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Optimization of Controlled Release Granule Properties by Screw Design in a Continuous Granulation System

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PURPOSE

Challenges exist in developing a robust continuous twin screw granulation process. One of the past challenges encountered has been the formation of "noodle-like" granules at the end of the extruder[1]. "Noodle-like" granules have unacceptable characteristics for post processing such as tableting. The objective of this study was to evaluate the performance of different barrel and screw designs of a novel continuous granulation system on the granule properties of a hydroxy-propyl methylcellulose (HMPC) based formulation.

METHODS

Blends of 20% HPMC (Dow Methocel™ K4M), 64% lactose (Foremost™ 316 Fast-Flo®), and 16% microcrystalline cellulose (JRS Pharma, Emcocel® 50M) were prepared in a "V" blender (Keith Machinery Corp. 3 ft^3). The blends were then granulated with water and dried in a continuous granulation system (Granuformer® Gf-215, Freund-Vector). The Granuformer® system consisted of a gravimetric feeder, twin screw extruder, liquid addition pump, conical mill with 2 mm aperture, novel drying tube, and cyclone for separating product from drying air stream. Variations of extruder design with solid and jacketed barrels and four different kneader element placements along the twin screws (see Figure 1) were made to understand the impact of cooling and screw design, respectively, on granule properties. Powder feed rate, liquid addition percentage, extruder screw speed, mill speed, drying air flow and temperature were held constant throughout all trials. Process parameters are shown in Table 1. Resulting granulations were tested for X_{50} particle size (QicPic, Sympatec) and bulk/tap density.

Table 1. Process Parameters

Parameter	Trial A	Trial B	Trial C	Trial D	Trial E	Trial F	Trial G
Barrel Type	Solid	Solid	Solid	Jacketed	Jacketed	Jacketed	Jacketed
Jacket Inlet Temperature (°C)	NA	NA	NA	18	18	18	18
Screw Design	4	1	1	1	2	3	4
Powder Feed Rate (g/min)	75	75	75	75	75	75	75
Extruder Speed (RPM)	150	150	150	150	150	150	150
Target Moisture Addition (%)	24-25	24-25	24-25	24-25	24-25	24-25	24-25
Mill Speed (RPM)	300	300	300	300	300	300	300
Drying Air Flow (SCFM)	150	150	150	150	150	150	150
Drying Air Temperature (°C)	120	120	120	120	120	120	120

METHODS

Figure 1. Screw Design

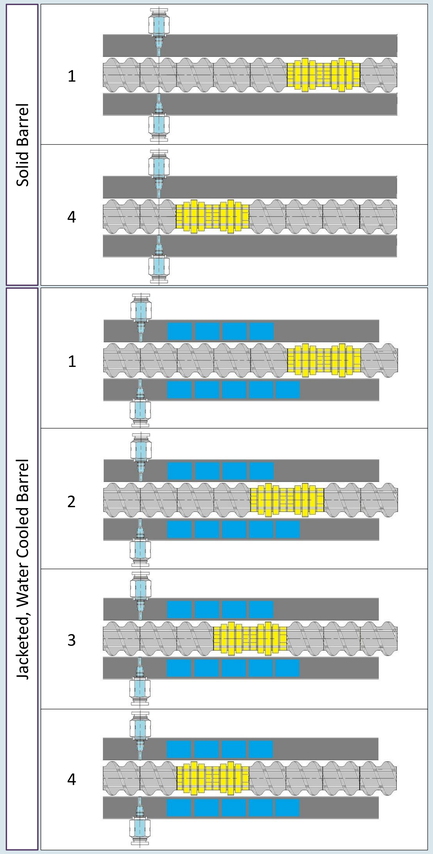
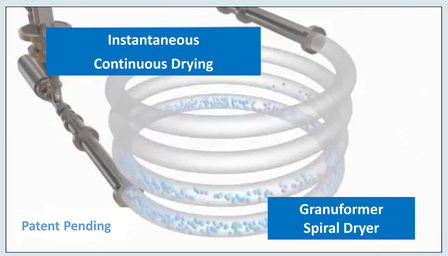


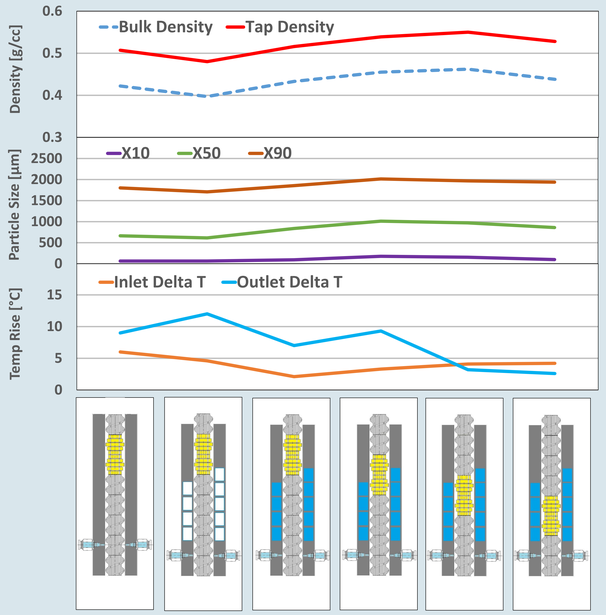
Figure 2. Dryer Design



RESULTS

- "Noodles" not observed
- Solid Barrel Design
  - Aggressive granulation (seizing) when kneaders placed immediately after liquid injection
  - Continuous granulation when kneaders placed just prior to last conveying elements
    - 663 µm X_{50} particle size
    - 0.422 g/cc bulk density; 0.503 g/cc tap density
- Jacketed Barrel Design
  - No cooling –
    - Smaller granules (613 µm on average)
    - Less dense granules (0.023 to 0.027 g/cc decrease)
  - Cooling with 18°C fluid and kneaders in middle positions as compared to closest to or furthest away from liquid injection
    - Larger granules (~ 150 µm on average)
    - Denser granules (increased by average of 0.023 g/cc)

Figure 3. Density, Particle Size, and Temperature Trends



CONCLUSIONS

- Twin screw extruder design used in this study eliminates the problem of "noodling" as previously experienced with HPMC with other extruder designs[1]
- Cooling of the extruder barrel provides greater flexibility in controlling granule characteristics and allows more versatility in screw design
- Increased granule size and density is best achieved by placement of the kneading blocks in the middle section(s) of the screw design
- Additional processing flexibility may be achieved with other kneader element designs (future testing required)

REFERENCE

[1] Thompson, M.R.; O'Donnell, K.P. "Rolling" phenomenon in twin screw granulation with controlled-release excipients. Drug Dev. Ind. Pharm. 2015, 41, 482–492.

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