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Experimental Investigation Linking Granulation Performance with Residence Time and Granulation Liquid Distributions in Twin-Screw Granulation

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Abstract Text:

Twin-screw granulation is a promising technique for the continuous production of pharmaceutical solid dosage forms based on wet granulation. In a short period, solid-liquid mixing must be achieved by arrangement of transport and kneading elements to produce granules with a particle size distribution appropriate for tableting. The residence time distribution and the solid-liquid mixing governed by the field conditions (such as location and length of mixing zones) in the twin-screw granulator thus contain interesting information about mixing and different granulation rate processes such as aggregation and breakage. In this study, the impact of process (feed rate, liquid-to-solid ratio and screw speed) and equipment parameters (number of kneading discs and stagger-angle) on the residence time, the granulation liquid-powder mixing and the resulting granule size distributions during twin-screw granulation were investigated. Residence time and axial mixing information was extracted from tracer maps and the solid-liquid mixing was quantified from moisture maps, both obtained by monitoring the granules at the granulator outlet using near infra-red chemical imaging (NIR-CI). The granule size distribution was measured by sieving. The screw speed most dominantly influenced the residence time distribution based responses, i.e. mean residence time and axial mixing. Increasing the screw speed caused reduction in mean residence time and an increase in axial mixing. Also, an interaction between screw speed and material throughput dictating the fill ratio caused a reduction in residence time and an increase in axial mixing when the throughput-force increased by the high fill ratio. The frequency and amplitude of perturbation in the mean moisture profiles (derived from the moisture maps) indicated that unlike residence time, the solid-liquid mixing is dominantly driven by the material throughput and the number of kneading discs. Increasing the number of kneading discs reduced the frequency of variation indicating reduction in the heterogeneity of liquid mixing, which is desired for a good granulation yield. Correlating these results with the particle size fractions, the low residence time and high axial mixing obtained at a high screw speed resulted in a reduced oversized (>1400 µm) fraction and an increase in yield fraction (>150 µm and < 1400 µm). However, increasing the material throughput, which had a similar effect as screw speed on the residence time and the axial mixing, resulted in a reduction of the yield fraction. This was due to the inferior solid-liquid mixing at high material throughput which ultimately negatively affected the granulation performance. This improper solid-liquid mixing at high throughput resulted in more oversized particles. Thus, a balance between material throughput and screw speed should be found to achieve the required granulation time and solid-liquid mixing for high granulation yield. The results from this experimental study improved the understanding regarding the interplay between granulation time and the axial and solid-liquid mixing responsible for the granulation yield after twin-screw granulation.

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