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Consolidation and compaction of powder mixtures: II. Binary mixtures of different particle size fractions of α-lactose monohydrate

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Summary

Binary mixtures of different particle size fractions of α-lactose monohydrate were compacted into tablets. The results showed decreased crushing strengths and decreased internal specific surface areas of the tablets as compared with the values calculated by linear interpolation of the data obtained for the corresponding single powder fractions. The extent of decreased strength and decreased surface area of the tablets was found to depend upon the weight ratio of the finer sieve fraction in the blend and to increase with the diameter ratio between coarse and finer particles. These results indicate an interaction with respect to consolidation and compaction which is explained by decreased fragmentation potentials, caused by increased packing densities of the binary mixtures of different particle size fractions of crystalline lactose. All data on crushing strength and internal specific surface area of the tablets fitted the unique linear relationship between these parameters, as found previously for tablets compressed from binary mixtures of equal particle size fractions of different types of crystalline lactose.

Introduction

Vromans et al. (1985) and De Boer et al. (1986) examined the consolidation and compaction properties of different types of crystalline lactose. The investigations showed the existence of a unique relationship between tablet strength and tablet pore surface area, valid for all types of crystalline lactose and all particle size fractions tested. From these studies it was concluded that fragmentation is the predominant mechanism of consolidation for crystalline lactoses. Moreover, the actual binding type between the particles is likely to be the same for all types of crystalline lactose.

The experimentally found relationship between crushing strength and specific surface area of the tablets has been explained by Leuenberger et al. (1989) in a theoretical model for the calcu-

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lation of the tensile strength of tablets. Assuming that a tablet is made up of spherical isometric particles and that the strength of all types of crystalline lactose tablets originates from Van der Waals dispersion forces, acting at the coordination points of the particles, a proportionality is obtained between the tensile strength and the internal specific surface area of the tablet.

Obviously the crushing strength of crystalline lactose tablets is determined by the tablet pore surface area, initially present and created by fragmentation during the process of consolidation.

Many studies have been published dealing with the effect of particle size on the tensile strength of tablets (Shotton and Ganderton, 1961; Fell and Newton, 1971; Hersey et al., 1972, 1973; Butcher and Newton, 1974; Alderborn and Nyström, 1982; Duberg and Nyström, 1982). For lactose these studies showed that the compact strength generally tends to increase with decreasing particle size. Although fragmentation is the predominant mechanism of consolidation of all types of crystalline lactose, the extent of fragmentation is apparently not sufficient to eliminate differences in initial surface area of different particle sizes.

Next, it should be borne in mind that the degree of fragmentation of particulate matter under compression is dependent upon both the intrinsic property of a particle to fragment, which can be regarded as a fragmentation propensity, and the extent of fragmentation of the particle within the powder system, the fragmentation potential.

The fragmentation propensity is a material-related parameter and expresses the ability of a single particle to fragment under compression (Alderborn et al., 1985). Several studies confirmed the Griffith theory of increasing mechanical strength of a crystal with decreasing particle size, corresponding with a decrease in fragmentation potential with an increase in particle size (Griffith, 1920; Shotton and Ganderton, 1961; Hersey et al., 1972, 1973; Butcher and Newton, 1974).

De Boer et al. (1986) studied the consolidation behaviour of different sieve fractions of crystalline α-lactose monohydrate. The results showed strongly decreasing degrees of fragmentation with both decreasing particle size and increasing compaction load. Moreover, the lactose compacts exhibited for all compression loads an increase in overall porosity with a decrease in particle size of the starting material. These differences in porosity can be considered as differences in fragmentation potential of the particles within the particulate system.

The many studies on the consolidation and compaction of powder sytems have generally been performed on narrow sieve fractions. Commercially available excipients for direct compression generally show, however, a broad range of particle diameters.

The present work has been performed in order to extend existing knowledge on the consolidation and compaction of powder mixtures. The first paper of the series discussed the consolidation and compaction of binary mixtures of equal particle size fractions of different types of crystalline lactose: α-lactose monohydrate, anhydrous α-lactose, crystalline β-lactose and roller dried β-lactose (Riepma et al., 1990). The results showed that both crushing strength and surface area of the tablets were linearly related to the weight ratio of the binary blends compressed. Moreover, all data on crushing strength and internal surface area of the tablets fitted the unique linear relationship between these properties, as found for the single materials (Vromans et al., 1985). From this, it was concluded that no interaction with respect to consolidation and compaction occurs between two different types of crystalline lactose if the mixture contains equal sieve fractions of the powders.

The present paper discusses the consolidation and compaction properties of binary mixtures of different sieve fractions of crystalline α-lactose monohydrate.

Materials and Methods

The materials used were different sieve fractions of α-lactose monohydrate, supplied by DMV, Veghel, The Netherlands (Table 1). All handling was performed at constant temperature

TABLE 1

Sieve fractions of α-lactose monohydrate used in the study

Sieve fractions (μm)	Mean particle diameter (μm)	Ratio D_c / D_f
24– 32	28	10.00
32– 45	38.5	7.34
45– 63	54	5.23
63– 80	71.5	3.95
100–125	112.5	2.51
125–160	142.5	1.98
180–200	190	1.49
250–315 (coarse sieve fraction)	282.5 (= D_c)	

The mean particle diameter is expressed as the arithmetic mean of the sieve openings. D_c / D_f, diameter ratio between coarse (D_c) and finer (D_f) sieve fractions.

(20 ± 1°C) and constant relative humidity (50 ± 5%). The powders were stored under the same conditions for at least 2 days before mixing and compression.

Different weight ratios of a coarse sieve fraction (250–315 μm) of lactose with one of the finer sieve fractions listed in Table 1 were blended during a period of 30 min in a Turbula mixer model 2P (W.A. Bachofen, Basle, Switzerland) at 90 rpm. The binary blends were compacted into 500 mg flat-faced tablets with a diameter of 13 mm using a programmable hydraulic press (Mooi ESH Testing, Brierley Hill, U.K.). The die was prelubricated with magnesium stearate.

Specific powder volumes of the binary blends were measured by pouring 100 g of the powder into a measuring glass cylinder. The data given are the mean of three measurements.

Tablet strength and tablet dimensions were determined 30 min after compaction with a Schleuniger 4M tester (Dr Schleuniger Production AG, Solothurn, Switzerland) and an electronic micrometer (Mitutoyo, Tokyo, Japan), respectively. The data given are the mean of five tablets.

Specific tablet volumes were derived from the tablet dimensions and tablet weights.

The specific surface areas of both the powders and tablets were measured with a Quantasorb gas adsorption apparatus (Quantachrome Corp., Syosset, U.S.A.) using nitrogen as adsorbate. The tablets were stored immediately after compaction under a nitrogen atmosphere to suppress the adsorption of moisture. The data given are the mean of six tablets.

Results and Discussion

Fig. 1a depicts the crushing strength of tablets compressed from binary mixtures of a coarse (250–315 μm) and a fine (32–45 μm) sieve fraction of α-lactose monohydrate vs the composition of the binary blends. As seen, the tablets exhibited a lower crushing strength than that calculated by linear interpolation of the values for the

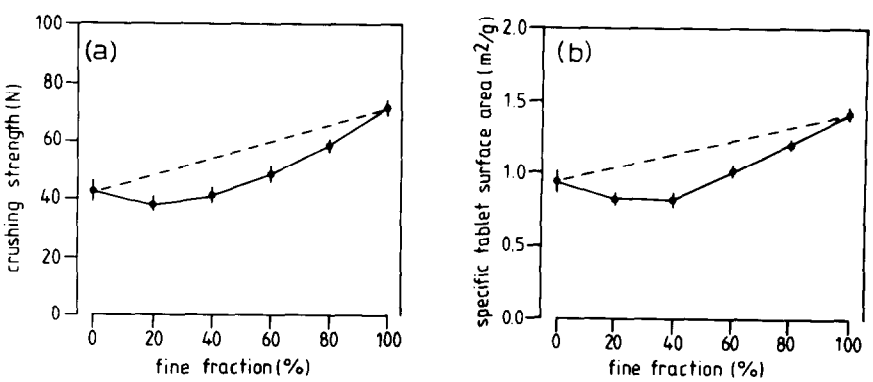

Fig. 1. Crushing strength (a) and specific surface area (b) of tablets compressed from binary mixtures of a coarse (250–315 μm) and a fine (32–45 μm) fraction of α-lactose monohydrate plotted vs the weight percentage of the fine fraction in the blend. The mixtures were compacted at 20 kN compression force into 500 mg, 13 mm diameter tablets.

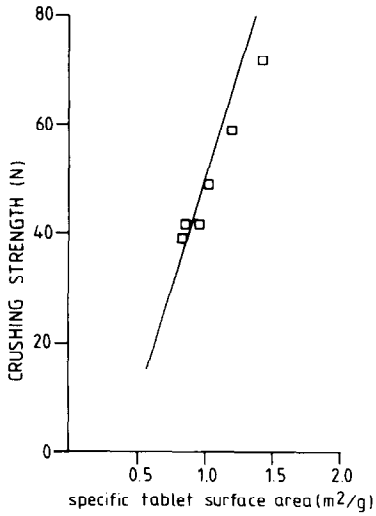

Fig. 2. Crushing strength vs specific surface area of the tablets from Fig. 1. The line refers to the relation as found for tablets compressed from binary mixtures of equal particle size fractions of different types of crystalline lactose (Riepma et al., 1990).

single fractions. The pore surface area of the tablets, measured by nitrogen adsorption, demonstrated a similar deviation from the interpolated values (Fig. 1b). The similarity between the profiles in Fig. 1a and b is emphasized by plotting the data of crushing strength vs internal surface area of the tablets (Fig. 2). The line drawn in the figure represents the relation as found for binary mixtures of equal particle size fractions of different types of crystalline lactose (Riepma et al., 1990). As observed, both the tablets compressed from binary blends of equal particle size fractions of different types of crystalline lactose and those compressed from binary blends of different particle size fractions of α-lactose monohydrate follow the same linear relationship between crushing strength and internal surface area of the tablets.

Referring to the conclusions from previous studies (Vromans, 1987; Riepma et al., 1990), it may be assumed from Fig. 2 that the actual binding mechanism between the particles in lactose tablets is the same for both single powder systems and binary blends of crystalline lactose(s). The observed deviation from linearity between tablet pore surface area and composition of the binary blends of differently sized powder fractions (Fig. 1b) suggests differences in fragmentation potential of the particles in the various powder systems.

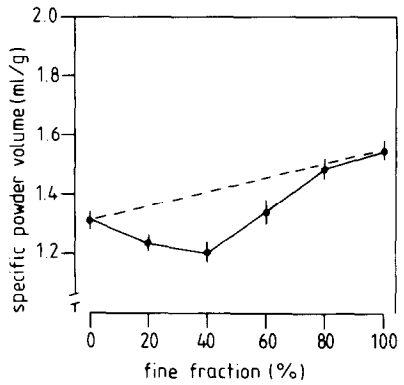

Fig. 3. Specific powder volume of binary mixtures of a coarse (250–315 μm) and a fine (32–45 μm) fraction of α-lactose monohydrate plotted vs the weight percentage of the fine fraction in the blend.

Fig. 3 depicts the specific powder volume of binary mixtures of a coarse (250–350 μm) and a fine (32–45 μm) fraction of α-lactose monohydrate vs the composition of the powder blends. As expected from literature (Cumberland and Crawford, 1987), the specific powder volumes showed a non-linear relation with the composition of the blends. A similar specific volume-composition profile was found for the tablets, compressed from the corresponding powder blends (Fig. 4). The specific volume of both the powder blends and tablets exhibited decreased volumes

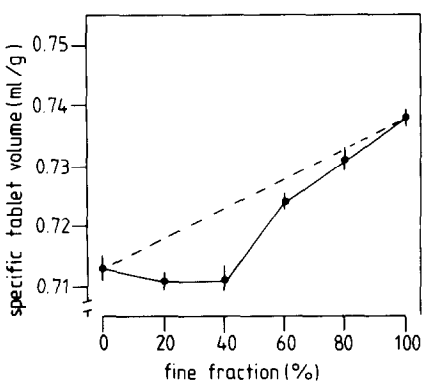

Fig. 4. Specific volume of tablets compressed from the binary mixtures from Fig. 3 plotted vs the weight percentage of the fine fraction in the blend.

as compared with the linear interpolated values. The results illustrate, for both the specific powder and tablet volume, a maximum deviation from linearity for the blend containing 40% of the fine fraction.

Obviously the 'decreased' specific powder volume of the binary mixtures, as compared to the linear interpolated values, still exists after compression. Comparison of the results from Fig. 3 and 4 with Fig. 1a and b, where similar minima in crushing strength and specific surface area of the tablets were found, indicates that the extent of particle fragmentation within the binary powder blends is affected by the porosity of the system.

The extent of particle fragmentation during compression of binary mixtures of a coarse (250–315 μm) and a fine (32–45 μm) fraction of α-lactose monohydrate is quantified in Table 2. The data given for the specific surface area of the binary powder blends were calculated from the composition of the blends and the measured specific surface area of the single fractions. The degree of fragmentation, $(S_t - S_p)/S_p$, has been expressed as the relative increase in surface area when compressing a powder (blend) with specific surface area S_p into a tablet with specific surface area S_t. The calculations show more fragmentation for the coarse fraction than for the fine fraction, which is in agreement with earlier findings (De Boer et al., 1986). Of particular interest is the observation of a lower degree of fragmentation for the blends of the two powder fractions. If fragmentation of the coarse and fine particles were to remain unaffected by differences in porosity of binary blends of different particle size

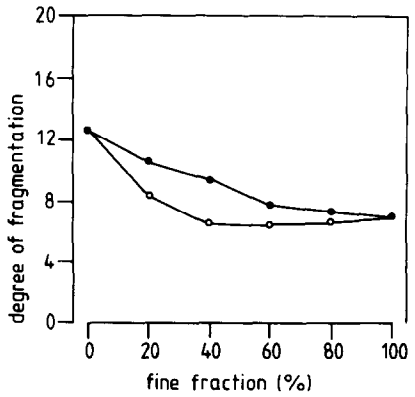

Fig. 5. Degree of fragmentation of binary mixtures of a coarse (250–315 μm) and a fine (32–45 μm) fraction of α-lactose monohydrate, compacted at 20 kN compression force into 500 mg, 13 mm diameter tablets plotted vs the weight percentage of the fine fraction in the blend. (●) Degree of fragmentation for the case when fragmentation potential is not affected by decreased porosities for the blends; (○) experimentally found degree of fragmentation.

fractions of α-lactose monohydrate, the specific surface area (S_t^*) of the tablets would change linearly with the composition of the blend. The degree of fragmentation would consequently be expressed by the value of $(S_t^* - S_p)/S_p$, if no interaction with respect to consolidation and compaction were to occur between the different particle size fractions. The lower degrees of fragmentation, $(S_t - S_p)/S_p$, as found experimentally for the blends endorse the phenomenon of decreasing fragmentation potentials for the crystalline lactose particles when present in differently sized powder mixtures (see Fig. 5).

From the literature, it is known that the pack-

TABLE 2

Degree of particle fragmentation of single powder fractions and of binary blends of a coarse (250–315 μm) and a fine (32–45 μm) fraction of α-lactose monohydrate on compaction into tablets

% fines	0	20	40	60	80	100
S_p (m^2/g)	0.07	0.09	0.11	0.14	0.16	0.18
S_t (m^2/g)	0.95	0.83	0.84	1.02	1.22	1.44
S_t^* (m^2/g)	(0.95)	1.05	1.15	1.24	1.34	(1.44)
$(S_t - S_p)/S_p$	12.57	8.22	6.63	6.28	6.63	7.00
$(S_t^* - S_p)/S_p$	12.57	10.66	9.45	7.86	7.38	7.00

S_p, specific powder surface area; S_t, specific tablet surface area; S_t^*, specific tablet surface area, assuming a linear relationship between the surface area and the composition of the blend; $(S_t - S_p)/S_p$, degree of fragmentation; $(S_t^* - S_p)/S_p$, degree of fragmentation, assuming no interaction of the size fractions on the fragmentation potentials.

ing density of binary mixtures of spheres of the same material is a function of both the weight and diameter ratio of the fractions in the mixture (McGeary, 1961; Cumberland and Crawford, 1987). The packing density increases with increasing diameter ratio between the large and small spheres. Obviously, the smaller the diameter of the fine particles, the greater the extent to which the voids between the coarse particles are eliminated by the addition of the fine particles. There is a critical ratio of occupation for the diameter of a small sphere that can exist inside the void between the large spheres without disturbing the systematic packing of the large spheres. Next, there is a critical ratio of entrance for the smaller sphere that can just pass through the pore formed by the large spheres. It is self-evident that both critical ratios are dependent on the arrangement of the large spheres. Practical densities are always found to be lower than the theoretical values, since the coarse and fine particles cannot be arranged in dense random packing as postulated by theory. Each component disturbs the order of the other. The mutual disturbance of the two components decreases with increasing diameter ratio.

Thus, taking into account that the packing density or porosity of binary mixtures of differently sized powders is affected by the diameter ratio between the coarse and the finer particles in the mixture, it could be expected that the fragmentation potential is also dependent upon this diameter ratio. This was studied by blending a coarse (250–315 μm) fraction of α-lactose monohydrate with different finer sieve fractions and compressing these binary mixtures into tablets. The particle sizes of the finer fractions ranged from 24–32 up to 180–200 μm (see Table 1). The crushing strengths of the tablets are expressed in Fig. 6 as relative deviation from the linear interpolated values of the strengths of the tablets compressed from the corresponding single fractions. The results indeed show that the crushing strengths of the tablets were dependent upon both the weight ratio of the finer fraction in the

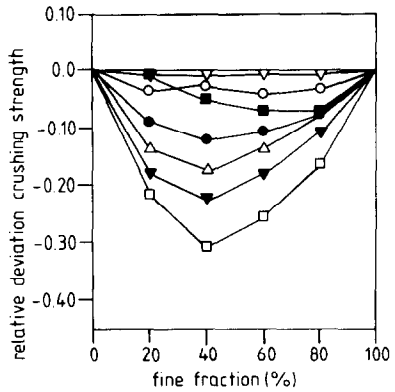

Fig. 6. Crushing strength, expressed as relative deviation from the linear interpolated values of the strength of tablets compressed from the corresponding single fractions, plotted vs the weight percentage of the finer fraction in the blend. Binary mixtures of a coarse (250–315 μm) with a finer fraction of α-lactose monohydrate were compacted at 20 kN compression force into 500 mg, 13 mm diameter tablets. Finer fractions: (□) 24–32 μm; (▼) 32–45 μm; (△) 45–63 μm; (●) 63–80 μm; (○) 100–125 μm; (■) 125–160 μm; (▽) 180–200 μm.

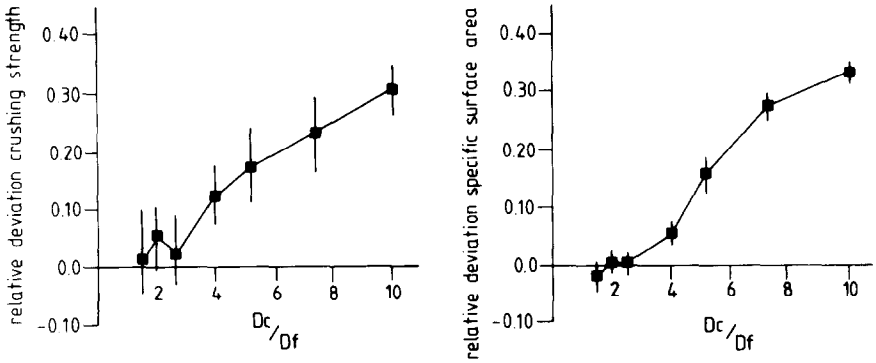

Fig. 7. Crushing strength (a) and internal surface area (b), expressed as relative deviation from the linear interpolated values of strength and specific surface area, respectively, of tablets compressed from a coarse (250–315 μm) and a finer (see Table 1) fraction of α-lactose monohydrate plotted vs the diameter ratio between the coarse and finer fraction in the blend.

blend and the diameter ratio between the coarse and finer powder fraction. One can observe the deviation from linearity increased with increasing diameter ratio. Moreover, it is noted that a maximum deviation was found for the blends containing (about) 40% of the finer fraction. These maximum deviations at 40% finer fraction in the blend are plotted in Fig. 7a against the diameter ratio between the coarse and finer fraction. The results show, up to a diameter ratio of about 2.5, no significant deviation from the linear interpolated values of the crushing strength of the tablets. Obviously, the finer particles need to be smaller than about 110 μm, as compared to 250–315 μm for the coarse fraction, in order to affect the fragmentation potentials of the powder mass. This decrease in fragmentation potentials is caused by the lowered porosity of the powder bed and finally results in deviating crushing strength of the tablets. The effect of the diameter ratio on the decrease in pore surface area of tablets compressed from binary mixtures of different sieve fractions of α-lactose monohydrate is finally illustrated in Fig. 7b by plotting the relative deviation of tablet surface area vs the diameter ratio between the coarse and the finer sieve fraction in the blend.

In conclusion, binary blends of different sieve fractions of α-lactose monohydrate show an interaction with respect to consolidation and compaction. The crushing strength of the tablets depend on both the weight and the diameter ratio between the fractions. Percolation of the finer fraction in the matrix of coarse particles decreases the fragmentation potential of the single particles. Compaction of these blends results in tablets with decreased crushing strength as compared to the values calculated from the weight ratio by linear interpolation of the strength of the tablets compressed from the single fractions. The crushing strengths and specific pore surface areas of the tablets behave according to the unique linear relationship between tablet strength and tablet surface area as found for tablets compressed from binary mixtures of different types of crystalline lactose.

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