was considered to reflect the interparticulate contact area in a cross-section of a tablet. If the tensile strength of the tablet correlates to this contact area coefficient, it is reasonable to suppose that the tensile strength is controlled by the area of contact formed between particles during compression rather than by differences in the type of bonds formed between the particles in the compact or by fracture mechanic effects. In Fig. 5, the tensile strength of the tablets is plotted as a function of this contact area coefficient. A spread in values was obtained in the upper region of the graph which corresponds to tablets of a porosity below 10%. In the lower region of the graph, the tablet tensile strength increased nearly rectilinearly with an increased contact area coefficient. It is difficult to rank-order the relationships obtained for the respective MC values of the material. Thus, for tablet porosities above 10%, the values seem to be represented by a single relationship with a correlation coefficient of 0.96. The slope of this line should theoretically represent the strength of the bonds cohering the particles together within the tablet, i.e. the bond strength seemed independent of the MC of the particles, indicating that the same type of bonds controls the interparticulate bonding process in the tablet. An extrapolation of the regression line gives a negative intercept. The results presented in Fig. 5 can thus be described with the following equation:

$$\sigma_c = \sigma_b C_{CA} - a_0$$

where σ_c is the tablet tensile strength, σ_b is the bond strength, C_{CA} is the dimensionless contact area coefficient calculated as σ_a/P_y, and a_0 is the intercept of the line. This intercept can be described as a compensation for the fact that a certain compaction pressure must be applied to the powder in order to obtain the minimum contact area needed to form a coherent tablet.

The relationship presented in Fig. 5 supports the view that the tensile strength is controlled by the total bond strength in the failure plane of the compact and that the total bond strength is controlled by the contact area formed between the particles during compression of the powder. This contact area will be controlled by the applied compaction force and the deformability of the particles. A moisture-induced change in particle deformability will thus explain the effect of MC on the compactability of amorphous lactose particles.

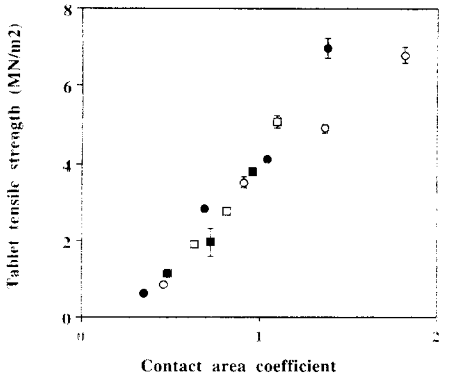

Fig. 5. Tensile strength as a function of the contact area coefficient for tablets, formed at 50, 100, 150 and 200 MPa of spray-dried lactose stored at different RHs before compaction. Symbols as in Fig. 2a. Bars represent 95% confidence limits of the mean.

Relationships between determined tablet tensile strength and the expression σ_a/P_y have been presented earlier for four crystalline materials (Eriksson and Alderborn, 1995). It was observed that the slope of the profile for the relationship was material-dependent. The highest slope value was obtained for milled, fine particulate sodium chloride. The slope for the relationship between determined tablet tensile strength and the expression σ_a/P_y obtained in this study for amorphous lactose has the same order of magnitude as that for milled sodium chloride. These two materials have the same dominating compression mechanism (permanent particle deformation) and probably have a disordered solid-state structure at the particle surfaces (the lactose particles were completely amorphous and the sodium chloride particles were milled before tableting). The high slope values for these materials can be due to the fact that disordered surfaces represent high-energy surfaces (Hüttenrauch et al., 1985) which can form strong adsorption bonds, or that milled sodium chloride and amorphous lactose are materials which are prone to form diffusional bonds which will be of significant importance for their compactability.

4. Conclusions

The effect of MC on compactability of partially amorphous lactose was investigated earlier (Sebhatu et al., 1994b). In that study, it was concluded that an increased MC of the material increased the tensile strength of tablets formed at a given compaction pressure. By the use of more or less fully amorphous lactose, this finding has been confirmed in this study. In addition, from the experiments reported in this study, we reach the following conclusions:

(a) Amorphous lactose powder was reduced in volume during compaction due to particle deformation, and compression of the powder was facilitated by an increased MC. It is suggested that the increased powder compressibility was due to an increased deformability of the particles in their glassy state. However, a glass–rubber transition seemed to occur during the compression, but had a limited effect on the relationship between MC and compressibility of the powder.

(b) The particle deformability will control the area of contact formed between the particles during compression; this is suggested to be the main explanation for the effect of MC on the compactability of amorphous lactose.

(c) Amorphous lactose particles also seemed to form strong interparticulate bonds in terms of their bond strength, either due to strong adsorption bonds or due to the formation of diffusional bonds. The results supported the existence of both types of bonds, but their relative proportion was dependent on the MC and the compaction pressure.

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