Experimental and computational characterization of flow and mixing behavior in a continuous powder mixer

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Abstract

In recent years, there has been a lot of interest in the pharmaceutical industry towards continuous processing. In order to convert the current batch based manufacturing into a continuous process, developing predictive understanding of continuous powder mixing process is highly critical. In this study, continuous mixing process was investigated from both experimental and computational standpoint.

A convective continuous blender, Gericke GCM 250 was used in this study. Several parameters related to the continuous blender including impeller rotation rate (40-250 RPM), flow rate (30, 45 kg/hr) and impeller design (All forward, Alternate) were investigated. Powder flow behavior in the continuous blender was captured by experimentally measuring the residence time distributions (RTDs). To quantify the strain, the number of blade passes experienced by the powder in the blender was calculated using the residence time measurements. Blender performance, defined by the achievable relative standard deviation (RSD) of the blend composition at the blender discharge and the variance reduction ratio (VRR) of the blender was measured. Blending experiments were performed for two different formulations including APAP-Avicel 200 blend and Caffeine-Dicalcium phosphate blend. Fokker Plank equations (FPEs) were used to model RTDs. Variance component analysis was applied in order to quantify different sources of variability in the output composition. RTD measurements were utilized to determine the contributions of feeding variability, powder segregation and RTD variability on output composition variance.

Simulations based on discrete element modeling (DEM) were performed to model the flow behavior in the continuous mixer. Soft particle based approach, Hertz Mindlin contact model was used to model flow of spherical particles. Different parameters related to the RTDs including mean residence time, dispersion coefficient, powder hold-up and number of blade passes were computed. Excellent agreement was achieved between simulations and experimental data. This indicated DEM method to be a promising way of modeling macroscopic powder flow behavior in the continuous blender.