Experimental investigation of the link between granulation performance, residence time and granulation liquid distribution in twin-screw granulation

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Twin-screw granulation is a promising technique for the continuous production of pharmaceutical solid dosage forms. In a short process time window, solid-liquid mixing must be achieved by an 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 field conditions in twin-screw granulators thus contain valuable 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 evaluated. Residence time and axial mixing information was extracted from tracer maps and the solid-liquid mixing was quantified from the moisture maps, obtained by monitoring the granules at the granulator outlet using near infrared chemical imaging (NIR-CI). The granule size distribution was measured by sieving. The screw speed dominantly influences the mean residence time, which decreased with increasing screw speed. An interaction between screw speed and other parameters such as the feed rate, liquid-to-solid ratio, number of kneading discs and stagger angle was also observed. Furthermore, the level of axial mixing, indicated by the mean-centered variance of the residence time, was most influenced by the screw speed. A high axial mixing and low residence time obtained at high screw speed reduced the oversized fraction (>1400 µm) and increased the fines (<150 µm) fraction. The material throughput has no significant effect upon axial mixing, but it dominantly controls the solid-liquid mixing. More variations in granulation liquid distribution were observed at a low throughput condition. However, a better solid-liquid mixing at high throughputs yielded more oversized particles. The results from this experimental study improved our understanding regarding the interactions between granulation time, the axial mixing and the solid-liquid mixing responsible for the granulation yield after twin-screw granulation.