ABSTRACT

Kumar, Rahul Ph.D., Purdue University, August 2014. Modeling Coating Variability in a Continuous Tablet Coating Pan. Major Professor: Carl R. Wassgren, School of Mechanical Engineering.

Continuous coating of tablets is a recent trend in the pharmaceutical industry and is expected to improve the efficiency of the coating process. In this work, coating variability, which is one of the most important critical quality attributes of the coating process, is studied. Both inter-tablet coating variability and intra-tablet coating variability are studied.

For a continuous coater, the inter-tablet coating variability depends on the residence time of the tablets in the coater which in turn is dependent on the axial motion of the tablets. A mathematical framework based on renewal theory is developed and an expression for inter-particle coating variability is obtained that accounts for the variance in the residence time of particles inside the coater. This model makes no assumptions on the nature of the particle axial motion. Discrete element method simulations have shown, however, that the particle axial motion can be accurately modeled by a combination of advective and diffusive motion characterized by an axial Peclet number. Using this advective-diffusive model, it was found that in order to maintain an inter-particle coating variability of less than 1%, typical of what might be required for functional pharmaceutical tablet coatings, a Peclet number of 20,000 is required. Such a large Peclet number would require essentially plug flow for typical continuous coater lengths of 1–2 m, or coater lengths of at least 15 m for

typical particle diffusion coefficients and feed rates. These findings suggest the use of a compartmentalized continuous coater very similar to a batch coater with tablets moving along the length of the drum.

Assuming a compartmentalized continuous coater, a compartment-model based population balance (PB) model is developed to reduce the computational time required to study the motion of tablets using Discrete Element Method (DEM) modeling. A compartment model consisting of a spray zone and active and passive bed zones is proposed based on the motion of the particles in a rotating drum. The parameters for the resulting coupled set of PB equations are estimated by fitting the time varying coating mass variability curve from the first few tens of seconds (35 s – 85 s) of DEM simulation data. The long term coating mass variability (1,000 s) is predicted using the PB model and compared with direct measurements from the DEM simulations. Excellent agreement was obtained between the model and DEM simulations with a relative error of less than 5% for the three cases studied.

In order to study the intra-tablet coating variability, a new image based algorithm is developed which is at least an order of magnitude faster than ray-tracing based methods. The surface of the tablet is divided into panels and the coating mass on each of the panels is identified using a GPU based method. The coating mass distribution on the tablet surface is compared to experimental measurements of coating thickness over the tablet surface. Good agreement is obtained between the simulations and experiments for the average coating mass distribution on the tablet surface. A new approach is also developed to obtain the asymptotic value of intra-tablet coating variability for a given tablet shape and operating conditions. The new approach takes into account the occlusion of tablets which is shown to have a significant influence on the coating mass distribution over the tablet surface.