StarTab®
Directly Compressible Starch

Colorcon®

Flow Properties, Morphology and Compression Characteristics of a Directly Compressible Starch Before and After Feeding through Continuous Feeder

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Introduction

Continuous manufacturing is becoming the preferred manufacturing process in many pharmaceutical companies as it may lead to reduced development time, potential production cost saving while improving product quality. A continuous manufacturing line uses loss in weight feeder (LIW) or volumetric feeder to continuously feed the ingredients to the in-line blender, or the tablet press. LIW feeders are typically preferred over volumetric feeder to achieve a stable mass flow rate and accuracy of dispensing the raw materials.[1] Understanding the flowability and cohesivity of raw materials are essential to achieve consistent feeding rate and content uniformity of the tablets. As material passes through the continuous feeder, constant shear forces between the feeder wall and screw can potentially lead to particle attrition, density changes and generation of electrostatic charge. These undesired changes in raw material properties may inadvertently affect the consistency and compression characteristic of the tablets.

In this study, powder flow and compression characteristics of StarTab®, directly compressible starch were analyzed before and after feeding through the continuous feeder. StarTab was subjected to advanced powder characterization using dynamic tap density measurement, electrostatic charge buildup and rotating drum measurement to assess the changes in its cohesiveness and flow properties. StarTab was also characterized for changes in particle size distribution and compression characteristics before and after feeding through the continuous feeder.

Methods

A feeding study, using StarTab, was carried out using a twin-screw loss-in-weight feeder (GEA Compact Feeder, GEA Process Engineering, Belgium) at the feed rate of 3 kg/hr and 7 kg/hr using a fine screw feeder (Figure 1). A gain-in-weight catch scale (Mettler Toledo LLC, USA) was used to collect data at every second, with an average of 5 seconds calculated. Relative standard deviation (RSD) and relative difference from the mean (RDM) were calculated to evaluate feeder performance. Use of a slower feed rate, 3 kg/hr, subjected StarTab to higher shear forces in the continuous feeder. StarTab (pre and post feeder study at 3 kg/hr) was evaluated for dynamic bulk and tapped density measurement (GranuPack™, GranuTools, Belgium), the ability of the powder to create electrostatic charges during a flow (GranuCharge™, GranuTools, Belgium), flowing properties and cohesiveness (GranuDrum™, GranuTools, Belgium), and particle size distribution (Malvern Instruments Ltd., UK). Pre and post-feeder study materials were separately lubricated with 0.25% w/w magnesium stearate (previously screened through mesh #60) and compressed on a rotary tablet press (Piccola B/D 370 press, USA) fitted with 10 mm round flat-faced B-tooling at 50 rpm turret speed, tablet target weight of 400 mg using compression forces of 10-30 kN. All tablets were evaluated for tablet weight uniformity, hardness, and thickness (Multicheck V, Erweka, Germany), friability (Varian, USA), and disintegration in 900 mL of DI water at 37°C (Erweka ZT 224, Erweka, Germany).

Results

Figure 1: Experimental Set-up using GEA Compact LIW Feeder

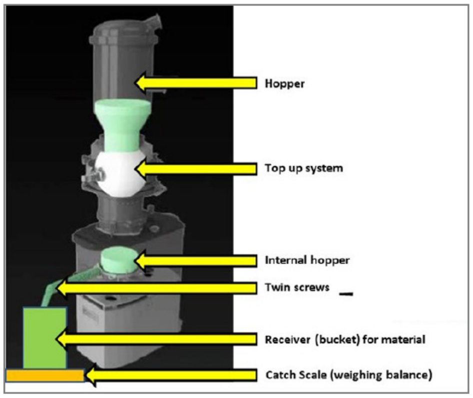


Figure 2a: GranuPack, High Resolution Tapped Density Analyzer

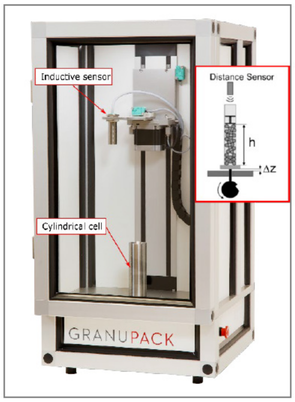


Figure 2b: GranuCharge, Granular Material Electric Charge Analyzer

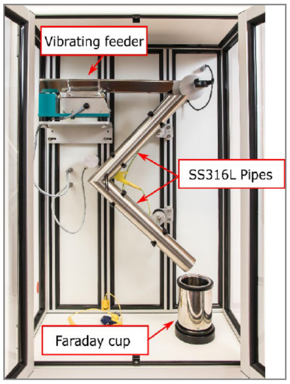
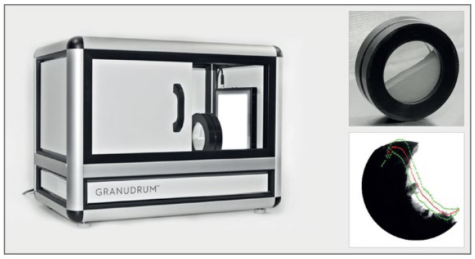


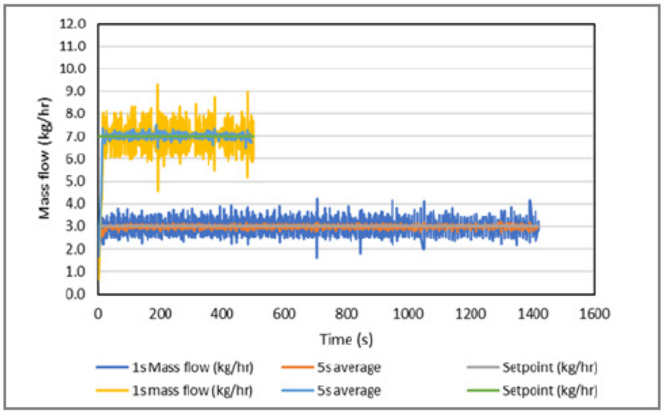
Figure 2c: GranuDrum, Granular Material Flow Analyzer



Feed Rate Study

Figure 3 displays the mass flow rate profiles of StarTab at 3 and 7 kg/hr feed rate. A low value of standard deviation (SD <5%) for both feed rates suggests StarTab has a consistent flow. Samples from a slower feed rate i.e. 3 kg/h with longer residence times (experiencing higher stresses) were chosen for pre- and post-feeding powder evaluation.

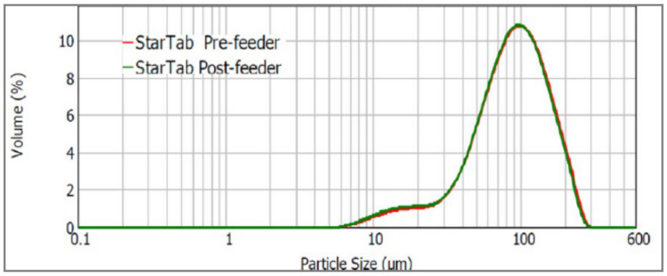
Figure 3: Mass Flow Rate of StarTab for Feeder Standard Run (3 kg/h and 7 kg/h) Using Fine Screw



Particle Size Evaluation

The particle size distribution of StarTab before and after feeding study is shown in Figure 4. The particle size characterization showed no difference before and after the feeding study.

Figure 4: Particle Size Comparison of Pre and Post Fed StarTab



Dynamic Bulk and Tapped Density Measurement

The dynamic tap density measurement provided insight into the rate of consolidation and time to achieve the optimal consolidated state. Both pre- and post-feed StarTab showed a low Hausner ratio denoting good packing behavior. Moreover, the dynamic packing parameter (n1/2), which measures the number of taps to achieve half of the final packed density, showed similar values for pre- and post-fed StarTab, indicating no major changes in packing kinematic (Table 1).

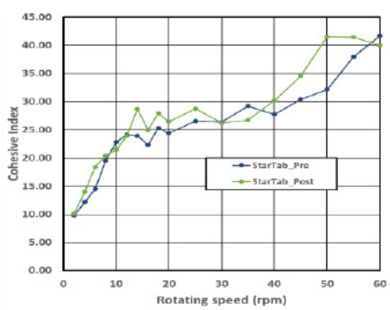
Table 1: Dynamic Bulk and Tapped Density Measurement

Sample Name	Initial Bulk Density, ρ(0) (g/ml)	Final Packed Density, ρ(n) (g/ml)	n½ (secs)	Hausner's Ratio
Post-fed StarTab	0.617	0.708	9.9	1.15
Pre-fed StarTab	0.609	0.698	13.9	1.15

Table 2: Electrostatic Charge Evaluation

Sample Name	Initial Charge Density, q0 (nC/g)	Final Charge Density, qf (nC/g)	Charge Density Difference, Δq (nC/g)	% Charge lost
Pre-fed StarTab	-0.33	-1.21	-0.88	1.33
Post-fed StarTab	-0.43	-1.30	-0.86	1.07

Figure 5: Pre- and Post-fed StarTab Cohesivity Evaluation using GranuDrum



Evaluation of Compression Characteristics

Tablets compressed pre- and post-fed StarTab showed similar hardness, disintegration, and compression characteristics (Figures 6a, 6b, 6c).

Figure 6a: Pre- and Post-fed StarTab Compression Profile (Hardness Vs. Compression Force)

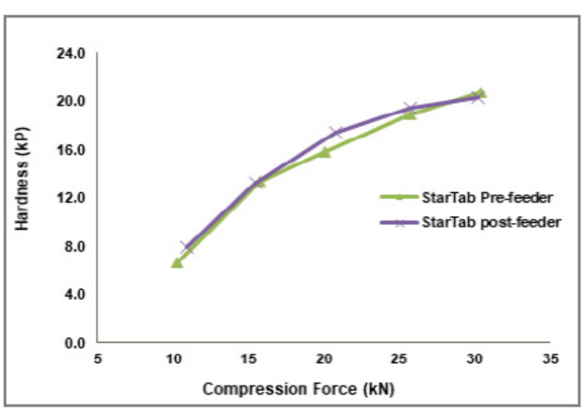


Figure 6b: Pre- and Post-fed StarTab Compression Profile (Friability Vs. Compression Force)

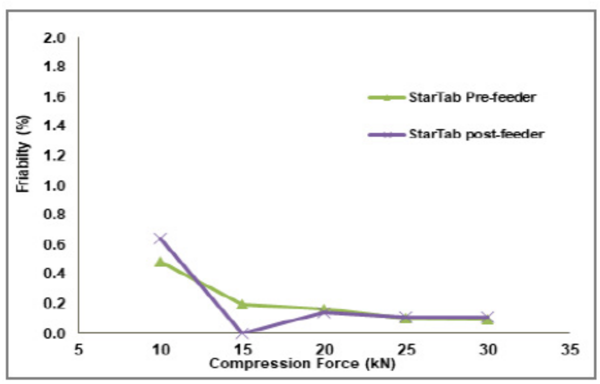
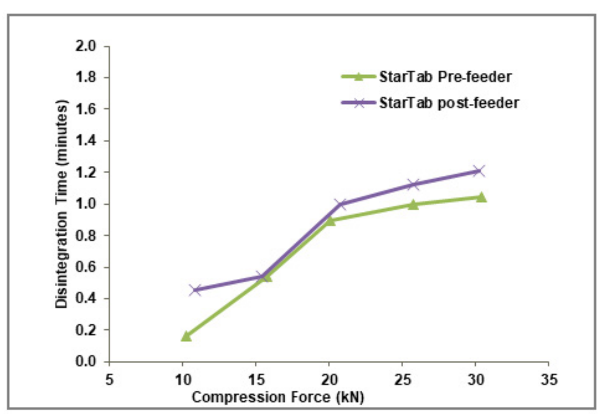


Figure 6c: Pre- and Post-fed StarTab Compression Profile (Disintegration Time vs. Compression Force)



Conclusions

- StarTab, directly compressible starch, demonstrated excellent flow behavior and low variability when fed through a LIW continuous feeder at different feed rates.
- No differences in particle size or morphology were observed for pre- and post-fed StarTab.
- Further, advanced characterization of compaction behavior, assessment of cohesivity index and electrostatic charges of pre- and post-fed StarTab also confirmed no changes in the powder properties.
- This evaluation highlights the suitability of StarTab as a direct compression excipient in continuous manufacturing.

Reference

1. M. Hopkins, "LOSS in weight feeder systems," Meas. Control, vol. 39, no. 8, pp. 237–240, 2006.

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