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TABLETING PROPERTIES OF EXPERIMENTAL AND COMMERCIALLY AVAILABLE LACTOSE GRANULATIONS FOR DIRECT COMPRESSION

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ABSTRACT

Lactose granulations (125-250 μm) were prepared from two different α-lactose monohydrate powders and one roller dried ß-lactose powder respectively, by wet granulation with only water as a binder. As an effect of the granulation process, the flow properties improved, but the compactibility decreased. Moreover, the lubricant sensitivity of the granule fractions was higher than found for the starting materials. The compactibility of the granule fractions was found to be dependent on the type of lactose, the surface area of the starting powder and the granule bulk density. For lubricated lactose granulations, the lubricant sensitivity, expressed as Lubricant Sensitivity Ratio (LSR), increased with an increase of bulk density. The ß-lactose content of roller-dried ß-lactose is hardly affected by the granulation process, which explains the good compactibility of the granule fractions prepared from this type of lactose. On the other hand, anhydrous α-lactose present in the roller-dried ß-lactose starting material is converted into α-lactose monohydrate during the granulation process, which improves tablet disintegration.

The compaction properties of commercially available lactose granulations have been compared with those of the experimental granulations and with a free flowing sieved α-lactose monohydrate. As an effect of the higher powder surface area and the relatively low bulk density, Tablettose^R has a better compactibility than α-lactose monohydrate 100 Mesh. The excellent compactibility of another commercially available lactose granulation, Pharmatose^R DCL 15, was attributed to the presence of more ß-lactose, providing strong intergranular cohesion.

INTRODUCTION

In Pharmaceutical Industry, lactose is one of the most used excipients. The most common quality, ground α-lactose monohydrate, is generally used as a filler in tablets, prepared by wet granulation. The compactibility of α-lactose monohydrate is strongly dependent on both the powder surface area before compaction and the degree of fragmentation during the compaction process (1-3). The binding capacity increases with an increasing specific powder surface. Moreover, it was demonstrated that there exists a linear relation between the tablet pore surface area and the crushing strength of tablets, prepared from different types of crystalline lactose, including different particle size fractions of α-lactose monohydrate. In spite of the rather good dry binding properties of small particles, the poor flowability makes ground fractions of α-lactose monohydrate unsuitable for direct compression. Sieved fractions of α-lactose monohydrate with a proper particle size distribution, such as the 100 Mesh quality, have good flow properties, but a moderate compactibitity. For this reason and because of the low price, α-lactose monohydrate 100 Mesh is extensively used as a directly compressible filler-binder in combination with excipients with good binding properties such as microcrystalline cellulose.

In contrast to hydrous lactose, roller-dried ß-lactose has good compaction properties, which has been attributed to a combination of the high specific surface area of the very irregular particles and the large tendency to fracture during compaction (1,3). As roller-dried ß-lactose meets the same linear relationship between specific tablet surface area and crushing strength as found for other crystalline lactoses such as α-lactose monohydrate, it was concluded that the actual binding mechanism is the same for all types of crystalline lactose. Commercially available roller-dried ß-lactose for direct compression, commonly referred to as anhydrous lactose, consists of agglomerated, extremely fine crystals, produced by roller-drying of a solution of pharmaceutical grade α-lactose monohydrate followed by subsequent comminution and sieving. These commercial products, marketed as Pharmatose® DCL 21 by DMV and Anhydrous DT Lactose by Sheffield, contain about 85% ß-lactose and about 15% anhydrous α-lactose. Both products have good binding properties and a low lubricant sensitivity.

Because of the moderate compaction and/or flow properties of α-lactose monohydrate, some special types of hydrous lactose were developed as directly compressible filler-binders. They include spray-dried lactose, agglomerated lactose and co-processed products based on α-lactose monohydrate. Until now, little attention has been paid to agglomerated lactose for direct compression. Only two products are commercially available. Tablettose®, produced in a fluid-bed granulator, is made up almost entirely of aggregated crystals of α-lactose monohydrate (4). It contains no amorphous lactose. Its compactibility lies between those of α-lactose monohydrate 100 mesh and spray-dried lactose or roller-dried ß-lactose (5-7). For a second product, Pharmatose® DCL 15 which

has been marketed recently, the producer claims that it has better compaction properties than Tablettose[R].

A previous publication of the present authors evaluated the compaction properties of binderless lactose granules (8). The granulations were prepared by different wet granulation techniques or by dry granulation from several ungranulated powders of two types of crystalline lactose: α-lactose monohydrate and roller-dried ß-lactose, respectively. It was demonstrated that the compactibility of unlubricated lactose granule fractions was dependent, among others, on the type of the starting material (α-lactose monohydrate or roller-dried ß-lactose) and on the bulk density of the granulations. With an increase of the bulk density, the compactibility of a granule fraction decreased. This effect was explained by the lower deformation potential of lactose granules with a high density.

The objective of the present paper was an evaluation of lactose granulations as directly compressible filler binders. The tableting properties of commercially available agglomerated lactoses will be compared with those of experimental granule fractions, prepared by wet granulation with only water as a binder from α-lactose monohydrate and roller-dried ß-lactose, respectively.

MATERIALS AND METHODS

The materials used were two ground fractions (200 Mesh and 450 Mesh) and one sieved fraction (100 Mesh) of α-lactose monohydrate; two roller-dried ß-lactoses (<450 Mesh and Pharmatose[R] DCL 21) and agglomerated lactose (Pharmatose[R] DCL 15), all supplied by DMV, Veghel, The Netherlands. Another agglomerated lactose (Tablettose[R]) was obtained from Meggle GmbH, Wasserburg, Germany. Magnesium stearate Eur.Ph. was supplied by Centrachemie, Etten-Leur, The Netherlands.

The α/ß-ratio of the lactoses was determined by gas liquid chromatography (GLC). Before injection the lactose was transferred into the corresponding trimethylsilyl derivate to make it sufficiently volatile (9). The ratio between α-lactose monohydrate and anhydrous α-lactose was determined by differential scanning calorimetry (DSC), as described previously (10).

Granules were prepared from the lactose powders by wet massing using only water as a binder in a planetary mixer or in a rotating dish, as previously described (8). Granule fractions of 125-250 μm were used for the experiments.

The bulk density of the products was measured by pouring about 50 g of the material into a measured glass cylinder. The data given are the mean of six measurements.

The specific BET-surface areas of the powders were measured with a Quantasorb gas-adsorption apparatus (Quantachrome Corp., Syosset, USA) using nitrogen as adsorbate in single point determinations. The specific permeametry surface area was measured using an apparatus as described by Casal et

al. (11). Measurements were performed on a powder column with a diameter of 2 cm and a height of about 10 cm. Calculations were performed according to the Kozeny-Carman equation.

The flow properties of starting materials, granule fractions and commercial products were measured by determining the minimum aperture through which the powder blend would flow without assistance, according to Klein (12).

If not specified otherwise, tablets with a diameter of 13 mm and a weight of 500 mg were prepared with a specified force using a programmable hydraulic press (ESH Testing, Ltd, Brierley Hill, UK) with a loading rate of 2 kN/s. Before the compaction of unlubricated tablets, the die was prelubricated with magnesium stearate. Lubricated tablets were compacted after previous mixing for 2 min. with 1.0% magnesium stearate in a Turbula mixer (model 2P, W.A.Bachofen, Basel, Switzerland) at 90 rpm.

In one experiment, 9 mm tablets with a weight of 250 mg were compressed on an instrumented Kilian RLE rotary press (Kilian, Köln, Germany) at different compaction forces and a speed of 30.000 tablets/hour. Before compression, the powders were mixed for 5 min with 0.5% magnesium stearate in a Turbula mixer at 90 rpm.

Compact strength was determined 30 min after compaction with a Schleuniger 4M tester (Dr.Schleuniger Production AG, Solothurn, Switzerland). The presented data are the mean of 10 compacts.

Tablet disintegration times were determined using the Eur.Ph. apparatus without disks. The data given are the mean of the disintegration times of 6 individual tablets.

RESULTS AND DISCUSSION

Experimental Lactose Granulations

Table 1 shows the bulk density, the specific surface area measured by nitrogen adsorption, the specific surface area measured by permeametry, the flow properties and the compactibility of ungranulated powders of α-lactose monohydrate and roller-dried ß-lactose, respectively, and of granule fractions (125-250 μm) prepared from the powders. Crushing strength data are given both for unlubricated tablets and tablets containing 1 percent magnesium stearate. Moreover, Table 1 shows the Lubricant Sensitivity Ratio (LSR), being a quantitative measure to express the sensitivity to mixing with a lubricant of tableting materials. The LSR is the ratio between the decrease in crushing strength of tablets, due to mixing with a lubricant and the crushing strength of unlubricated tablets:

$$LSR = (Cs_u - Cs_l) / Cs_u$$

where Cs_u and Cs_l are the crushing strengths of tablets prepared without and with a lubricant, respectively (13).

The flow properties of the starting materials were very poor: flow class 6 means that the powders did not flow through an orifice of 18 mm. As expected,

TABLE 1

Powder bulk density, specific surface area, flow properties, compactibility and lubricant sensitivity ratio of granule fractions (125-250 μm), prepared from α-lactose monohydrate 200 Mesh, α-lactose monohydrate 450 Mesh and roller-dried ß-lactose < 450 Mesh, respectively.

Starting material and granulalation method	Bulk density (g/cm^3)	Sp* (m^2/g)	Sn* (m^2/g)	Flow class	CS* (N) unlubricated	CS* (N) lubricated	LSR*
α-lactose monohydrate 200 Mesh							
ungranulated	0.47	0.31	0.46	6	56 ± 5	62 ± 5	0.00
planetary mixer (11.4% water)	0.49	0.06	0.23	1	58 ± 4	27 ± 2	0.53
planetary mixer (15% water)	0.53	0.05	0.22	1	50 ± 4	29 ± 2	0.42
planetary mixer (20% water)	0.55	0.05	0.20	1	48 ± 3	26 ± 2	0.46
planetary mixer (22.5% water)	0.55	0.05	0.20	1	47 ± 3	21 ± 3	0.55
rotating dish (32% water)	0.59	-	0.25	1	45 ± 6	15 ± 3	0.67
α-lactose monohydrate 450 Mesh							
ungranulated	0.43	0.46	0.76	6	79 ± 9	77 ±11	0.03
planetary mixer (11.4% water)	0.40	0.09	0.43	1	69 ± 4	45 ± 2	0.35
planetary mixer (15% water)	0.47	0.07	0.37	1	55 ± 4	36 ± 4	0.35
planetary mixer (20% water)	0.49	0.06	0.33	1	50 ± 5	34 ± 4	0.32
rotating dish (27% water)	0.49	-	0.32	1	48 ± 5	35 ± 5	0.27
Roller-dried ß-lactose <450 Mesh							
ungranulated	0.44	0.32	0.69	6	136 ±11	139 ±13	0.00
planetary mixer (11.4% water)	0.37	0.09	0.70	1	127 ± 7	119 ± 7	0.06
planetary mixer (15% water)	0.41	0.08	0.61	1	120 ±11	108 ± 5	0.10
planetary mixer (20% water)	0.49	0.06	0.56	1	109 ± 6	85 ± 5	0.22
rotating dish (27% water)	0.67	-	0.56	1	83 ±10	37 ± 3	0.55

* Sp = Specific powder surface area, determined by permemetry
Sn = Specific powder surface area, determined by nitrogen adorption
CS = Crushing strength
LSR = Lubricant sensitivity ratio

the flowability increased after granulation: all the granule fractions flowed freely through an orifice of 2.5 mm (flow class 1) (12). In contrast to the improved flow properties, the binding properties of the granule fractions were generally worse than those of the ungranulated starting materials. Moreover, the lubricant sensitivity, expressed as the LSR, was much higher for tablets prepared from the granulations than for tablets, prepared from the starting materials.

In previous work, Vromans et al. (3) found that the compactiblity of crystalline lactose powders is dependent, among other things, on the powder surface area. Table 1 shows that the powder surface area of the granule fractions, measured by nitrogen adsorption, was lower than that of the starting materials. Moreover, the differences in surface area between the starting materials α-lactose monohydrate 200 Mesh and α-lactose monohydrate 450 Mesh have not disappeared completely using the wet granulation process. The decreased powder surface area can be attributed to both the use of sieve fractions of the granulations and a decrease in surface area by dissolution and precipitation of lactose during the granulation and drying procedure. Consequently, for α-lactose monohydrate the largest reduction in specific area was found for granules, prepared from the 450 Mesh quality. The smaller decrease of the surface area of roller-dried ß-lactose as compared with that of α-lactose monohydrate may be caused by dissolution of anhydrous α-lactose and its immediate precipitation in the form of α-lactose monohydrate (14).

Figure 1 depicts the relationship between granule bulk density and tablet crushing strength both for unlubricated tablets and for tablets containing 1% magnesium stearate. The figure shows the existence of a linear relationship between granule bulk density and crushing strength both for tablets prepared from unlubricated granulations and from granulations containing lubricant. The decrease of the compactibility of unlubricated granule fractions with an increase of the bulk density was explained in a previous publication by the lower deformation potential of lactose granules with a high density (8). Consequently, it must be concluded that the decrease in compactibility of lactose powder after wet granulation is caused by both a decreased powder surface area and an increased bulk density as effected by the granulation process.

Lubrication with magnesium stearate resulted in both an increase of the granule bulk density and a decrease of the tablet crushing strength. Figure 1 shows that the granule bulk density had a larger effect on the compactibility of lubricated granule fractions than on unlubricated granule fractions. This applies particularly for granule fractions, prepared from roller-dried ß-lactose. Figure 2 depicts that the LSR depends heavily on the bulk density of the lubricated granule fractions. Similar relationships between bulk density and lubricant sensitivity ratio were found previously for a variety of lactose samples, differing in particle size and particle texture (15) and for granulations based on native starches or on modified celluloses (16). Although bulk density is a

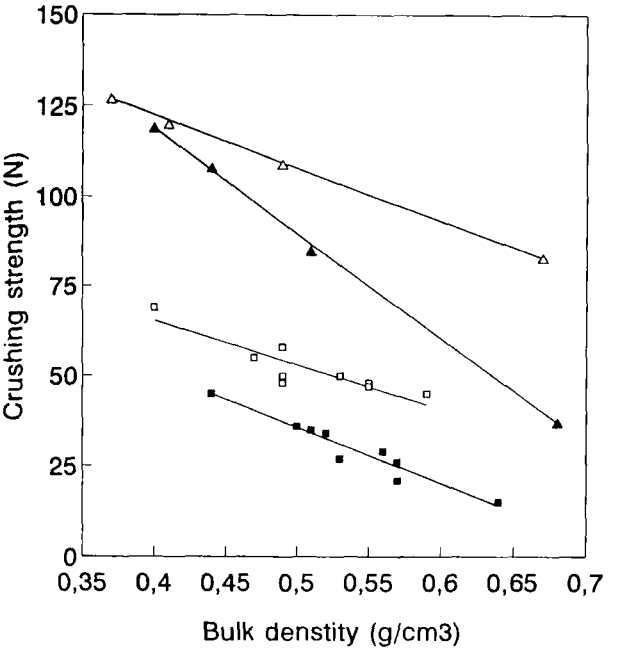

FIGURE 1

Crushing strength of tablets compressed from different lactose granulations (125-250 μm) vs the bulk density of the granulations before compression. The granulations were prepared from α-lactose monohydrate (□,■) and roller-dried ß-lactose (△,▲), respectively. Open symbols: unlubricated granulations; closed symbols: granulations, lubricated with 1% magnesium stearate.

secondary parameter, depending on fundamental properties such as true density, particle size, shape, texture and surface roughness, Vromans et al. proposed some theoretical considerations to explain the relationship between bulk density and lubricant sensitivity ratio (15): Firstly, a low bulk density is an indication for poor flowability of a powder, which might delay or even prevent the formation of a lubricant film during the mixing process. Secondly, a lower bulk density will result in a larger contribution to particle rearrangement and consequently higher friction during consolidation. This could disturb an already formed lubricant film and enhance bond formation. For granulations, the flowability of the particulate system was thought to be the predominant mechanism in the sensitivity to lubrication with magnesium stearate. This is consistent with results in Table 1: the ungranulated lactose powders had very poor flow properties, whereas the compactibility was not influenced by mixing with

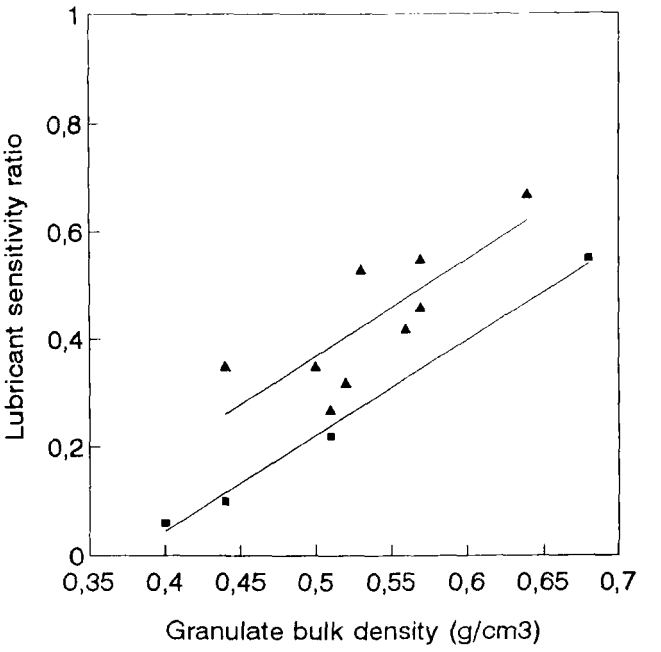

FIGURE 2

Lubricant sensitivity ratio vs powder bulk density for lubricated lactose granulations, prepared from α-lactose monohydrate (▲) and roller-dried ß-lactose (■), respectively.

magnesium stearate (LSR = 0). The granule fractions, however had better flow properties, a higher bulk density and a much smaller external surface area, as indicated by permeametry measurements. The good flow properties and the small surface area will promote film formation on granule particles during mixing with magnesium stearate, whereas the high bulk density decreases the possibility of a breakdown of lubricant films during the consolidation process. The combination of these factors results in a higher LSR for the granule fractions than found for the starting materials.

Table 1 shows that the LSR was generally higher for granules, prepared from α-lactose monohydrate 200 Mesh, than for granules prepared from the 450 Mesh quality. This effect may be caused by the rougher surface texture of granules, prepared from α-lactose monohydrate 450 mesh. The more rough surface area, as indicated by the permeametry data in Table 1, leads to both a more difficult film formation and a lower bulk density, as compared with granules, prepared from α-lactose monohydrate 200 Mesh.

Figure 2 shows different relationships between LSR and bulk density for granules, prepared from α-lactose monohydrate and roller-dried ß-lactose, respectively. This effect will be caused by differences in consolidation behaviour of the two types of lactose. Riepma et al. (17) showed that during compaction of α-lactose monohydrate, a coherent matrix of magnesium stearate is highly sustained during compression of the particulate system. Failure of tablets happens therefore principally along the interfaces of the original excipient particles, which effect results in a high LSR. For roller-dried ß-lactose a coherent network of magnesium stearate, created by dry mixing the excipient with the lubricant, is interrupted by fragmentation and consolidation of the particulate system which results in a non-coherent lubricant network in the tablets. Failure of tablets takes place across the original particles, which effect results in a low LSR. Moreover, the more or less rough surface texture of granules prepared from roller-dried ß-lactose will hinder film formation and contribute to the a low LSR.

The increase in lubricant sensitivity ratio at increasing granule bulk density (figure 2) explains why the compactibility of lubricated granulations decreased more with an increase in bulk density than that of the unlubricated granulations (figure 1). Hence, it can be concluded that the higher compactibility of lubricated lactose granulations with a low bulk density, as compared with granulations with a high bulk density, is caused by both an increased deformation potential and a decreased lubricant sensitivity.

In contrast to α-lactose monohydrate powders, ungranulated roller-dried ß-lactose has good binding properties (see Table 1). This effect has been attributed to the high initial powder surface area in combination with extensive fragmentation under load, which results in a high surface for bonding (1,3). The differences between the binding properties of the two types of lactose have not disappeared by the granulation process.

Table 2 lists the percentages hydrous α-lactose, anhydrous α-lactose and ß-lactose, respectively, for the three starting materials before granulation and after granulation with 11.4% water in a planetary mixer. The α/ß-ratio of α-lactose monohydrate is not influenced by granulation with water. However, the chemical composition of roller-dried ß-lactose changes as an effect of the granulation process. The ß-lactose content is largely retained, which effect explains the good compactibility of the granule fractions. However, the anhydrous α-lactose part, present in the starting material is converted into hydrous α-lactose during the granulation process.

The absence of anhydrous α-lactose in granulations prepared from roller-dried ß-lactose, has consequenses for the disintegration time of the tablets. In previous work, Van Kamp et al. (14) showed that the relatively long disintegration time of tablets, prepared from roller-dried ß-lactose is caused by the presence of anhydrous α-lactose in the product. In the course of the water penetration process, anhydrous α-lactose will dissolve and precipitate in the small pores, which will retard further water penetration. The absence of anhydrous α-lactose in the granulated roller-dried ß-lactose prevents a conver-

TABLE 2

Effect of wet granulation on the composition of different lactose powders.

	hydrous α-lactose	anhydrous α-lactose	ß-lactose
α-Lactose monohydrate 200 Mesh			
before granulation	96 %	0 %	4 %
after granulation	96 %	0 %	4 %
α-Lactose monohydrate 450 Mesh			
before granulation	96 %	0 %	4 %
after granulation	96 %	0 %	4 %
Roller-dried ß-lactose < 450 Mesh			
before granulation	9 %	15 %	76 %
after granulation	29 %	0 %	71 %

sion during the disintegration process. As a consequence, the disintegration time of tablets prepared from granulated roller-dried ß-lactose were shorter than for tablets prepared from the starting material or from commercially available roller-dried ß-lactose Pharmatose® DCL 21 (Table 3). Hence, it can be concluded that granulations with excellent tabletting properties can be prepared from roller-dried ß-lactose with only water as a binder.

Commercially Available Lactose Granulations

Table 4 shows some physical properties of three different commercially available α-lactose monohydrate products for direct compression. α-Lactose monohydrate 100 Mesh is a sieved lactose fraction with excellent flow properties (7). Both Tablettose® and Pharmatose® DCL 15 are granulations prepared from ground α-lactose monohydrate as a starting material, meeting the specifications of the USP. Figure 3 shows compaction profiles of tablets prepared from the three products, both unlubricated and lubricated with 1 % magnesium stearate. The tablets were prepared using a hydraulic press. Figure 4 gives compaction profiles for tablets containing 0.5% magnesium stearate, prepared on a rotary press. Both figures show that there are large differences between the compactibilities of the three products. The compactibility increased in the order α-lactose monohydrate 100 Mesh < Tablettose® < Pharmatose® DCL 15. The differences between the compaction properties of α-lactose monohydrate 100 Mesh and Tablettose® will be caused by the larger surface area and smaller bulk

TABLE 3

Crushing strength and disintegration time of tablets prepared from different lactose products. The tablets were unlubricated or lubricated with 1% magnesium stearate.

	unlubricated		lubricated	
	crushing strength	disintegration time	crushing strength	disintegration time
Pharmatose® DCL 21	102 N	221 ± 7 s	80 N	520 ± 25 s
Roller-dried ß-lactose powder < 450 Mesh	136 N	215 ± 11 s	139 N	536 ± 55 s
Granule fraction prepared from roller-dried ß-lactose < 450 Mesh	120 N	66 ± 6 s	108 N	444 ± 7 s

TABLE 4

Bulk density, specific surface area, flow class and composition of three different commercially available α-lactose monohydrate products.

Lactose product	Bulk density (g/cm^3)	Sn* (m^2/g)	Flow class	Percentage α-lactose	Percentage ß-lactose
α-lactose monohydrate 100 Mesh	0.73	0.08	1	97	3
Tablettose®	0.59	0.34	1	97	3
Pharmatose® DCL 15	0.61	0.12	1	87	13

* Specific powder surface area, determined by nitrogen adsorption

density of the latter (Table 4). For a comparison with the experimental granulations, prepared from α-lactose monohydrate, a fraction of 125-250 μm was sieved from Tablettose®. Figure 5 depicts that the Tablettose® fraction fits the relationship between the bulk density and the tablet crushing strength, as found for the experimental α-lactose monohydrate granule fractions (see Figure 1).

The high crushing strength of tablets prepared from Pharmatose® DCL 15 can neither be explained from the powder surface area, which is smaller than that of Tablettose® nor from the powder bulk density, which is almost the same as for Tablettose® (see Table 4). The differences in binding properties are introduced by differences of the production process. As an effect of the

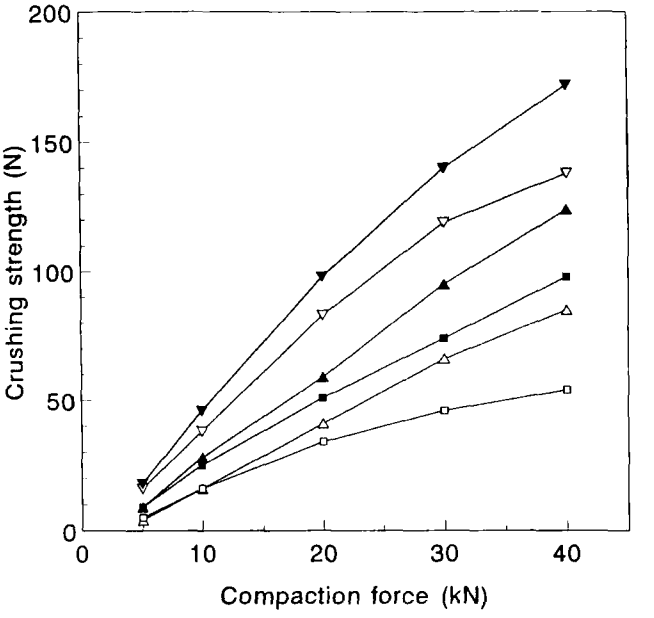

FIGURE 3

Crushing strength vs applied compaction force for tablets compressed on a hydraulic press from Pharmatose[R] DCL 15 (▼,▽), Tablettose[R] (▲,△) and α-lactose monohydrate 100 Mesh (■,□), respectively. Closed symbols: unlubricated tablets; open symbols: tablets, lubricated with 1% magnesium stearate.

production procedure of Pharmatose[R] DCL 15, apart of the starting material α-lactose monohydrate is precipitated as ß-lactose. For this reason, Pharmatose[R] DCL 15 contains 13 percent ß-lactose, whereas the ß-content of the other two products is very low (see Table 4). It may be expected that the ß-lactose is located at the surface of the Pharmatose[R] DCL 15 granules. It has previously been pointed out that the strength of tablets, compressed from α-lactose monohydrate granules is determined by the weakest bonds, being the intergranular bonds (18). In Pharmatose[R] DCL 15 the strength of the interparticular bonds will be favoured by the presence of ß-lactose at the granule surface. Because ß-lactose undergoes more fragmentation and deformation under load than α-lactose monohydrate, a larger intergranular bond surface area will be formed. This conclusion is affirmed by the relation between granule bulk density and tablet crushing strength. Figure 5 shows that a fraction of 125-250 μm sieved

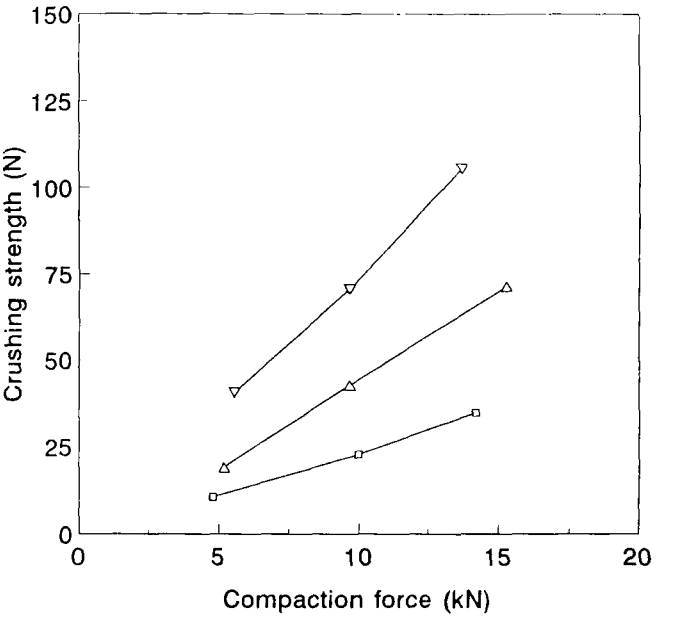

FIGURE 4

Crushing strength vs applied compaction force for tablets compressed on a rotary press from Pharmatose[R] DCL 15 (▽), Tablettose[R] (△) and α-lactose monohydrate 100 Mesh (□), respectively. The tablets were lubricated with 0.5% magnesium stearate.

from Pharmatose[R] DCL 15 fits the relationship for roller-dried ß-lactose and not the relationship for α-lactose monohydrate .

In conclusion, granulation of α-lactose monohydrate powder or roller-dried ß-lactose powder with water increased the flowabilty but decreased the compactibily as compared with the starting materials. The compactibility was dependent on both powder surface area and bulk density of the granulation. The higher compactibility of lubricated lactose granulations with a low bulk density, as compared with lubricated granulations with a high bulk density, is caused by both an increased deformation potential and a decreased lubricant sensitivity. As an effect of a conversion of the anhydrous α-lactose part to α-lactose monohydrate during granulation of roller-dried ß-lactose, the disintegration properties of tablets, prepared from granulated roller-dried ß-lactose were better than those prepared from the starting material.

As an effect of the higher powder surface area, lactose granulations, prepared from ground α-lactose monohydrate such as Tablettose[R] have a better

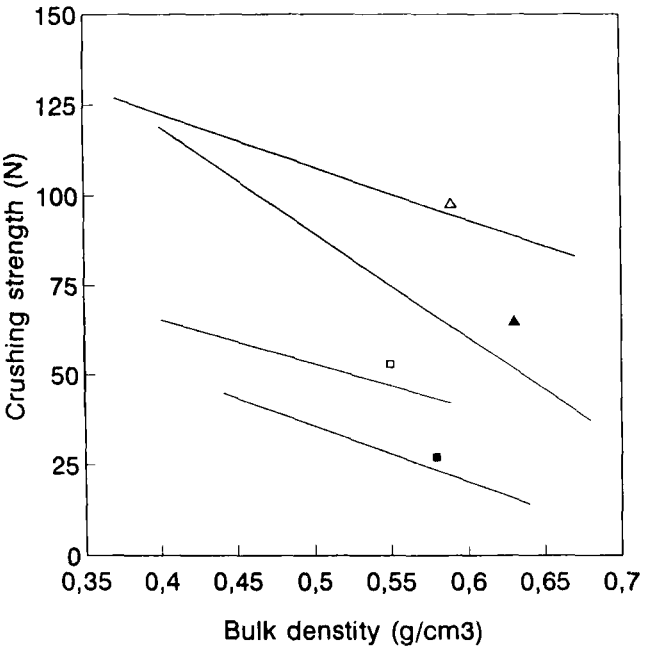

FIGURE 5

Crushing strength of tablets compressed from 125-250 μm fractions of Pharmatose^R DCL 15 (▲,△) and Tablettose^R (□,■), respectively, vs the bulk density of the fractions before compression. The lines refer to the relationships as shown in Figure 1 for granulations prepared from roller-dried ß-lactose (upper lines) and α-lactose monohydrate (lower lines), respectively. Open symbols: unlubricated tablets; closed symbols: tablets, lubricated with 1% magnesium stearate.

compactibility than the free flowing, sieved fraction α-lactose monohydrate 100 Mesh. The excellent compactibility of another commercially available lactose granulation, Pharmatose^R DCL 15, can be attributed to the presence of more ß-lactose, providing strong intergranular cohesion, as compared with α-lactose monohydrate granulations with a low ß-lactose content.

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REFERENCES

1. H.Vromans, A.H.de Boer, G.K.Bolhuis, C.F.Lerk, K.D.Kussendrager and H.Bosch, Pharm. Weekblad Sci. 7, 186 (1985).
2. A.H.de Boer, H.Vromans, C.F.Lerk, G.K.Bolhuis, K.D.Kussendrager and H.Bosch., Pharm. Weekblad Sci. 8, 145 (1986).
3. H.Vromans, G.K.Bolhuis, C.F.Lerk and K.D.Kussendrager, Int. J. Pharm. 39, 207 (1987).
4. E.Nürnberg and S.Ritsert,. Technische Nachrichten Fette, 92(1), 1 (1992).
5. J.Bossert and A.Stamm, Labo-Pharma Problèmes et Techniques. 28, 531 (1980).
6. M. Nicklasson and H.Nyqvist, Int. J. Pharm. Tech. & Prod. Mfr. 3, 115 (1982).
7. G.K.Bolhuis, G.Reichman, C.F.Lerk, H.V.van Kamp and K.Zuurman, Drug Dev.Ind. Pharm. 11, 1657 (1985).
8. K.Zuurman, K.A.Riepma, G.K.Bolhuis, H.Vromans and C.F.Lerk, Int. J. Pharm. 102, 1 (1994).
9. T.J.Buma and H.K.C. van der Veen, Neth. Milk Dairy J. 29, 225 (1975).
10. C.F.Lerk, A.C.Andreae, A.H.de Boer, P.de Hoog, K.Kussendrager and J.van Leverink, J. Pharm. Sci. 73, 856 (1984).
11. J.Casal, J.Arnaldos and N.Pellicer, Powder Techn. 58, 93 (1989).
12. K.Klein, Seifen-Öle-Fette-Wachse, 94, 849 (1968).
13. C.E.Bos, "Tropical tablets", Krips Repro, Meppel, 1990, p.41.
14. H.V. van Kamp, G.K.Bolhuis, K.D.Kussendrager and C.F.Lerk, Int. J. Pharm. 28, 229 (1986).
15. H.Vromans, G.K.Bolhuis and C.F.Lerk, Powder Technol. 54, 39 (1988).
16. C.E.Bos, H.Vromans and C.F.Lerk, Int. J. Pharm. 67, 39 (1991).
17. K.A.Riepma, H.Vromans and C.F.Lerk, Int. J. Pharm. 97, 195 (1993).
18. K.A.Riepma, H.Vromans, K.Zuurman and C.F.Lerk, Int. J. Pharm. 97, 29 (1993).