Development of a Population Balance Model for Continuous Twin-Screw Granulation in Pharmaceutical Manufacturing

Ashish Kumar[1,2], Krist V. Gernaey[3], Thomas De Beer[2] and Ingmar Nopens[1], (1)Department of Mathematical Modelling, Statistics and Bioinformatics, Ghent University, Gent, Belgium, (2)Department of Pharmaceutical Analysis, Ghent University, Ghent, Belgium, (3)Department of Chemical and Biochemical Engineering, Technical University of Denmark (DTU), Kgs. Lyngby, Denmark

Abstract Text:

Continuous processing in pharmaceutical manufacturing could be implemented for cost-efficiency. This opportunity for moving beyond the traditional batch processing is possible due to a change in attitude of the regulatory environment through the publication of the PAT guidance. However, in order to fully utilise this opportunity, a detailed process understanding about the key processes in pharmaceutical manufacturing is required. The wet granulation process step in continuous manufacturing can be achieved by a twin-screw granulator. The screw used has a modular structure, and mixing is achieved in a short time as the result of a combination of screw design and alignment, and process settings (e.g. feed rate, screw speed, etc.). Therefore, a thorough understanding of the dominating granulation sub-processes as well as the change in granule size distribution and dynamics along the granulator barrel is needed to allow optimisation and control. Process dynamics will obviously be a function of the individual screw modules and their interaction. In an initial study, we experimentally analysed the mixing behaviour inside the granulator using the residence time distribution, and the granule size distribution inside the screw barrel for gaining knowledge regarding continuous twin-screw granulation. To extend our understanding in this direction, now we endeavour to develop a population balance model for a continuous twin-screw granulator. The focus in this study was on modelling the rate processes which are considered dominant in the kneading element regions of the granulator, i.e. aggregation and breakage, based on the inflow and outflow granule size distribution. Experimental data for the granule size distribution at different locations were used to obtain the unknown model parameters and also for calibrating the model for individual screw modules in the twin-screw granulator to provide an improved insight into the system. After having calibrated the unknown parameters of the aggregation and breakage terms in population balance model, a good agreement of the experimental and numerical results was observed. The results enriched our knowledge regarding the role of kneading discs in the spatial evolution of granule size during twin screw granulation. Results from this modelling study and experimental calibration will be further used as a unified base for the development of a multi-dimensional PBM to understand the liquid distribution by involving granule properties such as the moisture content for the twin-screw granulation process.

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First Author

Presenting Author
Ashish Kumar
Email: Ashish.Kumar@UGent.be

Second Author

Krist V. Gernaey
Email: kvg@kt.dtu.dk

Third Author

Thomas De Beer
Email: thomas.debeer@ugent.be

Fourth Author

Ingmar Nopens
Email: ingmar.nopens@ugent.be

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