Effect of screw configuration on twin screw wet granulation process: an experimental study

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The importance of continuous production in the pharmaceutical industry has increased significantly over the past years as there are many advantages associated with this mode of manufacturing which are all related to economic drivers for change (quality, cost and time). In the current work, twin screw granulation, being a continuous wet granulation method for particle size enlargement, was studied. The objective was to understand the effect of screw configuration, screw speed, powder feed rate, and liquid content on particle size distribution of the granules produced in a twin-screw granulator.
Experiments were conducted using a high-shear twin screw granulator, being part of the ConsiGma™-1 unit (mobile R&D unit of ConsiGma™ series, continuous tablet manufacturing systems). A premix of α-lactose monohydrate and PVP (ratio: 97.5/2.5, w/w) was granulated along with a 0.01% cochenille red aqueous solution. Using a dedicated experimental design, the effects of screw configuration (number of kneading elements: 2, 4, 6 and 12), powder feed rate (10-25 kg/h), screw speed (600 and 900 rpm) and liquid content (4.58-6.72% (w/w), based on wet mass) on the granule size (F) distribution (GSD) were evaluated. The barrel temperature was kept constant (25 °C). Granules produced were collected and dried to measure the GSD by sieve analysis (sieve size 75-2000 µm). The quality of the granules is good when in the size range of 150-1000 µm. The mass of granules in this range is therefore defined as percentage yield for the constant throughput based on powder feed rate..
Increased liquid content and powder feed rate resulted in a lower amount of fines (F <150µm). The results showed that the degree of fill inside the barrel, controlled by screw speed and powder feed rate, had the most significant impact on the yield. Increasing the filling degree of the barrel lowered the yield values from 46-33% to 38-31% for the size range of 150-1000 µm. Furthermore, a lower amount of oversized granules (F >1000µm) (yield reduced from maximum of 49 % to 22%) could be obtained at decreased liquid content and increased screw speed. This was attributed to the high granulability of the α-lactose monohydrate and PVP mix. The effect on the granulation process (torque) and shape within the scope of the applied experimental design are under evaluation and will be provided when becoming available. Such endeavour will significantly contribute to the physical interpretation required for future mechanistic modelling of the twin-screw granulator.

Keywords: continuous twin screw granulator, experimental design, particle size distribution, process yield