Particle size distribution in the product stream after roll compaction/dry granulation

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Introduction

Roll compaction/dry granulation (RCDG) is a commonly used process in pharmaceutical manufacturing to produce granules from a powder mixture. RCDG is used in continuous manufacturing as product is continuously fed, processed and discharged [1].

Previous work has shown that the granule size distribution (GSD) is inhomogeneous in the product stream and in-line determination of the product GSD is challenging [2]. Until now, no further investigations were made to characterize the GSD in the product stream. An assumption is that larger sized granules fall more freely than smaller particles because of their higher mass. This work summarizes investigations to characterize the RCDG-product stream in detail. The aim of this work is to enhance knowledge to be able to develop an on-line method for RCDG-GSD determination.

Materials and Methods

Dicalcium phosphate anhydrous (Di-Cafos® A150, Budenheim, D) was used as excipient for all experiments. It was compacted and granulated using a BRC 25 (L.B. Bohle GmbH, D) and a Mini-Pactor (Gerteis Maschinen + Processengineering AG, CH) at 12 kN/cm specific compaction force. The two roll compactors used in this work differ in arrangement of the compaction rolls and used granulation unit. The BRC 25 was equipped with a 360° rotating turbo sieve (BTS, L.B. Bohle GmbH, D) while the Mini-Pactor utilizes an oscillating sieve (Figure 1 and 2).

At the compactor outlet, the product stream was separated into five sections using a sample splitter (Figure 3). The GSD was determined using laser diffraction (Mastersizer 3000, Malvern Instruments, UK).

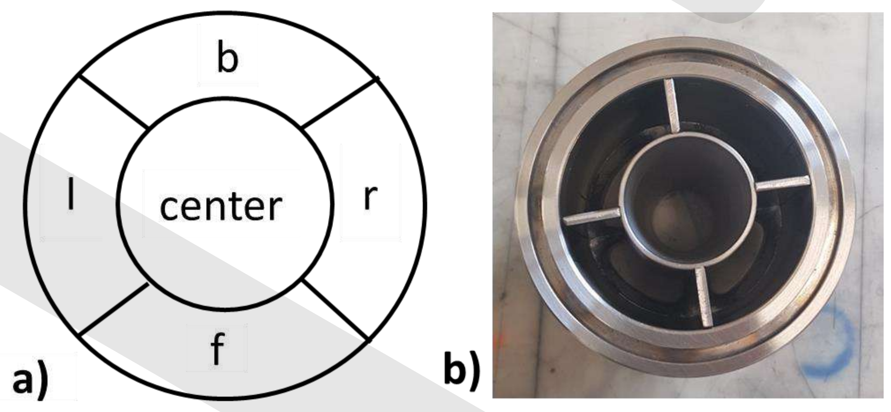

Figure 3. a) Schematic layout of the five parted sample splitter. Naming of the sections: center, left (l), back (b), right (r), and front (f). b) Photograph of the sample splitter

Results

Figure 1. BRC25 granulation unit

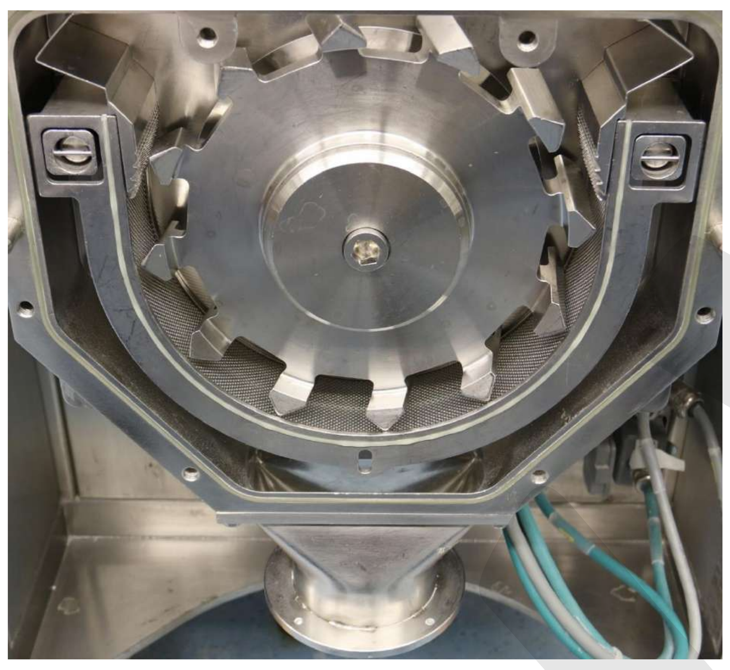

Figure 2. Mini-Pactor granulation unit

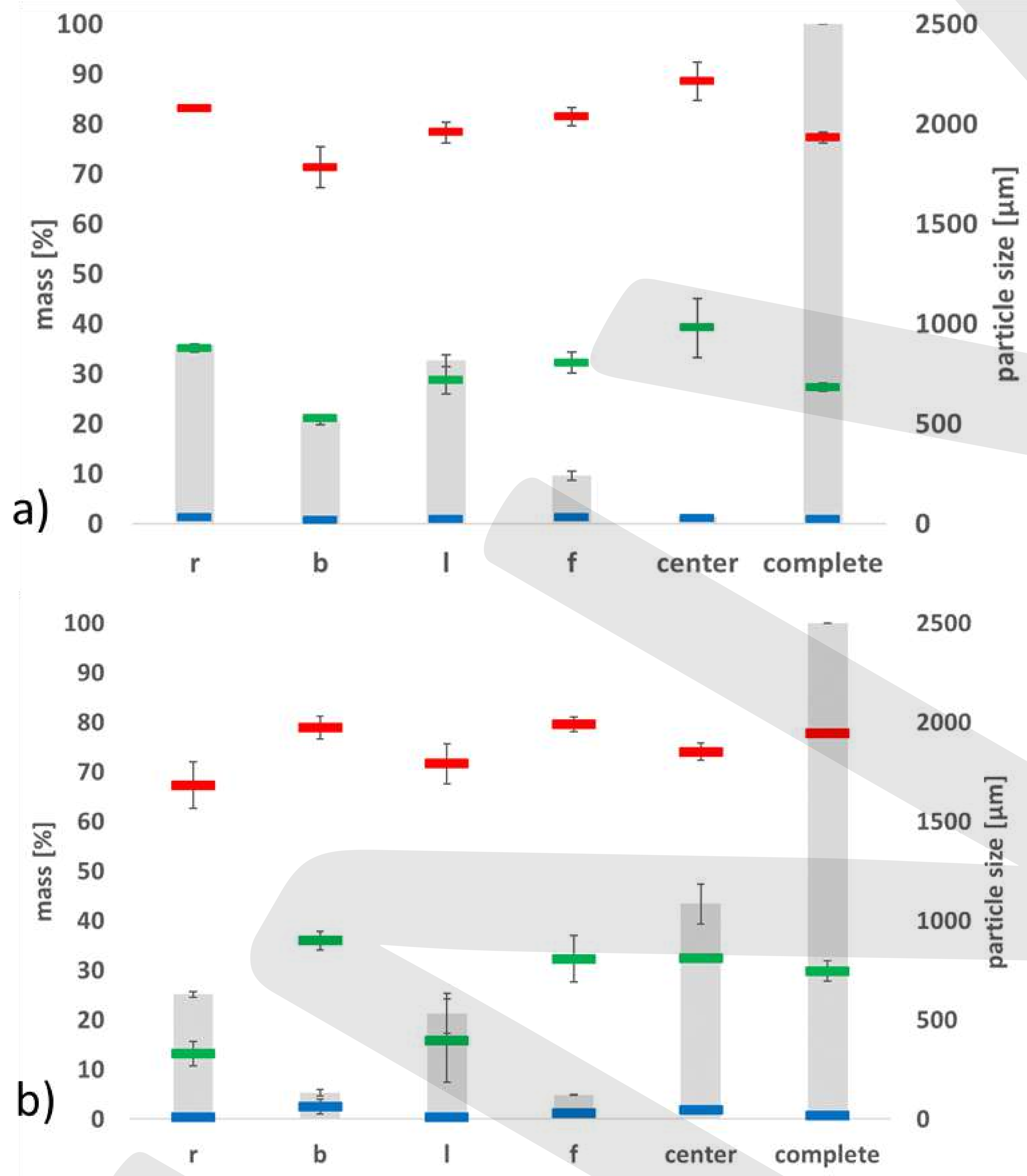

Figure 4. Granules compacted using a) BRC 25 b) Mini-Pactor. the mass percentages of the different fractions on the primary y-axis. The GSD key parameters D90 (red), D50 (green) and D10 (blue) are shown at the second y-axis. n = 3 x 1 (BRC 25, center), n = 3 x 3 (all other fractions and complete) ; mean ± sd

Discussion

The product mass is not distributed evenly throughout the product stream. The sieving unit setup of the BRC 25 blocks the “center” section of the sample splitter (Figure 1). Hence, little product is collected there. During compaction, the ribbons enter the sieving unit primarily from the “right” side and the impeller is rotating in counter-clockwise direction, leading them to the back first and afterwards to the left and the front. The high mass collected in the right fraction can be caused by high initial breakage of the ribbon. It is surprising that little mass is collected at the back fraction, compared to the front and left (Figure 4a). The stress on the ribbons during a 180° rotation might lead to increased breakage compared to a 90° rotation.

Regarding the results of the GSD, the back and center section differ substantially from the complete sample. The back section consists of particles with smaller particle sizes while the center section is composed of larger granules. As proposed, we can see a cluster of bigger particles falling in the “center” section for this compactor. However, this section is accountable for less than 2% of overall sample mass and shows the highest deviation in granule size (Figure 4a).

The turning points of the Mini-Pactor oscillating sieves are at the edges of the product outlet (Figure 3). At those sides and the “center” section, large amounts of product are collected. As the sieve has no forward or backward motion, only small amounts of granules are collected at the front and back of the product outlet (Figure 4b).

Mini-Pactor results (Figure 4b) were obtained with the sieve oscillating at 50 rpm in both directions. Particles in the front, back and center of the particle stream have larger sizes than the complete sample while the majority (>50%) of the sample is falling at the sides of the particle stream and is showing a smaller particle size. The smaller particle sizes at the sides can be explained, as the oscillating sieve changes direction and high stress is applied on granules there.

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CONCLUSION

The particle stream of RCDG is heterogeneous with regard to mass and particle size distribution. The sieving system used in the roll compactor seems to be the primary source of these differences. Further investigations are needed to develop a method to sample RCDG product for on-line GSD determination.

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