

Properties of a Co-Processed Compound versus the Physical Blend based on Lactose and Starch

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INTRODUCTION

The use of a combination of lactose as a filler and starch as a disintegrant is very common. However, native starch has insufficient flow and compression properties and on the other hand pregelatinized starch has a lower disintegration potential¹. The change in physical properties by co-spray drying is reported for several excipients^{2,3}. There is a new co-processed excipient, based on 85% lactose and 15% starch commercially available (StarLac®). In our investigation we focused on the most important characteristics for direct compression like compaction behavior, stability of the compound, flowability, Mg-stearate sensitivity and disintegration as well as dissolution. Purpose of the study is to compare the powder and tablet characteristics of the compound vs. the physical blend.

MATERIALS & METHODS

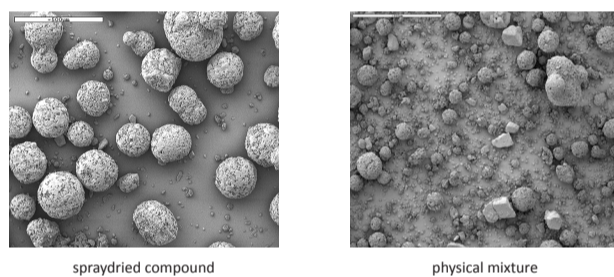
Spray dried lactose (trade FlowLac®, Meggle), spray dried compound of lactose and starch (trade name StarLac®, Meggle & Roquette) and native white corn starch (Roquette), DC-ascorbic acid (Roche C 90) and fine powdered ascorbic acid (Merck KGaA, ordering item 1.50078), Mg-stearate (Merck KGaA, ordering item 1.00663) and 2,4-dichlorophenolindophenol (Merck KGaA). Spray drying equipment was a top bottom spray dryer (Industrie Werke Karlsruhe, Germany) water evaporation capacity approx. 500 kg/h. Tablets were compressed on a rotary press (Kilian type S 100/22 AU-B, speed approx. 20.000 tablets/h instrumented, punch 10 mm, flat faceted tablet weight 320 mg) or on a single punch press (Korsch EK 0, punch 8 mm, flat faceted, tablet weight 240 mg).

ANALYTICAL EQUIPMENT:

- SEM-pictures - Jeol JSM 5410LV,
- Tablet hardness - Erweka, type TBH 30; disintegration - Erweka, type ZT 3-2; dissolution - Pharmatest PTW; flowability/angle of repose - Pfrengle equipment according ISO 4324; Testing of the parameters according to standard pharmacopoeial methods.

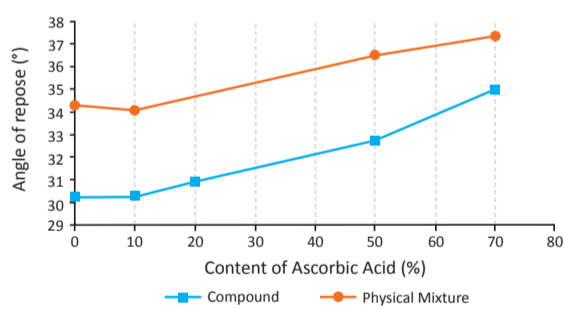
RESULTS & DISCUSSION

Figure 1. SEM compound vs. physical mixture.



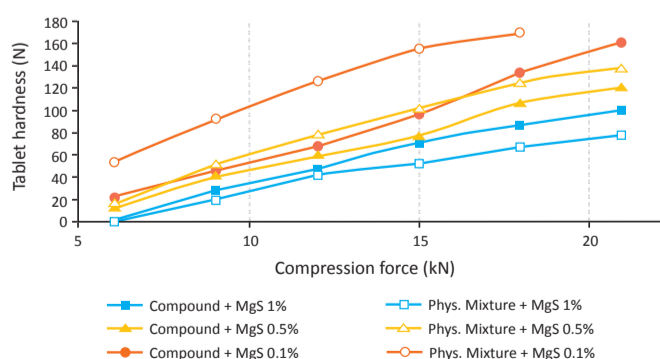
SEM pictures (fig. 1) demonstrate that the co-processed mixture of 85% lactose and 15% white corn starch is a so called "one body compound" with spherical granules.

Figure 2. Angle of repose of the compound vs. the physical mixture depending on the Ascorbic Acid concentration.



Due to the spherical shape of the granules the compound showed significant improved flow properties compared to the physical blend. The angle of repose was 30° of the compound and 34° of the physical blend. Flowability of formulations containing ascorbic acid (AA) was also improved, i.e. the angle of repose was 31° - 34° (compound) vs. 34° - 38° (physical blend), depending on the concentration of AA (fig. 2).

Figure 3. Compression profile of the compound vs. the physical mixture.



Less segregation was observed in all formulations with the compound and the standard deviation of ascorbic acid in the tablets was 0.31% compared to 0.9%. Minimum lubricant requirement for all Lactose-Starch based combinations were 0.1%. At different compression forces (6-21 kN) a tablet hardness of up to 155 N (compound) and up to 175 N (physical blend) was obtained, depending also on the lubricant concentration (fig. 3).

Figure 4. Disintegration profile of the compound vs. the physical mixture.

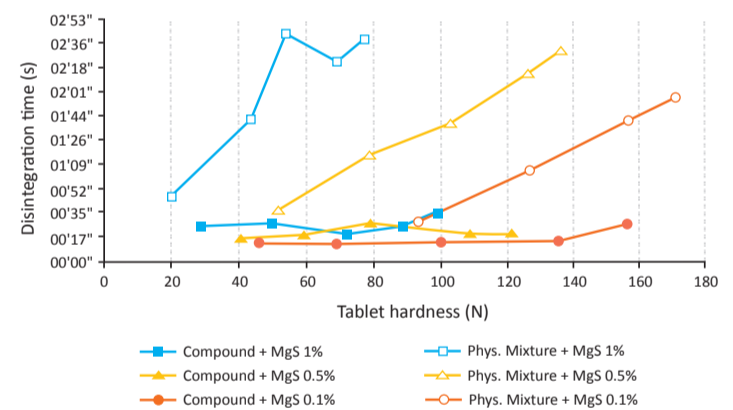
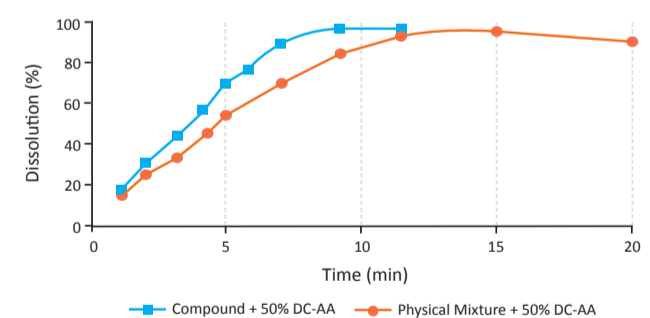


Figure 5. Comparison of the dissolution of Ascorbic Acid from a formulation containing the compound vs. the physical mixture.



At comparable compression force and low concentration of lubricant the physical blend formulations resulted in higher tablet hardness. However, the tablet hardness of the physical blend formulations were more affected by the lubricant concentration. Disintegration time of tablets (placebo) was 13 - 35 sec for the compound and 25 - 157 sec for the physical blend (fig. 4). Consequently, the dissolution of AA was 35% faster for a formulation with the compound (fig. 5).

CONCLUSION

The powder and tablet characteristics of the lactose-starch compound StarLac® vs. the physical blend show some considerable differences. The compound as well as the formulations with an active showed better flowability and lower tendency of de-mixing. Most important, there is practically no influence of the Mg-stearate concentration and over a wide range of the tablet hardness on the disintegration or dissolution, which is faster compared to the physical mixture.

REFERENCE

1. P. Lefevre et al. (2001): Comparison of Tableting Properties of a DC Lactose/Starch Compound Versus a Physical Mixture of DC Lactose and DC Starch, AAPS, Denver, USA.
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3. C. Dolge et al. (1999) Comparison of Co-Spray Dried Calcium Carbonate/Carbohydrates Mixtures vs. Mechanical Mixtures, AAPS, New Orleans, USA.