Directly compressible lactose: high speed compaction.

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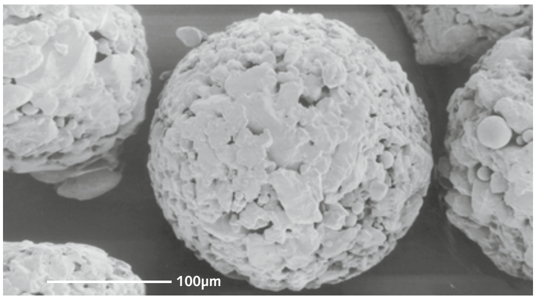
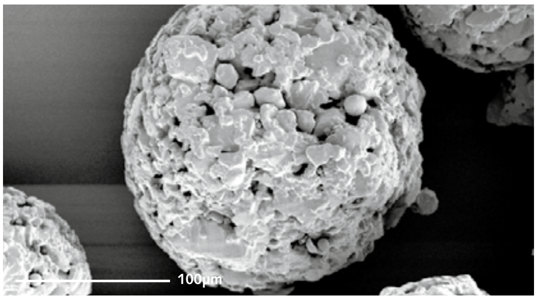
Summary

The compaction speed sensitivity of filler-binders for direct compression is of great practical importance because of the use of high capacity rotary presses in the pharmaceutical industry. After a brief introduction on compaction mechanisms and the relevance of a combination of brittle and ductile deformation behaviour, this bulletin describes a study on compaction speed sensitivity of spray dried lactose, SuperTab 11SD and SuperTab 14SD, using a programmable compaction simulator.
The results of this study show that both types of spray dried lactose, unlubricated and lubricated have a low compaction speed sensitivity with respect to compactibility. The new spray dried lactose SuperTab 14SD performed best and only showed a reduction in compactibility of about 10% at a 100 fold increase of the punch velocity (from 3 to 300mm/s). The results confirm that the spray dried lactoses SuperTab 11SD and SuperTab 14SD are excellent filler-binders for direct compaction, due to a combination of easy fragmentation and plastic deformation under load.



SuperTab 11SD.



SuperTab 14SD.

ESH high speed compaction simulator.

Introduction

Spray dried (SD) lactose was the first filler-binder used successfully in direct compaction (DC) of tablets[1] and still is one of the most popular excipients for this application. This is mainly due to the combination of excellent flowability and high compactibility[2]. The compaction mechanism of SD lactose is largely elucidated and is based on a combination of fragmentation and plastic deformation during the short time of compact formation in the die.

The ability of spray dried lactose to form strong tablets mainly depends on two product characteristics :

1) the presence of a certain percentage of amorphous lactose and
2) the size and surface area of the primary α-lactose monohydrate crystals embedded in the amorphous matrix of the spherical product particles[3].

Based on this knowledge improved SD lactose products for DC have been developed, such as SuperTab 14SD[4].

Despite the comprehensive knowledge on compaction mechanisms, little attention has been paid to the sensitivity of SD lactose to compaction speed, i.e. to the effects of high speed tabletting machines on compactibility.

Because of the practical relevance - nowadays rotary tabletting machines are used that produce over a million tablets per hour, with compression cycles between 10 and 50 milliseconds and punch velocities up to approx 300mm/sec - the sensitivity for high speed compaction was studied for two types of spray dried lactose, SuperTab 11SD and SuperTab 14SD, using a compaction simulator.

After a brief introduction on relevant aspects of deformation and compaction, this bulletin describes the approach and outcome of this study.
The study was performed in cooperation with the University of Groningen, Department of Pharmaceutical Technology and Biopharmacy, Groningen, The Netherlands.

Powder compaction

Compactibility is defined as binding capacity, the ability to form coherent compacts, and mostly expressed in tensile strength or tablet strength of tablets prepared under a certain load. The tensile strength, S, is used to study tablets independent of tablet dimensions and defined as:

$$S = 2.TS / \pi .D.d. \quad (S \text{ in Pa})$$

TS = tablet strength in N. D = tablet diameter;
d = tablet thickness (D and d in m).

Compactibility is predominantly determined by material properties such as surface energy and deformation. For example for the production of tablets with sufficient strength, filler-binders with a certain plasticity are preferred to create enough area of contact during consolidation.

On the other hand interparticle bonding of plastic filler-binders decreases dramatically upon mixing with lubricants such as magnesium stearate, and extreme plasticity is unwanted[5].

Bonding as an effect of compression

Figure 1 shows the general relationship between tensile strength and tablet porosity for filler-binders, as described by the Ryshkewitch-Duckworth equation:

$$\ln S_\varepsilon / S_o = -k\,\varepsilon$$

S_ε is the tensile strength of a compact with porosity ε, S_o is the calculated tensile strength at zero porosity and *k* is a constant, called 'bonding capacity', and is a measure for the attraction between the particles. Figure 1 shows that the tensile strength of tablets depends on two factors, namely bonding capacity and tablet porosity.

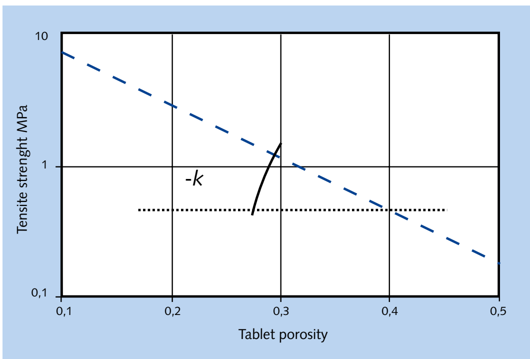


fig. 1: Tensile strength as a function of porosity, after tablet relaxation.

Brittle and ductile materials

The distinction between brittle and ductile materials is of great practical relevance. Brittle materials with a high fragmentation propensity show a low lubricant sensitivity but also a relative low contact area for bonding, while ductile materials (those which show plastic deformation) have a relatively high lubricant sensitivity but on the other hand a high contact area for bonding.

The tablet strength depends on the final tablet porosity which is a result of tablet consolidation and tablet relaxation.

Tablet relaxation depends to a large extent on deformation behaviour and stored elastic energy in the tablet. In general, for ductile materials the stored energy is high, especially at high compaction speed.

For brittle materials energy storage is generally low and less affected by speed of compaction. Figure 2 indicates the possible effects of compaction speed on tablet strength.

Increase in compaction speed

↓

Increase in amount of stored elastic energy in the tablet under load

↓

Elastic energy causes tablet relaxation

↓

Increase in porosity

↓

Decrease in tablet crushing strength

fig. 2: Effects of compaction speed.

Ideally a filler-binder should show sufficient consolidation (low porosity tablets), low tablet relaxation, low lubricant sensitivity and high bonding capacity.

Agglomerated excipients are considered to be most suitable to meet above requirements because they commonly are rather brittle and after fragmentation their primary particles may show brittle and/or plastic deformation[5,6].

Spray dried lactose study

Objective

Evaluation of the compression speed sensitivity, lubricated and unlubricated, using a high speed compaction simulator.

Methods

SuperTab 11SD and SuperTab 14SD were subjected to compaction tests, using a programmable compaction simulator (ESH Testing, Brierley Hill, UK). Flat faced tablets of 500mg and a diameter of 13mm were prepared at different compression forces, in the range of 8 - 27kN, and at compression rates of 3mm/s and 300mm/s, simulating slow (rotary) lab presses and high speed industrial rotary presses respectively. Tablets were prepared without and with lubrication (0.5% magnesium stearate, 2 minutes mixing in a Turbula mixer at 90rpm).

Crushing strength of the tablets was measured with a Schleuniger 6D tester after storage of the tablets for at least 18 hrs at 20°C and 30% RH. The SD lactoses/tablets were evaluated for compaction speed sensitivity, lubricant sensitivity and yield strength.

Results and discussion

In table 1 some relevant characteristics of both types of spray dried lactose are listed.

	11SD	14SD
Water, KF (%)	4.9	4.9
Amorphous (%)	15	16
β-lactose (%)	12	13
Particle size, d50, µm*	117	115
Primary particle size,* d50, µm	32	22

* By laser diffraction.
table 1: Product characteristics.

Both types of spray dried lactose possess similar physical characteristics, except for the size of the primary particles inside the spray dried particles.

Compactibility

Figure 3 shows the compactibility profiles of SuperTab 11SD and 14SD at low and high speed compaction, without lubrication. It is obvious that the increase in tabletting speed from 3mm/s to 300mm/s affects the compactibility of both products only to a small extent.

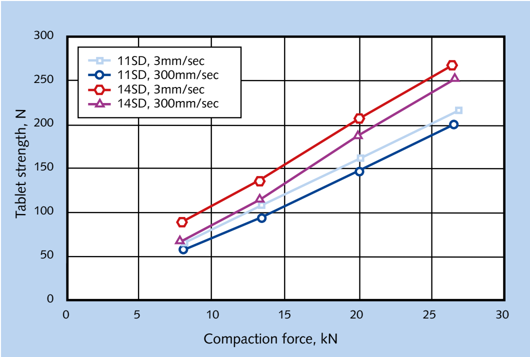


fig. 3: The effect of compaction speed on compactibility of SuperTab 11SD and SuperTab 14SD, without lubrication.

In figure 4 the compaction profiles at low and high speed, after lubrication, are depicted.

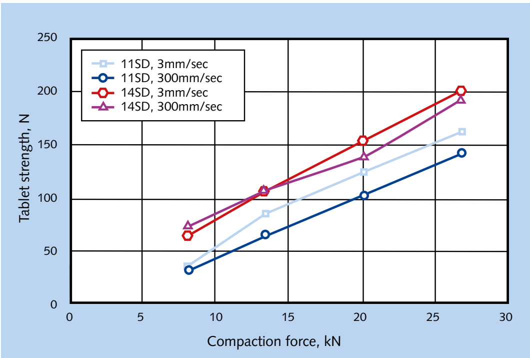


fig. 4: The effect of compaction speed on the compactibility of SuperTab 11SD and SuperTab 14SD, lubricated with 0.5% magnesium stearate.

In this case it appears that the compactibility of SuperTab 14SD is practically not affected by the speed of compaction. The speed sensitivity of lubricated SuperTab 11SD is relatively small. For example, at compression forces of 15kN, the reduction in tablet strength, as a consequence of the 100 fold increase in velocity of the upper punch, is 2% and 22% for SuperTab 14SD and SuperTab 11SD respectively.

In table 2 the reduction in compactibility as a consequence of increase of punch velocities from 3 to 300mm/s is summarized, as calculated at a compaction force of 15kN.

	11SD	14SD
Compactibility ratio, high/low speed, no lubricant	0.89	0.86
Compactibility ratio, high/low speed, lubricated	0.78	0.98

table 2: Compactibility ratios at 15kN force.

Lubricant sensitivity

The lubricant sensitivity for bonding, as calculated from the compactibility data, is expressed in % reduction in compactibility and in table 3 the values for both spray dried lactose products are listed, at a compaction force of 15kN, and at low and high compaction speed.

at 15kN force	11SD (%)	14SD (%)
3mm/s	19	21
300mm/s	28	9

table 3: Lubricant sensitivity for bonding at low and high compaction speed.

At low speed the lubricant sensitivities of SuperTab 11SD and 14SD are similar, with relatively low values, of about 20%. At high speed compaction the tablet strength of SuperTab 14SD was significantly less affected by lubrication compared with that of SuperTab 11SD, with a reduction in compactibility of about 10% and 28% respectively, at 15kN force. This is possibly due to a more intensive fragmentation of the 14SD particles at high speed compaction.

Yield strength

The yield strengths, as calculated from Heckel plots, are presented in table 4.

	11SD	14SD
3mm/s, unlubricated	40.9	40.1
3mm/s, lubricated	42.0	39.2
300mm/s, unlubricated	42.4	41.3
300mm/s, lubricated	46.0	44.9

table 4: Yield strengths in MPa.

The yield strength quantifies permanent and large deformations and normally increases with rate of strain (deformation).

The values found are not significantly different for the two spray dried lactoses and are considered to be intermediate, as compared to the reported values (at 300mm/s) for the plastically deforming microcrystalline cellulose (24 MPa) and the brittle anhydrous β-lactose (67 MPa)[7].

The increase in yield strength (σ_c) at increasing compaction speed is small for both SD lactoses.

In table 5 the yield strengths expressed in terms of 'strain rate sensitivity ratio' (SSR), in the range of punch velocities of 3mm/s to 300mm/s are presented. In this case the SSR is expressed as:

$$SSR = \frac{\sigma_c\,(300mm/s) - \sigma_c\,(3mm/s)}{\sigma_c\,(300mm/s)}$$

	11SD	14SD
Unlubricated	0.04	0.03
Lubricated	0.09	0.13

table 5: SSR's in the range of 3 - 300mm/s.

These values are considered to be low and suggest a high degree of fragmentation in the initial stage of the compaction process, followed by plastic deformation of the amorphous part and, probably, plastic deformation of the small primary α-lactose monohydrate crystals. It is reported that the so-called brittle - ductile transition of α-lactose monohydrate crystals occurs at a particle size of 45µm[5].

The low strain rate sensitivities calculated from the yield strength values are in agreement with the low compaction speed sensitivities as shown from the compactibility profiles in figures 3 and 4.

Conclusions

The sensitivity for high speed compaction, in terms of compactibility, for the spray dried lactose products SuperTab 11SD and SuperTab 14SD is low, both for the unlubricated and the lubricated products.

It can also be concluded that the lubricant sensitivity for bonding is very limited for both products.

Comparing the two types of spray dried lactose, SuperTab 14SD performs best with regard to sensitivity for high speed compaction for the lubricated powders. This is possibly due to a difference in particle structure as caused by the incorporation of smaller primary crystals in the amorphous matrix.
Next to an increased binding capacity compared to SuperTab 11SD because of a larger particle surface (smaller primary particles) covered by amorphous lactose, this structure is also extra favourable with regard to speed sensitivity after lubrication.

These findings show and confirm that these spray dried lactose products are excellent filler-binders for direct compaction in high speed rotary presses.

References

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