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Correlation between excipient material attributes and powder feeder systems

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Purpose

With continuous manufacturing gaining ever so importance in the pharmaceutical industry, use of consistent excipients is vital. Hence, the performance of excipients in different process units such as powder feeders, blenders, continuous granulators etc., needs to be understood.

Raw material feeding is usually one of the first unit operation and variations in this step could affect finished product quality. The variations in a feeder can be caused due to the inconsistency in the material attributes or process inaccuracy.

Loss-in-weight (LIW) gravimetric feeders with a control system (twin screw with varying rpm) are generally used to counter these variations. However, intrinsic material attributes such as particle size distribution (PSD), flow, bulk density, wall friction etc., could impact the accuracy of powder feeding. Hence, to study and understand these correlations, standard Pharmatose® 200M (DFE Pharma, Germany) along with custom made fine and coarse grade of Pharmatose® 200M were analyzed.

Method(s)

Pharmatose® 200M and the custom made fine and coarse grades of Pharmatose® 200M were supplied by DFE Pharma, Germany. Powder feeding systems was manufactured by Gericke AG , Switzerland.

The feeder was operated in two modes, volumetric (disabled mass control system, fixed twin screw speed) with decreasing hopper level (no material refill) and gravimetric mode (using control system, variable twin screw system) with constant material refill (~ 360 s). Two feed rates of 9.5 kg/h and 14 kg/h were studied.

The discharged excipients were collected in a bin placed on a Mettler Toledo weight scale. Weight measurements were taken every 1 s and the data was analyzed by a software developed by Gericke using LabView.

Fig 1: Experimental setup using a gravimetric loss in weight feeder (Gericke).

Result(s)

The excipient material attributes for different grades of Pharmatose® 200M can be seen in Table 1a. A screw speed of 530 rpm was used to feed the excipients in a volumetric mode. Figure 1 shows the feed rate of the three grades at varying hopper levels(The hopper is completely filled at the start and is allowed to drain till empty). As seen in the figure, the feed rate of Pharmatose® 200M was consistently dosed in between the feed rate range of custom made coarse and fine grade of Pharmatose® 200M. Due to the tight particle size distribution and density of Pharmatose® 200M, the variations caused during feeding were reduced. Therefore it shows the need for consistent excipients to maintain constant feeding in a volumetric mode.

In a gravimetric mode, the variations between the three grades of Pharmatose® 200M was reduced due to the control system of the feeder. The feeder in this mode compensates for the variations in the material attributes by adjusting the twin screw rpm and delivers a constant feed rate for all the three grades as can be seen in Figure 2. The relative standard deviation and relative error for all the three grades were low (Table 1b). Pharmatose® 200M showed the least variation, but the differences were small. Similar results were obtained at 9.5 kg/h (results not shown).

Material attributes	Pharmatose 200M®	Custom made coarse	Custom made fine
x50 (µm)	42.6	56.8	32.6
Bulk density (g/ml)	0.59	0.67	0.56
Tapped density (g/ml)	0.92	1.02	0.90
Hausner ratio	1.56	1.53	1.62
Carr's index	36	35	38

Table 1a: Material attributes of Pharmatose® 200M along with custom made grades of coarse and fine Pharmatose® 200M.

Feeder outcome – Gravimetric mode	Pharmatose 200M®	Custom made coarse	Custom made fine
Relative standard deviation	0.91	1.45	1.00
Relative error from set point	0.28	0.49	0.42

Table 1b: Relative standard deviation and relative error for gravimetric feeding at 14 kg/h

Volumetric feeding

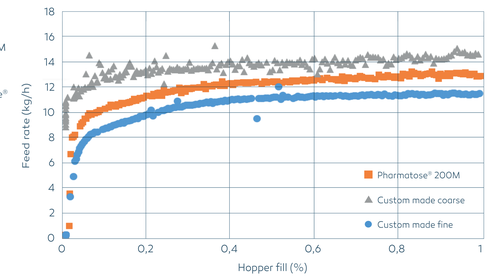

Fig 1: Volumetric feeding of Pharmatose® 200M with custom made grades of fine and coarse Pharmatose® 200M at 530 rpm

Gravimetric feeding

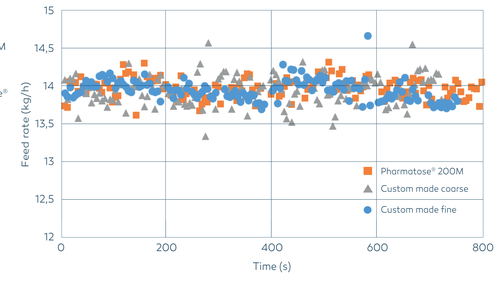

Fig 2: Gravimetric feeding of Pharmatose® 200M with custom made grades of fine and coarse Pharmatose® 200M at 14 kg/h

Conclusion(s)

The need for consistent excipients with a tight particle size and is vital to obtain accurate feeding. Volumetric mode operates in a fixed control system (fixed twin screw rpm) and therefore truly represents the material attributes such as particle size distribution , bulk density, etc. Using a gravimetric loss-in-weight feeder system, constant feeding can be achieved by varying the screw rpm. However, during refiling, the gravimetric system switches to a volumetric mode where material consistency again becomes crucial. Therefore it is important to have consistent excipients and a reliable gravimetric feeding system for processing in continuous manufacturing.

DFE Pharma offers ObD support and consistent pharmaceutical excipients for pharmaceutical development and manufacturing and suitable for Continuous Manufacturing.

Gericke

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