Characterization of a new multifunctional disintegrant for continuous manufacturing

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PURPOSE

Continuous manufacturing (CM) has gained interest in the pharmaceutical industry because of its economic and technical superiority to traditional batch manufacturing. One challenge of CM is the precise and reliable powder feeding requirement to meet critical quality attributes (CQAs) of pharmaceutical products. Thus loss-in-weight feeders (LWFs), which gravimetrically control powder feed rate, are typically employed, and feeder performance testing using LWFs can confirm CM feeding process robustness.

OBJECTIVE(S)

In this study, the powder flow and self-lubricating properties of a new multifunctional co-processed disintegrant was evaluated by the use of an LWF, and potential performance benefits were identified. This multifunctional disintegrant was found to exhibit superior powder flow and self-lubricating properties with the benefits of reducing processing steps, simplifying manufacturing, and enhancing manufacturing efficiency and product performance in Continuous manufacturing.

METHOD(S)

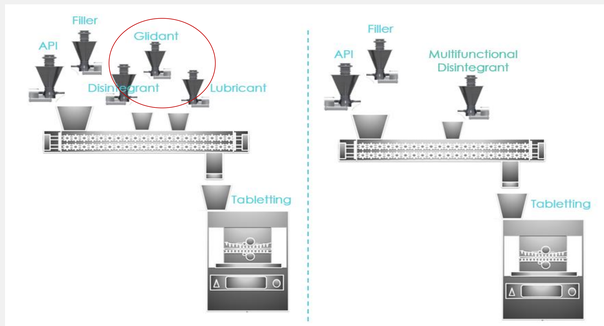
At first, the flowability of materials were evaluated using a Brookfield shear cell and a K-Tron KSU-II LWF using auger twin screws at a nominal feed rate of 12 kg/h. Next, feed studies were conducted using multiple K Tron feeders feeding into Gericke Tubular continuous blender at 7, 10, and 20 kg/h, using APAP as the model drug.

Number feeders	5	5	3
formulation	F1	F2	F3
ingredients		Tablet wt (%)	
APAP DC	75	75	75
MCC PH 102	5	5	5
polyplasdone™ plus			20
Crospovidone blend	Crospovidone -SSF*	Crospovidone-Mg. stearate	
crospovidone XL-10	18.5	18.5	
Fumed Silica	1.0	1.0	
SSF	0.5		
Mg stearate		0.5	
Total	100	100	100

*Sodium stearyl fumarate

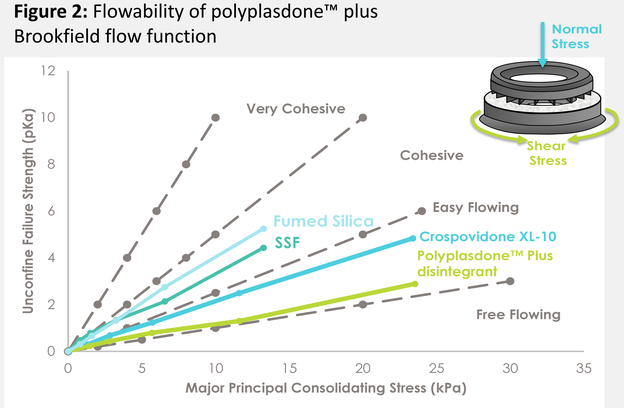
For the formulation with new multifunctional disintegrant three feeders were used, and for those with Crospovidone XL-10 five feeders were used (Figure 1). During each trial, the values of drive command percentage [i.e. motor velocity] (CMD %), net weight (kg), and mass flow rate (kg/h) were recorded. The blends from each feed rate were compressed into 500 mg tablets at 25kN using 11mm round tooling on an Elizabeth-Hata tablet press (38 stations) in production runs at 30 rpm for 15 minutes. Compression forces during the tableting press running cycle, ejection forces at each compression force, and tablet characterization of each blend were determined.

Figure 1: Feeder study design for APAP tablet blends



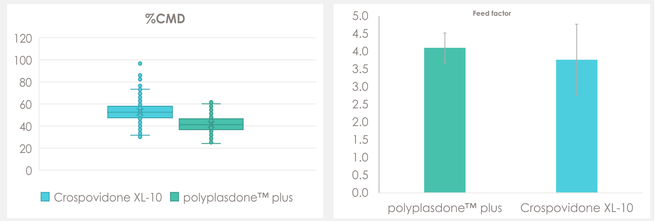
RESULT(S)

Figure 2: Flowability of polyplasdone™ plus Brookfield flow function



Pure material characterization revealed that the new multifunctional disintegrant was more freely flowing than Crospovidone XL-10, silica and sodium stearyl fumarate.

Figure 3: Gravimetric (loss in weight) feeder profile at 12 kg/h feed rate

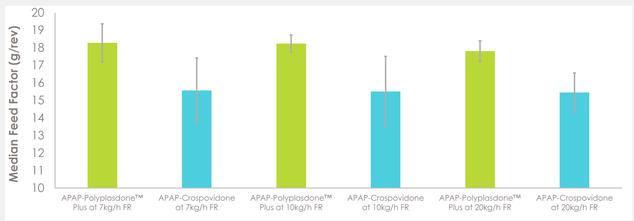


Drive Command % (CMD%) is a measure of motor velocity that requires the feeder to maintain the mass flow rate. Feed factor is a measure of the average grams of powder delivered per revolution of the feeder screw (g/rev). At a feed rate of 12 kg/h, the new Polyplasdone Plus demonstrated lower average CMD% and higher feed factor than Crospovidone XL-10 . Significant deviations in feed rate can cause quality issues in downstream product.

Polyplasdone™ Plus achieved:-

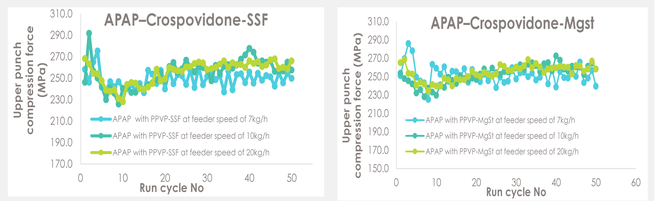
- 21% decrease CMD %
- 9% increase Feed Factor
- RSD decreased by 32%
- 29% increase Flow function

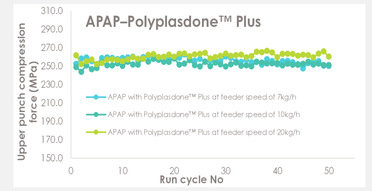
Figure 4: loss-in-weight feeding profile across 7, 10 and 20 kg/hr



The particles of the co-processed excipient were well coated with glidant and lubricant, and thus were less cohesive. For the feeding study, at ribbon speeds of 7, 10 and 20kg/h, the APAP formulation with new multifunctional disintegrant demonstrated a higher feed factor, lower average CMD%, and smaller RSD% for mass flow rate than the formulation with Crospovidone XL-10 blend.

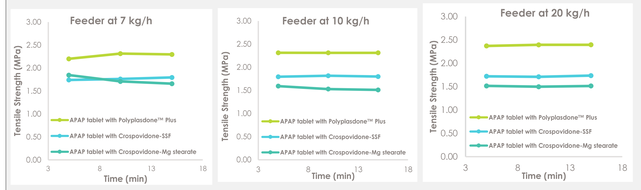
Figure 5: Tablet press running cycle during compression





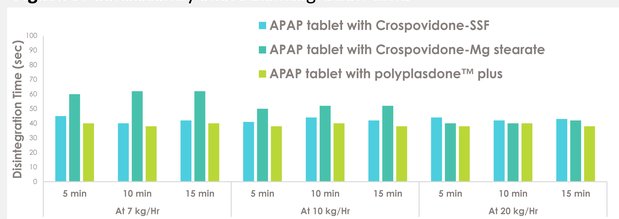
During tableting, the APAP formulation with the new multifunctional disintegrant showed less variation in compression force during the tableting cycle, less weight variation

Figure 6: Improved APAP Tablet strength across a wide feeding rate



Formulation with **polyplasdone™ plus multifunctional disintegrant** yields **much harder tablets** at various blend feeder speeds.

Figure 7: Consistently short disintegration time



APAP tablets with **polyplasdone™ plus multifunctional disintegrant** show **similar disintegration times** to tablets with crospovidone XL-10

CONCLUSION(S)

The new multifunctional direct compression superdisintegrant, co-processed with a glidant and lubricant possesses enhanced flow properties and provides better tableting performance with lower ejection force during continuous and batch processing. Benefits of all-in-one multifunctional disintegrant a high Feed Factor and low RSD in Loss-in-weight feeding (LWF), while enabling flexibility in choice of fillers and binders. It is designed to be economical to use by reducing production times simplifying both continuous and batch manufacturing.

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