Examination of Consistency During Roller Compaction Scale-Up

W1130-04-24

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PURPOSE

Roller compaction (RC) is a critical process in pharmaceutical manufacturing, with multiple equipment vendors offering different processing technologies. Achieving consistent results across different equipment during lab-scale or pilot-scale trials is challenging but essential for maintaining product quality and reliability throughout the drug development cycle. This study aims to understand, assess, and compare two different RC approaches and their impact on the Critical Quality Attributes (CQAs) of granules and tablets.

OBJECTIVES

The main goals were to: a) Integrate a lab-scale roller compactor from a different manufacturer / mechanism of operation (Freund-Vector) into our routine approach of simulating the Gerteis Mini-Pactor using the Styl'One® EVO and then transferring the product to pilot scale, and b) To understand the underlying mechanisms required to achieve consistent results when changing RC equipment.

METHOD

The study evaluated roller compaction of a placebo blend using the TFC Lab Micro from Freund-Vector and the Styl'One® EVO to simulate the Gerteis Mini-Pactor. CQAs included ribbon solid fraction (SF), granule particle size distribution (PSD), flowability, bulk density, and tablet tensile strength. A factorial Design of Experiments (DoE) approach was used to evaluate the effects of:

a) *Equipment Type* (Freund-Vector vs Styl'One® simulating the Gerteis Mini-Pactor) and
b) *Compaction force level (low, medium, high)*.

The following key parameters were kept identical across both machines: batch size, blending and lubrication time and speed, target SF of the ribbons (0.6, 0.7, and 0.8), roll speed of 2 rpm, and gap width of 3 mm. The milling parameters were also maintained the same by using the Gerteis Hand Mill with a screen size of 1.00 mm. Tabletability was evaluated by compressing tablets over a wide range of compression force of 50-300 MPa. The experimental design scope and placebo formulation is presented in Figure 1.

	Component	Composition (wt%)
Intragranular	MCC (Avicel PH-101)	65.00
	Mannitol (Pearlitol 200 SD)	30.00
	Croscarmellose sodium (Ac-Di-Sol)	3.00
	Magnesium Stearate	0.75
Extragranular	Kolliphor SLS Fine	0.50
	Magnesium Stearate	0.75
	Total	100.00

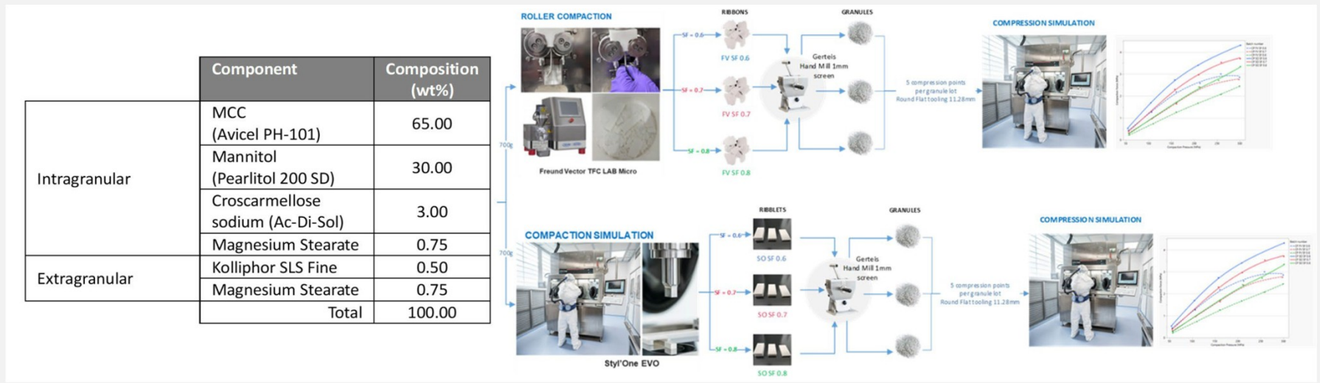


Figure 1. Design of the Study

RESULTS

Final Blend

The final blends were fully characterized, and the results are presented in Figure 2. When examining each RC approach individually, results follow expected trends, where increasing ribbon SF leads to increasing density and fewer fines. However, when comparing the two RC equipment, despite targeting the same SF, the final blends showed different properties. The final blend produced by the Styl'One® simulating the Gerteis Mini-Pactor consistently showed 15% lower bulk density and 20% more fines (at 0.6 & 0.7 SF) than the blend produced by the Freund-Vector.

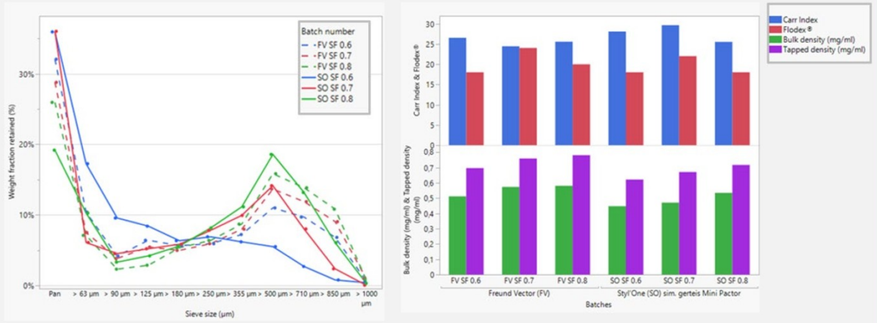


Figure 2. Final blend physical properties

Compression

Individually, each RC approach showed consistent results, with a loss in tabletability as the SF of the ribbons increased. However, the tabletability profiles do not overlay when comparing the two RC equipment (Figure 3), which is not surprising given the different physical properties of the final blends. Tablets produced from Styl'One® simulating the Gerteis Mini-Pactor had 25% more tabletability than Freund-Vector vs Styl'One® simulating the Gerteis Mini- Pactor.

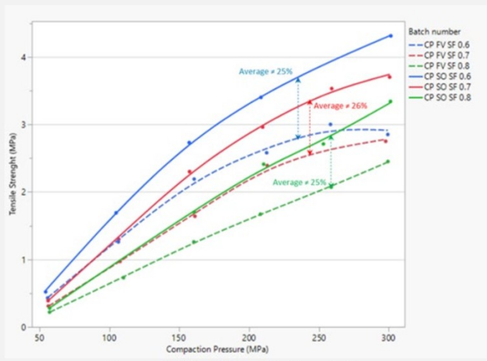


Figure 3. Final blend tabletability

DISCUSSION

Matching ribbon solid fraction alone was not sufficient to achieve equivalent granule properties and tabletability across the evaluated RC platforms. Key factors that may contribute to these differences include:

a) *Roller Design and Geometry* - Differences in roller surfaces, diameters, lengths, and shapes affect the compression zone, ribbon formation, and ribbon density uniformity.

b) *Roller Speed and Dwell Time* - Even if the SF is matched, the time under pressure differs with roller diameter, influencing ribbon compaction behavior and impacting material fragmentation or densification during granulation.

c) *Force Control System & Feed System* - The Gerteis Mini-Pactor uses a sophisticated gap control mechanism to adjust feeders that minimize variability in ribbon properties, while the Freund Vector uses a fixed feeder speed. Variability in pre-blend flowability impact the amount of powder fed into the rollers, affecting ribbon density and granule properties.

d) *Post-Compaction Milling* - The hand mill process may also add some variability, as this is a manual process without control of milling speed/angle, and may affect how the ribbons break apart during milling.

CONCLUSIONS

Scaling the roller compaction process from one equipment to another presents several challenges. Matching ribbon solid fraction alone was insufficient to achieve equivalent downstream granule and tablet performance across the evaluated RC platforms. Equipment-specific compaction and feeding behavior, as well as post-compaction milling, may contribute to these differences. Additional work is needed to establish equipment-specific correlations and transfer strategies.