Scale up of a Mesalamine Dry Powder Drug Layering Process Utilizing a Conical Rotor Fluid Bed Insert

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PURPOSE

The purpose of this study was to transfer a dry powder layering process from a lab scale 1.5 KG batch to a production scale 50 KG batch in a conical rotor fluid bed insert.

METHODS

In the lab scale batch, 1 KG of 20-25 mesh sugar/starch beads were loaded into a Freund-Vector Corporation GXR-35 Granurex® conical rotor insert. 666g of micronized Mesalamine powder was loaded into a KTron KT-20 Loss-in-weight powder feeder and was dry layered onto the sugar beads, using a 5% PVP K-30 solution as a binder. Processing parameters were recorded and yield, particle size, and process time was recorded.

In the scale-up batch, 30 kg of 20-25 mesh sugar/starch beads were loaded into a Freund-Vector Corporation GXR-95 Granurex® conical rotor insert. 20 KG of micronized Mesalamine powder was loaded into a KTron KT35 loss-in-weight powder feeder and was dry layered onto the sugar beads, using a 5% PVP K-30 solution. The scale up method used was based on the total time needed to apply the mesalamine powder in the lab scale batch. Feed rates and spray rates were scaled to achieve the same total process time from the small batch to the large batch. Airflow was scaled based on the area increase in the larger unit, and rotor speed was scaled to match the linear velocity of the product from the small batch.

EQUIPMENT

Freund-Vector Corporation GXR-35

Freund-Vector Corporation GXR-95

RESULTS

PROCESS CONDITIONS

Equipment	Airflow (Slit/ Drying)	Air Temperature	Product Temperature	Rotor Speed	Solution Spray Rate	Powder Feed Rate	Starting Batch Size
GXR-35	10/70 CFM	50°C	16.5-20°C	250 RPM	8 g/min	17 g/min	1 KG
GXR-95	130/700 CFM	50°C	18.3-20.3°C	120 RPM	235 g/min	500 g/min	30 KG

PROCESS RESULTS

Equipment	Total Amount Sprayed	Total Powder Added	Powder Addition Time	Powder rate to Spray rate Ratio	Process Efficiency	Finished Batch Size	Process Time
GXR-35	320 g	666 g	40 min	2.125:1	95.2%	1.66 KG	57 min
GXR-95	9,400 g	20,000 g	40 min	2.125:1	98.9%	50 KG	65 min

Using the process time method of scale-up for the powder feed and spray rates resulted in very similar process results on the large-scale batch as the lab-scale batch. Slight adjustments downward in the powder rate were needed in the early stages of the process to maintain high process efficiencies, but the rates were directly scalable later in the process. Slit airflow scaled well based on the area, but rotor speed needed to be slightly increased to maintain the same movement present in the lab-scale batch. Overall, the large-scale batch took 65 minutes with a 98.9% yield, compared to 57 minutes with a 95.2% yield on the lab-scale batch.

CONCLUSIONS

Powder layering processes on a conical rotor system can be effectively scaled to production sized batches utilizing powder addition time as the basis for scale up. Small changes to powder rates, especially early in the process might be necessary to maintain the highest process efficiencies, but those rates recover later in the process to directly scaled values based on the powder addition time.