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In-line Particle Size Detection in Roll Compaction

Garrett Alfred (Freund-Vector), Timothy J. Smith (Freund-Vector)

garrett.alfred@freund-vector.com

PURPOSE

Roll compaction as a form of dry granulation is a commonly used granulation technique to improve flowability, content uniformity and density prior to tablet compression. One of the main factors that determines flowability is particle size distribution. Small particles, or fines, can hinder bulk powder flowability due to their small size, high packing factor, and irregular shapes. Having reliable particle size data to determine the effectiveness of a granulation is key in predicting how the powder will perform on a high speed tablet press. There are several methods used to determine particle size offline, with a ro-tap and sieve stacks being a commonly used one to determine size fractions at different size cutoffs, to imaging methods including shadow capture, laser diffraction, or light scattering. All of these methods in the offline form take time to perform, which could result in a large amount of material being wasted while the samples are processing. Using the Parsum IPP-80 probe (Malvern Panalytical), particle size was able to be read instantaneously on granules coming off of a roll compactor, the TFC-220® (Freund-Vector Corporation). This study aimed to prove that particle sizes could be measured accurately in line with roll compaction when compared to offline measurements and determining the resulting physical characteristics such as flowability and density.

METHOD(S)

Roll compaction dry granulation was done using the roll compactor with flat, serrated rolls, milled with a 2.0mm punched hole mill screen, and the resulting particles were measured by three different analytical methods: In line with the Parsum IPP-80 probe (Malvern Panalytical), offline with the QICPIC particle size analyzer (Sympatec), and a sieve stack consisting of 10, 18, 30, 40, 70, and 270 mesh screens using the Ro-tap to separate the fractions. Two formulations were used in the study, a placebo formulation of 70% lactose monohydrate (Granulac 200), 29.5% microcrystalline cellulose (Emcocel 50M) and 0.5% magnesium stearate, and an active formulation of 85% APAP (semi-fine), 14% hydroxpropylmethylcellulose (HPMC E5), and 1% silicon dioxide (Aerosil 200). Compaction of the placebo raw material was done at the following process parameters: Force = 35kN, roll speed = 5rpm, screw speed = 15rpm, mill speed = 50rpm and deaeration vacuum on. For the active formulation, the parameters were: Force 50kN, roll speed = 5rpm, screw speed = 20rpm, and deaeration vacuum on. Product fell through the Parsum IPP-80 probe and was collected in a stainless-steel vessel for offline measurements in the Ro-tap and QICPIC. Hausner ratio and Carr's index were used to determine flowability characteristics of the granulated material.

RESULT(S)

The results described in this section use three different analytical methods to determine the D10, D50 and D90 particle sizes. The QICPIC (Sympatec) analyzes particle size based on shadow capture using a high speed camera against a light backdrop. The high speed camera is configured to capture each particle passing the lens in multiple orientations, and the images are then used to calculate particle size. The sieve stack takes different size mesh screens stacked on top of each other and are agitated with a ro-tap to force particles to fall through each mesh screen until they are too large to pass through, and then they come to rest. The particles are then weighed on each sieve screen and each fraction is mapped out and particle size can be determined accordingly. The Parsum IPP-80 probe measures particles based on a spatial filtering technique, illuminated by a laser and capturing the shadow of falling particles, then particle size date is captured on an external computer.

There are limitations to each device used to determine particle sizes, which lends itself to variability between measurement methods. However, there is a clear difference between the raw material and granulated material in terms of particle size, and that trend is captured by all three devices clearly showing significant particle size growth from the raw material to the final product.

The roll compaction process was adjusted slightly at the beginning to achieve a hard compact that had some resistance to breaking, while also not becoming too hard to the point that ribbon defects could be observed (i.e. ribbon splitting or ribbon flaking). The mill speed was adjusted to ensure that all of the ribbons were milled at the same rate that they were produced to avoid having buildup in the mill. Once the parameters were set, the process was run for 5 minutes to allow adequate time for process to stabilize and remove any of the bias that can occur early in the process. The roll compaction process was run with the following parameters for the placebo material:

Roll Force = 35kN

Roll Speed = 5rpm

Screw Speed = 15rpm

Mill Speed = 50rpm

The process parameters for the APAP blend were adjusted in the same fashion as the placebo blend to achieve a hard compact that could be milled without breaking the material down into the initial raw material. The parameters used are listed below:

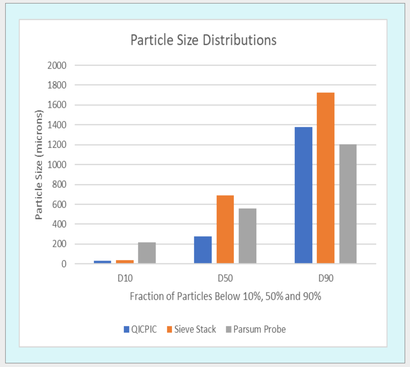
Roll Force = 50kN

Roll Speed = 5rpm

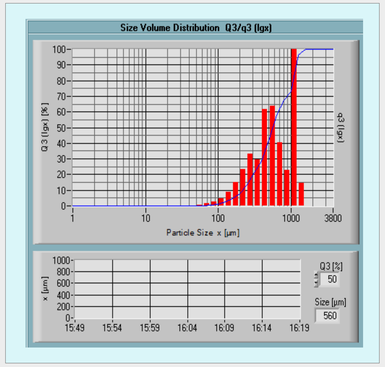
Screw Speed = 20rpm

Mill Speed = 50rpm

Two of the most common metrics for determining flowability of a powder are the Hausner ratio and Carr's Index. A Hausner ratio >1.34 and a Carr's index >28 generally indicate poor flowability. The placebo blend raw material had a Hausner ratio = 1.43 and corresponding Carr's index of 30.03. Conversely, the granulated powder had a Hausner ratio of 1.28 and Carr's index of 22.0, indicating significant improvement in flowability. The Hausner ratio and Carr's index for the APAP formulation, both raw material and final product was also measured. The raw blend had a Hausner ratio = 1.64 and corresponding Carr's index of 39.0 indicating very poor flowability, while the final product had a Hausner ratio = 1.31 and a Carr's index of 23.7.



The figure above shows a comparison of the three particle size analysis methods used in this study. The results are listed as D10, D50 and D90 for each of the samples run.



The figure above shows an example of a particle size graph produced by the Parsum IPP-80 probe using the placebo material blend.

The table below lists the particle size distributions for each particle size analysis method along with Hausner ratios and Carr's indices for each raw material and final product.

Material	Method	D10	D50	D90	Hausner Ratio	Carr's Index
Raw Material Placebo Blend (70% Granulac 200, 29.5% Emcocel 50M, 0.5% Magnesium Stearate)	Parsum Probe	53	87	162	1.43	30.03
	QICPIC	25	64	126		
	Sieve Stack	58	134	211		
Raw Material Active Product (85% Semi-fine APAP, 14% HPMC E5, 1% Aerosil Silicon Dioxide)	Parsum Probe	21	58	123	1.64	39.0
	QICPIC	16	46	83		
	Sieve Stack	40	118	195		
Final Product Placebo Blend (70% Granulac 200, 29.5% Emcocel 50M, 0.5% Magnesium Stearate)	Parsum Probe	219	560	1202	1.28	22.0
	QICPIC	32	280	1378		
	Sieve Stack	37	692	1727		
Final Product Active Product (85% Semi-fine APAP, 14% HPMC E5, 1% Aerosil Silicon Dioxide)	Parsum Probe	52	137	240	1.31	23.7
	QICPIC	28	223	597		
	Sieve Stack	88	530	1665		

CONCLUSION(S)

Using inline particle size analysis allows for increased response time to process upsets that can reduce out of specification material, as well as indicating the influence that changing process parameters will have on the resulting particles. It can also reduce the amount of sampling needing to be done by operators since it captures material as it's falling from the mill into the collection medium. If deviations occur in downstream processing, engineers have another data point to reflect on during root cause analysis of the failure, which can drastically reduce investigation times as well.