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Consolidation and compaction of powder mixtures. I. Binary mixtures of same particle size fractions of different types of crystalline lactose

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Summary

Binary powder mixtures of four different types of crystalline lactose: α-lactose monohydrate, anhydrous α-lactose, roller-dried β-lactose and crystalline β-lactose, were compressed into tablets. The results showed a proportional intercorrelation of the crushing strength and internal specific surface area of the tablets, respectively, with the composition of the powder blend, when compressed from binary mixtures of same particle size fraction. All data were found to fit the unique relationship between the crushing strength and the internal specific surface area of crystalline lactose tablets. It is concluded that binary mixtures of same particle size fractions of different types of crystalline lactose exhibit no interaction between the components during consolidation.

Introduction

The many obvious advantages of tabletting by direct compression have resulted in an abundance of publications on direct compression. The studies have been merely focussed on the tabletting properties of single excipients. Pharmaceutical tablets are, however, usually compacted from multicomponent mixtures of excipients and drug(s). If the properties of the mixtures are linearly related to the composition of the mixture, the strength of a tablet could be predicted from the strength properties of the individual components.

Fell and Newton (1970) reported that the tensile strength of tablets prepared at 20 kN compaction load from a blend of α-anhydrous and β-anhydrous lactose (particle size 0–32 μm) was directly related to the proportion of the components present in the system. When, however, the different forms of lactose were present in the same crystal, prepared either by spray drying or crystallization, the strength of the tablets, prepared by compaction of such crystals was not related to the composition of the mixture (Fell and Newton, 1971).

Bossart and Stamm (1977) found for binary mixtures of lactose with other diluents, like Emcompress and Avicel PH 102, that the tensile

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strength of the tablets changed linearly with the proportion of the components. Newton et al. (1977) reported however that the strength of tablets prepared from mixtures of dicalcium phosphate (Emcompress) and phenacetin was not a simple function of the strength of the tablets of the individual components.

Delacourte-Thibaut (1975) recorded force-displacement profiles of binary mixtures of Emcompress-butobarbital, Emcompress-potato starch and Avicel PH 102-aspirin, and concluded that the profiles of the powder mixtures could not be predicted from the properties of the single components. Similar results were obtained by Führer et al. (1977), Führer and Schmidt (1979, 1981) and Parmentier (1978). They studied powder compression on an eccentric tablet press and characterized the force-displacement curves by hyperbolic functions. For powder mixtures of Avicel PH 102 with Emcompress and potato starch, respectively, and of Elcema P 100 with (α-)lactose (monohydrate), all containing 0.5% magnesium stearate, no relation was found between the hyperbolic constants and the composition of the mixtures. The authors observed that when the deformability of the starting materials differed, the total energy necessary to form a tablet was not the arithmetic sum of the energy contributions of the individual components; up to a certain mixing ratio, the mechanically weaker component predominantly underwent deformation.

Kurup and Pilpel (1978) studied the compression characteristics of binary, ternary and quaternary powder mixtures of the ingredients of a typical griseofulvin tablet formulation. They analysed the results in terms of the compression equations of Heckel and of Cooper and Eaton, and in terms of Cheng's equation for tensile strength. The terms in these equations are a measure of the hardness and compressibility of the different mixtures. It appeared that the terms in these equations did not alter systematically with the composition, indicating that the pressure-density relationships of the mixtures were more complex than those of the individual ingredients.

Sheikh-Salem and Fell (1981, 1982) studied the compaction characteristics of mixtures of materials with dissimilar compaction mechanism. They showed for mixtures of sodium chloride and (α-)lactose (monohydrate) that simple relationships between the constants determined from pressure-density relationships, interpreted using the Heckel equation, and the proportions of the components of the mixture did not exist. Furthermore, the tensile strength of tablets prepared from mixtures of the materials exhibited a minimum. In contrast to this, Humbert-Droz et al. (1983) reported for mixtures of hydrochlorothiazide and sodium starch glycolate (Primojel) with microcrystalline cellulose (Avicel PH101) and dicalcium phosphate (Calipharm), respectively, a linear relationship between the mean yield pressure and the proportions of the ingredients.

Panaggio et al. (1984) demonstrated that mixtures of two or more matrices may have somewhat unexpected properties. They examined compaction and tablet properties of tablets containing varying proportions of dicalcium phosphate dihydrate (Emcompress) and pregelatinized starch (Sta-Rx 1500) in the presence of 0.5% magnesium stearate. The ejection force, disintegration time, tablet thickness and tablet hardness, did not vary linearly with the relative proportions of the two main components present. Cook and Summers (1985) found a marked peak in the tensile strength-composition curve for tablets compacted from mixtures of aspirin-Emcompress. Since porosity and lower-punch work showed nearly linear relationships with composition, changes in these factors did not appear to explain this increase in tablet strength. Leuenberger and co-workers (Leuenberger, 1982, 1985; Leuenberger and Jetzer, 1984, 1985; Leuenberger and Rohera, 1986a,b; Leuenberger et al., 1989) and Jetzer and colleagues (Jetzer et al., 1983; Jetzer, 1986) determined the compactability and compressibility of binary powder mixtures of substances of similar and of dissimilar compaction behaviour. The compactability of mixtures of anhydrous lactose-sucrose, anhydrous lactose-Avicel PH102 and aspirin-Emcompress did not vary linearly with the proportion of the components, but were less than predicted. The negative interaction between the components was attributed to the predominance of cohesive attraction between same substances over the adhesive attraction between different

substances. In contrast to this, mixtures of potassium bromide-potassium chloride showed positive interactions, explained by the formation of mixed crystals under compression. The compactibility of aspirin-caffeine and aspirin-metamizol mixtures were found to be linearly related to the relative proportions of the two components, indicating no interaction. The authors reported the compressibility of the mixtures to be the arithmetic mean of the relative proportion of the individual components, with the exception of the KBr-KCl system. An attempt has been made to deduce additive rules for the material-specific compressibility and compactibility parameters.

Based on the concept of bonding and non-bonding contact points present in a compact, Leuenberger (1982) derived mathematical expressions, correlating the deformation hardness of the compact with the compression stress and relative density of the powder compact. The Leuenberger equations have been applied (Leuenberger, 1985) in an attempt to deduce additive rules for the material-specific compressibility and compactibility parameters of binary powder mixtures.

Vromans and Lerk (1988) reported a positive interaction on the consolidation and compaction of binary mixtures of a microfine cellulose (Sanacel 90) with roller-dried β-lactose. The crushing strengths of the tablets were found to be much higher as compared to the linearly interpolated values. The increased compactibility was explained by an increased consolidation of the powder mixture, most probably caused by a lubricating action of the microfine cellulose present. The increased consolidation was demonstrated by tablet thicknesses which were much lower as compared to the linearly interpolated values.

In conclusion, different and conflicting results are reported in literature about the compression of binary powder mixtures. The different observations may be caused by partly non-documented differences in the experimental conditions, like moisture content and particle size fraction of the powder samples and the use of magnesium stearate.

The aim of the present investigation was both a continuation of a study of the tabletting properties of lactose and a systematic investigation of the interaction between the components of powder mixtures during compression. The study described in this paper examines the consolidation and compaction of binary mixtures of same particle size fractions of different types of crystalline lactose. The next publication discusses the interaction when different particle size fractions of lactoses were compressed.

Materials and Methods

The materials used were different sieve fractions of crystalline lactoses: α-lactose monohydrate, anhydrous α-lactose, crystalline β-lactose and roller dried β-lactose (Pharmatose DCL-21), all supplied by DMV, Veghel, The Netherlands.

All handling was performed in a room with constant temperature (20 ± 1°C) and relative humidity (50 ± 5%). The powders were stored in the same room for several days before mixing and compression. The different powder mixtures were blended in a Turbula mixer model 2P (W.A. Bachofen, Basle, Switzerland) at 90 rpm for 30 min. Compaction of 500 mg flat faced tablets with a diameter of 13 mm was carried out using an hydraulic press (Mooi/ESH Testing, Brierley Hill, U.K.). If necessary the die was prelubricated with magnesium stearate. Tablet strength and thickness were determined after a relaxation time of at least 30 minutes, using a Schleuniger 4M instrument (Dr. Schleuniger Production AG, Solothurm, Switzerland) and an electronic micrometer (Mitutoyo, Tokyo, Japan), respectively.

The data given are the mean of at least five determinations. The specific surface area of the tablets was measured with a Quantasorb gasadsorption apparatus (Quantachrome Corp., Syosset, U.S.A.) using nitrogen as adsorbate. The tablets were put in a nitrogenous atmosphere immediately after compaction in order to suppress capillary condensation. The data given are the mean of three measurements on samples of four tablets.

Results and Discussion

To exclude any interaction all six binary mix-

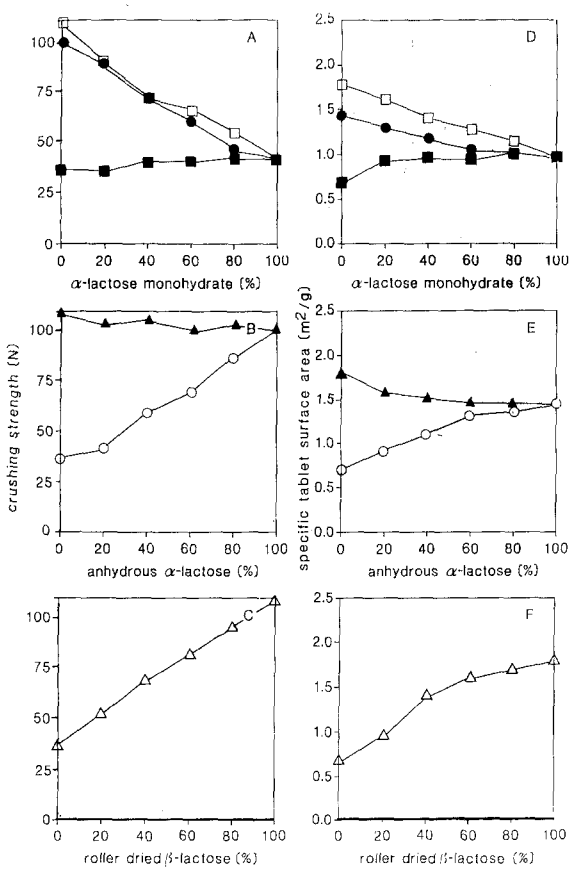

Fig. 1 (A–G) Crushing strength and specific tablet surface area as a function of the composition of the tablets. Sieve fractions of 250–315 μm of binary mixtures of crystalline lactoses were compressed at 20 kN into 500 mg tablets having a diameter of 13 mm. (●) α-Lactose monohydrate and anhydrous α-lactose; (□) α-lactose monohydrate and roller dried β-lactose; (■) α-lactose monohydrate and crystalline β-lactose; (○) anhydrous α-lactose and crystalline β-lactose; (▲) anhydrous α-lactose and roller dried β-lactose; (△) roller dried β-lactose and crystalline β-lactose.

tures of the four different crystalline lactoses, α-lactose monohydrate, anhydrous α-lactose, roller-dried β-lactose and crystalline β-lactose, were investigated. In Fig. 1 both the crushing strength and the specific surface area of the tablets are presented as a function of the composition of the powder mixture. The results show for all binary mixtures the crushing strength of the tablets to be linearly related to the composition of the blend (Fig. 1A–C).

Vromans et al. (1985) reported that neither the

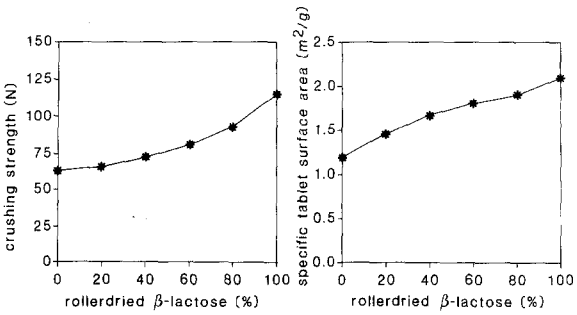

Fig. 2 Crushing strength and specific tablet surface area as a function of the composition of the tablets. Sieve fractions of 32–45 μm of blends of crystalline β-lactose and roller dried β-lactose (*) were compressed at 20 kN into 500 mg tablets having a diameter of 13 mm.

presence of water of crystallization nor the α/β-ratio has any influence on the binding properties of the crystalline lactoses. The crushing strength of all tablets showed to be linearly related to the tablet pore surface area, initially present in the powder and created by the process of fragmentation during consolidation. For the binary powder mixtures tested (Fig. 1), the experimentally found direct relationships between the internal specific surface area and the composition of the tablet (D–F) are consequently consistent with the linear relationships between the crushing strength and the proportion of the components present in the tablet (A–C).

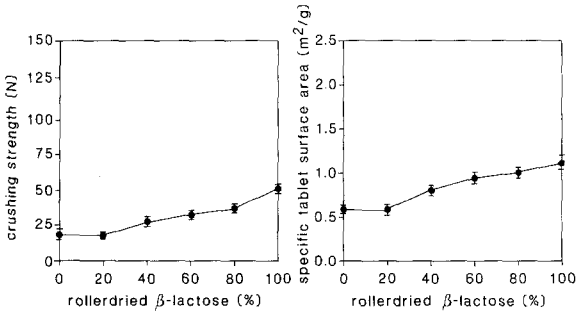

Fig. 3 Crushing strength and specific tablet surface area as a function of the composition of the tablets. Sieve fractions of 250–315 μm of blends of crystalline β-lactose and roller dried β-lactose were compressed at 10 kN into 500 mg tablets having a diameter of 13 mm.

As expected both the particle size fraction of the powder mixture and the applied compression force did not affect the direct proportionality of the crushing strength and the specific surface area of the tablets with the composition of the powder blends (Figs 2 and 3). Fig. 3 illustrates the small standard deviations of the measurements. For the sake of clarity these standard deviations have been omitted in Fig. 1.

All the experimental results are summarized and expressed by a unique relationship between the crushing strength and the internal specific surface area of the tablets, when compressed from binary powder mixtures of same particle size fractions of the different types of crystalline lactose (Fig. 4).

The thickness of the tablets finally showed to be constant or negligibly affected by the composition

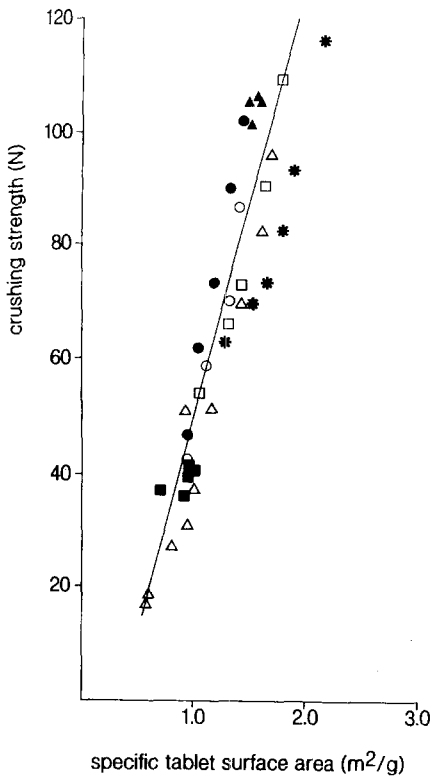

Fig. 4 Crushing strength of tablets compressed from binary mixtures of crystalline lactoses, as a function of the specific tablet surface area. Symbols as in Figs. 1 and 2.

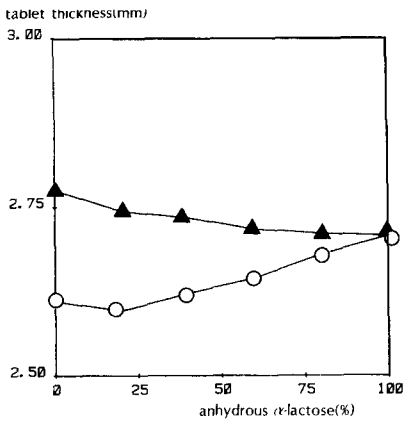

Fig. 5 Tablet thickness as a function of the composition of the tablets. Sieve fractions of 250–315 μm of respectively crystalline β-lactose and roller dried β-lactose with anhydrous α-lactose were compressed at 20 kN into 500 mg tablets having a diameter of 13 mm. Symbols as in Fig. 1.

of the powder mixture as shown in Fig. 5. This implies a proportionality between the crushing strength and the tensile strength of the compacts. These results agree with the theoretical model for the calculation of the tensile strength of tablets, presented recently by Leuenberger et al. (1989). Assuming that a tablet is made up of spherical isometric particles and that the strength of all types of crystalline lactose tablets is caused by 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. This theoretical approach enables the calculation of coordination numbers of the particles in a tablet and elucidates the unique relationship between the crushing strength and the internal specific surface area of a tablet, as found experimentally for all types of crystalline lactose.

Summarizing, both the crushing strength and the specific surface area of tablets of binary mixtures of the four different types of crystalline lactose, α-lactose monohydrate, anhydrous α-lactose, roller-dried β-lactose and crystalline β-lactose, all show a proportional intercorrelation with the composition of the tablet, when compressed from binary powder mixtures of same particle size fraction.

Realizing that all types of crystalline lactose are compacted by a similar binding mechanism, it may be concluded that binary powder mixtures of same particle size fractions of different types of crystalline lactose exhibit no interaction between the components during consolidation; the presence of the one component does not affect the consolidation of the other component, and vice versa.

Compression of binary mixtures of different particle size fractions of different types of crystalline lactose showed however a non-proportional intercorrelation of tablet strength with the composition of the powder mixtures. The observed phenomenon of (negative) interaction between the components will be presented in the next part of the series on the consolidation and compaction of powder systems.

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