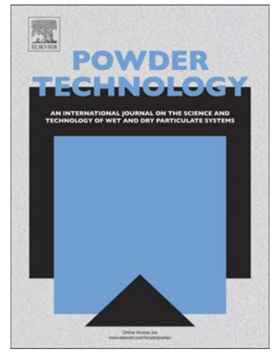

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Regime-separated approach for population balance modelling of continuous wet granulation of pharmaceutical formulations

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Abstract

A two-dimensional population balance model (PBM) was developed in order to predict granule size distribution (GSD) in continuous twin-screw granulation. The model predicts the GSD as well as granule liquid content at different spatial locations. In order to understand the different mechanisms involved in the twin-screw granulation process, a regime-separated approach was used in which the population balance model was solved for different zones along the extruder, i.e. kneading and conveying zones. For the conveying zone, the flow regime was assumed to be plug flow, whereas a well-mixed regime was assumed for modelling of particulate events in the kneading zone. In the development of the population balance model, breakage and aggregation phenomena were considered as particulate events. The unknown parameters of the model were estimated using experimental data obtained for granulation of pure microcrystalline cellulose using a 12 mm twin-screw granulator. Among five experimental runs, three runs were used for model calibration and two runs for validation. The results indicated that the model is rigorous and reliable for prediction of GSD as function of process parameters in twin-screw granulation. Moreover, in order to capture tri-modality in the granule size distribution, a partial wetting approach was used in which 50% of particles were assumed dry at low liquid to solid ratio. The latter assumption resulted in prediction of tri-modal GSD by the developed PBM. The results revealed that aggregation