Suitability of Different Excipients for Roller Compaction by Using a Pneumohydraulic Single-Punch Press as a Model Roller-Compactor

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Introduction

Often granulation is the first step in the production of tablets. Since the instrumentation of the roller compactor improved and the process can be sufficient controlled, it became a standard technique. Former publication described the decrease of tensile strength after second compaction [1].

Lactose-monohydrate and starch are very often used in pharmaceutical formulations for solid dosage forms. In our study we focused on the influence of the particle size distribution of milled lactose-monohydrate qualities as well as lactose/starch combinations.

Materials & Methods

Milled lactose-monohydrate qualities from Meggle, Germany:
Granulac 70 (d50: 100µm);
Granulac 140 (d50: 53µm);
Granulac 200 (d50: 28µm);
Sorbolac 400 (d50 : 9µm)
Spray dried lactose (d50 : 121µm) and co-processed lactose-starch combination (ratio 85 :15)
Starlac (d50 : 118 µm) from Meggle, Germany
Starch (d50 : 13µm) from Roquette, France
Mg-stearate from Merck, Germany

Tablet press: Single punch press (FlexiTab, Roeltgen GmbH&Co.KG, Germany)

First compaction forces 8, 12, 20, 36 kN, tablet weight 500mg, tablet diameter 13mm.
Crushing of tablets and sieving through a 1mm sieve. Addition of Mg-stearate (0.5%) for second compaction; mixing time 2minutes (optional).
Second compaction forces: 10, 16, 22, 28 36 kN, tablet weight 250mg, tablet diameter 10mm

Tablet hardness and disintegration were tested according to standard pharmacopoeia methods.

Results:

Compaction

Depending on the particle size distribution of the milled lactose we received during the primary compaction a tensile strength of 2.7 – 4.7 MPa at compaction pressure of approx. 270 MPa. Higher tensile strength was obtained by using the starch compound (up to 5.9 MPa for the compound). The compaction profiles are shown in figure 1.

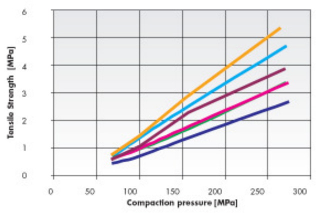

Figure 1: Compaction profiles of various milled lactose-monohydrate qualities and lactose starch combinations (first compaction)

For the milled lactose qualities (d 50: 100µm, 53µm and 28µm) we reached after the second compaction (36 kN equal to approx. 460 MPa) a tensile strength of 3.2-3.3, 4.1-4.3 and 4.1-4.5 MPa resp. There was no significant influence of the primary compaction force on the resulting tablet hardness after the second compaction (see figure 2-4).

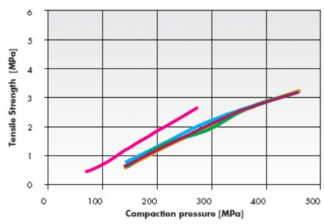

Figure 2: Compaction profile of GranuLac 70 after second compaction (primary compaction force in brackets)

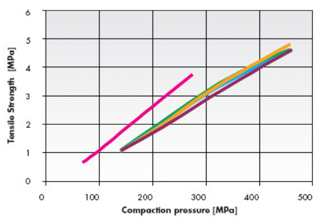

Figure 3: Compaction profile of GranuLac 140 after second compaction (primary compaction force in brackets)

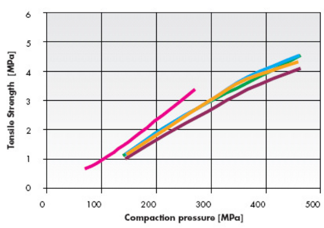

Figure 4: Compaction profile of GranuLac 200 after second compaction (primary compaction force in brackets)

However, for the fine milled lactose (d 50: 9µm) tensile strength depends on the primary compaction force and we obtained at 36 kN compaction force a tensile strength of 4.7 MPa at the highest primary compaction force or 5.6 MPa at the lowest primary compaction force, i.e. high first compaction force lowers the resulting tablet hardness of the final product (see figure 5).

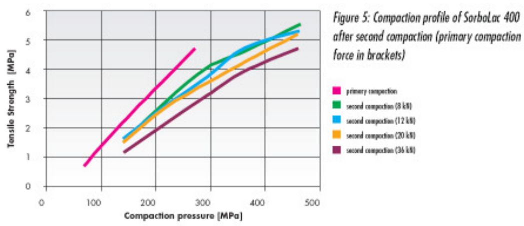

Figure 5: Compaction profile of SorboLac 400 after second compaction (primary compaction force in brackets)

Similar results we obtained for the lactose starch compound. The tensile strength varied from 4.9 -5.9 for the compound, but for the physical mixture the variation was only 4.4 -4.6 (see figure 6-7).

The addition of Mg-stearate lowered the tensile strength slightly. (results are not shown).

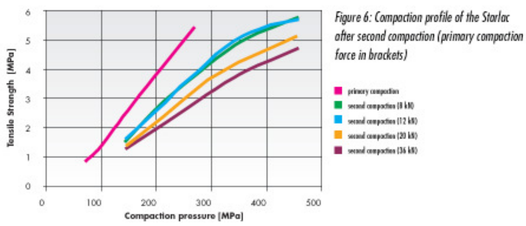

Figure 6: Compaction profile of the Starlac after second compaction (primary compaction force in brackets)

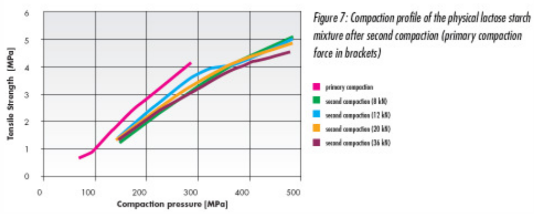

Figure 7: Compaction profile of the physical lactose starch mixture after second compaction (primary compaction force in brackets)

Disintegration

The disintegration time of the tablets depends also on the first compaction force. Tablets made from hard granules disintegrate slower than those from soft granules. There was no difference between the fine and coarse milled quality or the addition of starch (see figure 8-10).

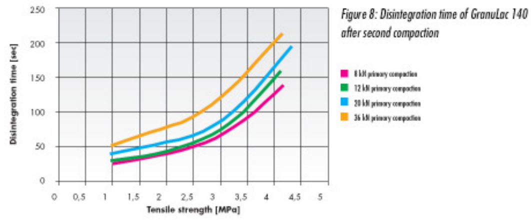

Figure 8: Disintegration time of GranuLac 140 after second compaction

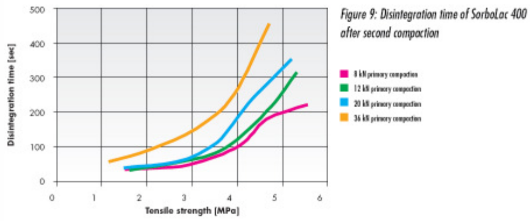

Figure 9: Disintegration time of SorboLac 400 after second compaction

Conclusion:

Purpose of the study was to investigate the influence of particle size distribution of milled lactose-monohydrate and addition of starch in first (roller compaction) and second compaction (tablet press). For the fine milled lactose and the lactose starch compound the resulting tablet hardness after the second compaction depends on the primary compaction whereas the lactose qualities with a d50 value of 100µm - 28µm and the physical mixture of lactose and starch were nearly independent from the primary compaction. Higher tensile strength was obtained by the compound and the fine milled quality. On the other hand the primary compaction influenced the disintegration time independently from the particle size distribution of the material or starch.

Literature:

[1] S. Erling: Trockengranulation: Entwicklung einer Basisrezeptur für die Walzenkompaktierung, Diplomarbeit University Bonn, Germany