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How relevant is ribbon homogeneity in roll compaction/dry granulation?

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INTRODUCTION

The most critical characteristics of dry granules obtained by roll compaction/dry granulation (RCDG) are granule size distribution and the granule's solid fraction [1]. Both of these characteristics predominantly depend on the ribbon's solid fraction, making it the key quality attribute in RCDG. It is described multiple times in literature that the solid fraction is not distributed evenly across the ribbon width. The detailed distribution patterns depend on the sealing systems used during manufacturing [2]. The cheek plate sealing system leads to high solid fractions in the centre and lower ones near the edges of the ribbon. When using rim rolls however, the solid fraction is distributed more homogeneously and the profile across the ribbon width is inverted. It is generally assumed that a higher homogeneity within ribbons (and by that in granules) positively affects the tablet characteristics. However, no detailed studies that critically test this hypothesis have been published to date.

MATERIALS AND METHODS

Microcrystalline cellulose (MCC) (Vivapur 102, JRS Pharma, D) and dibasic calcium phosphate anhydrate (DCPA) (Di-CaFos A150, Budenheim, D) were roll compacted using a Gerteis Minipactor (Gerteis, CH) at five specific compaction forces (2 - 10 kN/cm for MCC and 6 – 18 kN/cm for DCPA). The gap was automatically controlled at 2 mm and the roll speed set to 3 rpm. All experiments were conducted once using cheek plates (CP) and once using rim rolls (RR). Samples of ribbons were collected and analyzed regarding their overall solid fraction using powder pycnometry (GeoPyc, Micromeritics, USA). The ribbons were milled using an oscillating sieve with a mesh size of 1 mm, collected, their particle size distribution determined using laser diffraction (Master Sizer 3000, Malvern, UK), and compressed to concave tablets of 7 mm diameter on a pilot scale rotary tablet press (102i, Fette Compacting, D) at a speed of 100 000 tablets/h and compression pressures of 120 MPa (MCC) or 250 MPa (DCPA), respectively. The tablets were analyzed regarding their mass, outer geometry, and crushing strength (SmartTest 50, Dr. Schleuniger, CH). The compression of sieve fractions was performed on a tableting instrument (Styl'One Evolution, Medelpharm, F) using 10 mm flat-faced punches.

RESULTS AND DISCUSSION

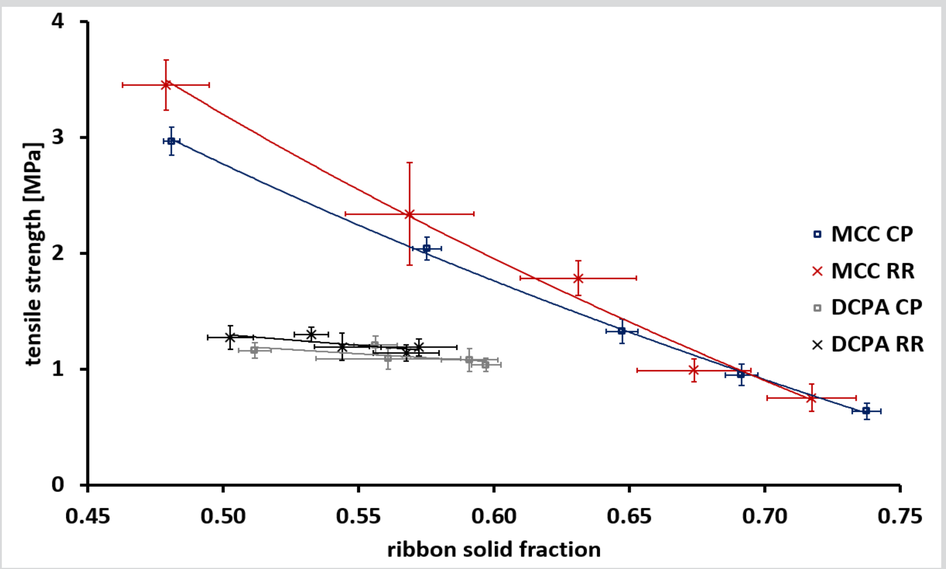

fig 1: tensile strength (σ) of tablets from dry granules over average solid fraction of corresponding ribbons

Figure 1 shows the tensile strength of tablets over the average solid fraction of the corresponding ribbons. In case of MCC, the tensile strength was reduced with increasing solid fraction of ribbons for both sealing systems. This loss in tabletability is well described in literature [3]. When comparing the profiles of both sealing systems, it can be seen that at similar average solid fractions, the tablets resulting from the less homogeneous cheek plate ribbons led to stronger tablets. The discrepancy was more pronounced for low ribbon solid fractions and was not found at higher ones. This is surprising, because in the more homogeneous rim rolls ribbons, no highly densified regions, which are expected to predominantly cause the loss of tabletability, are present. For DCPA, only a slight decrease in tabletability was observed and no difference between the two sealing systems found.

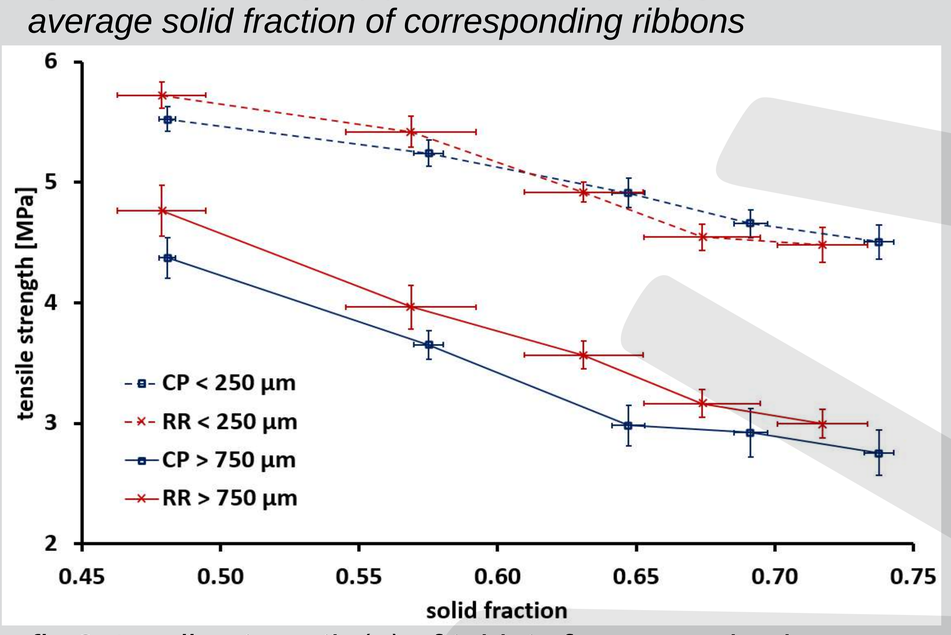

fig 2: tensile strength (σ) of tablets from granule sieve fractions over average solid fraction of ribbons (only MCC)

As ribbons are milled, the large granules originate from the dense regions of the ribbon. Ribbons of same overall density but different homogeneity will subsequently be processed to granules of different density when classified by size. The more porous granules from the homogeneous rim roll ribbons show less work hardening. This can be seen in figure 2 as tableting these granules (> 710 µm) led to stronger tablets compared to the similarly sized granules produced using cheek plates. For tablets produced from fines (< 250 µm), no differences could be detected between the two sealing systems.

The tableting behavior of the smaller granules combined with the higher fractions of fines that occured when using cheek plates seem to (over-) compensate the reduced tabletability of larger granules and thus cause that dry granules from more inhomogeneous ribbons led to stronger tablets.

The uniformity of mass is an equally important characteristic as the tensile strength. Hence the tablets from homogeneous and inhomogeneous ribbons were also compared in this regard (figure 3). At comparable ribbon solid fractions, no difference in mass variability between tablets originating from homogeneous and inhomogeneous ribbons was found with statistical significance. This was the case for MCC as well as for DCPA.

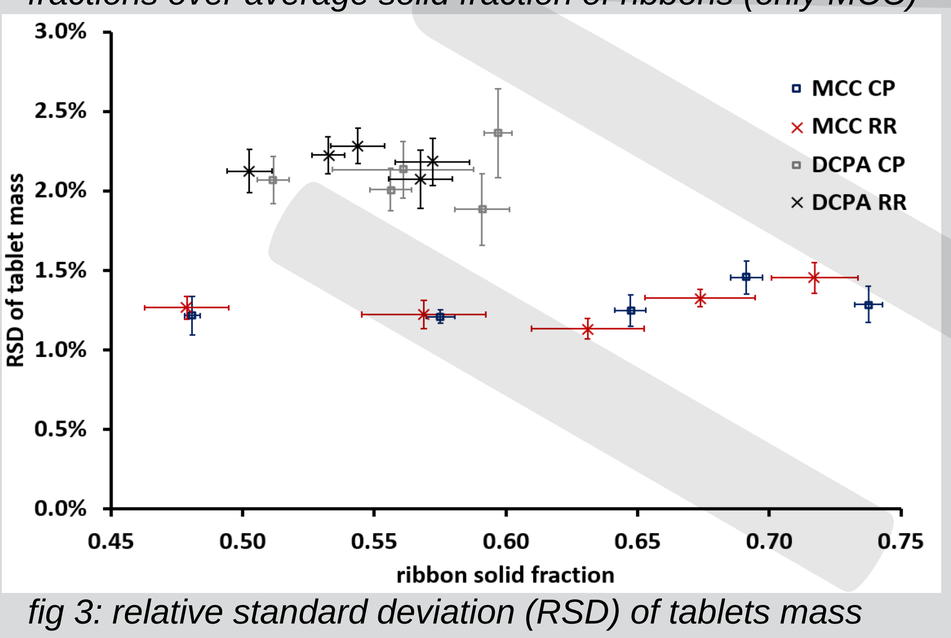

fig 3: relative standard deviation (RSD) of tablets mass over solid fraction of corresponding ribbons

CONCLUSION

The results from this study indicate that the relevance of ribbon homogeneity might commonly be overestimated. Surprisingly, it was found that dry granules made from ribbons of different homogeneity led to tablets of comparable strength and uniformity of mass. For MCC, only a small effect of ribbon homogeneity on the strength of resulting tablets was detected at low solid fractions. When using DCPA, no influence was found. Tablet compression of sieve fractions proved that this is due to compensating effects of highly densified and more porous regions within the ribbon. Regarding the tablet mass variability, no difference between homogeneous and inhomogeneous ribbons could be detected with statistical significance. It has to be considered that such negative effects might become more pronounced at larger batch sizes. On the studied scale however, homogeneous ribbons did not perform better than inhomogeneous ones.

[1] Nordström J, Alderborn G, The granule porosity controls the loss if compactability for both dry- and wet-processed cellulose granules J. Pharm. Sci., 2015; 104(6)
[2] Wiedey R, Kleinebudde P, Infrared thermography – A new approach for in-line density measurement of ribbons produced from roll compaction. Powder Technol., (in press)
[3] Mosig J, Kleinebudde P, Critical evaluation of root causes of the reduced compactability after roll compaction/dry granulation, J. Pharm. Sci., 2015; 104(3)

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