Model-based characterisation of twin-screw granulation system for continuous solid dosage manufacturing

A. **Kumar**[1,2], K.V. **Gernaey**[3], T. **De Beer**[2*], I. **Nopens**[1]
1. BIOMATH, Dept. of Mathematical Modelling, Statistics and Bioinformatics, Faculty of Bioscience Engineering, Ghent University, Belgium
2. Laboratory of Pharmaceutical Process Analytical Technology, Dept. of Pharmaceutical Analysis, Faculty of Pharmaceutical Sciences, Ghent University, Belgium
3. CAPEC-PROCESS, Department of Chemical and Biochemical Engineering, Technical University of Denmark, Denmark
Email for correspondence: Ingmar.Nopens@UGent.be, *Shared last authorship

Granulation is a key product design step in solid dosage manufacturing processes in the pharmaceutical industry. By using a combination of formulation and processing methods, the properties of the granules are modified and controlled. However, the granulation process is complex and therefore, despite having knowledge of all the variables during the process, precisely predicting the characteristics of the produced granules still remains a challenge. This leads to non-optimal unit operation and causes a significant failure rate during scale-up of the solid dosage manufacturing process to industrial scale. In this context, continuous twin-screw granulation has received increased attention as it can be embedded in a continuous manufacturing line which also includes dryer, product control hopper and tabletting machine making continuous powder to tablet production possible. A continuous process with 24/7 production capacity will eliminate scale-up requirements and intermediate storage. Moreover, the screws used in the granulator have a modular structure (interchangeable transport and kneading discs) allowing greater flexibility in equipment design. However, to cure the inefficiency issue, knowledge about continuous granulation should be further developed both under steady state and dynamic conditions. Application of mechanistic models that incorporate the understanding of the underlying mechanisms is therefore pursued. In this study, the principle constitutive mechanisms of a granulation system such as growth, aggregation and breakage are included in a population balance modelling framework. This was done for the different individual screw blocks of a continuous twin-screw granulator. The rate processes which are considered dominant in the kneading element regions of the granulator, i.e. aggregation and breakage, were included. Based on an experimentally determined inflow granule size distribution and mean residence time of the granulator, predictions of the outflow granule size distribution were made. The experimental data was used for calibrating the model for individual screw modules in the twin-screw granulator. This provided an improved insight into behaviour of the system. The results showed that the successive kneading blocks lead to a granulation regime-separation inside the twin-screw granulator. The first kneading block after wetting caused an increase in the aggregation rate, which was reduced after the second kneading block. Whereas, the breakage rate increased successively along the length of the granulator. Such a physical separation between the granulation regimes will be promising for future design and advanced control of the continuous granulation process.

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