Combined experimental and computational approach to elucidate the twin-screw granulation process

Ashish Kumar[1,2], Jurgen Vercruysse[3], Chris Vervaet[3], Jean Paul Remon[3], Krist V. Gernaey[4], Thomas De Beer [2,*], Ingmar Nopens[1]

1. BIOMATH, Department of Mathematical Modelling, Statistics and Bioinformatics, Ghent University, Belgium
2. Laboratory of Pharmaceutical Process Analytical Technology, Department of Pharmaceutical Analysis, Ghent University, Belgium
3. Laboratory of Pharmaceutical Technology, Department of Pharmaceutics, Ghent University, Belgium
4. CAPEC-PROCESS, Department of Chemical and Biochemical Engineering, Technical University of Denmark, Denmark
Email: Ingmar.Nopens@UGent.be, *Shared last authorship

Twin-screw granulation has recently emerged as a popular wet granulation technique for continuous secondary pharmaceutical manufacturing. A twin-screw granulator (TSG) achieves solid-liquid mixing and granulation by a complex interplay between the screw configuration and process settings (e.g. feed rate, screw speed, etc.) to produce a certain end-product specification in a short time. However, there is a rather limited understanding about the primary shaping mechanisms and the role that these variables play with regard to the granule size distribution in the TSG during wet granulation, due to the opacity of the multiphase system. As a result, the primary focus of most studies conducted thus far has been on the monitoring of the effect of these variables upon granule properties at the outlet of the TSG. In this study, a combination of experimental and mathematical approaches was applied to investigate the granule size evolution in the mixing zones of the twin-screw granulator. Near infrared chemical imaging was used for experimental characterisation of wetted material transport and mixing inside the confined spaces of the rotating screws and the residence times. In addition, the granule size distribution dynamics as a function of individual screw modules along the TSG barrel was investigated experimentally. A population balance model including the rate processes which are considered dominant in a twin-screw, i.e. aggregation and breakage, was calibrated using the experimental data for each kneading disc module separately in the TSG. The results showed that the aggregation is the dominant regime in the first mixing zone while a mixed granulation regime (both aggregation and breakage simultaneously) occurs in the second mixing zone. Additionally, under certain process conditions, a granulation regime separation inside the TSG can be achieved in the successive kneading blocks, where the first kneading block after wetting caused an increase in the aggregation rate, while the breakage rate increased in the second mixing block along the length of the granulator. This physical separation between the granulation regimes is a promising result for future design of the TSG and the screw configuration towards optimisation as well as advanced control of this granulation process. The modelling framework presented in this study also forms the basis of the analysis of the granulation mechanism as well as development of a predictive modelling tool in combination with micro-scale level models such as discrete element models in a hybrid framework.