

ABSTRACT

Discrete element method (DEM) modeling is a common way to model particulate systems and processes. Since the number of particles in most pharmaceutical processes is incredibly large, modeling these substantial magnitudes of particles individually using DEM is not computationally reasonable. To simplify the DEM modeling, agglomerates or groups of particles are modeled instead. This change creates a disconnect between the real particle parameter values and the simulated particle parameter values. Thus, efficient and accurate calibration is needed for effective modeling.

The methodology proposed in this thesis utilized a single commonly used bulk flowability measurement device, an annular shear cell, to calibrate for these DEM parameters with the help of dimensional analysis, design of experiments, and statistical tools. Three bulk responses were studied from the ring shear cell: the incipient yield internal friction angle, the critical state internal friction angle, and the bulk cohesion. The most important DEM parameters were isolated and subjected to a dimensional analysis to increase the generality of the results. A modified full-factorial study was then set up using the identified dimensionless parameters. The final calibration results were then validated using an independent flow through an orifice test using a Flodex™.

This thesis demonstrates this proposed calibration methodology using three different powder samples, lactose, (hydroxypropyl) methyl cellulose (HPMC), and ABT-089. Using the DEM simulation results and the experimental measurements, predictive models were created for all three powder samples. For HPMC, the calibration errors were large while using spherical particles, so a non-spherical particle shape was introduced using the glued-sphere model in DEM. The calibration process was repeated with simulated non-spherical particles with an aspect ratio of two to create a new model for HPMC.

The overall calibration procedure and the three models, when validated with the Flodex simulations and measurements, successfully predicted the Flodex results within one Flowability index range for all three powder samples. This demonstrates that this methodology can be used to successfully calibrate various DEM simulation parameters.