Department of Materials Science and Engineering
PhD Defense
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Adhesion of Pharmaceutical Powders on Tools During Compaction

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Abstract

A common concern in pharmaceutical tablet manufacturing is the propensity for powder to adhere to and accumulate on the tooling components, also known as *sticking*. This is a problem that needs to be addressed in the development stage because it becomes excessively disruptive and expensive to deal with during technology transfer and scale-up of manufacturing.

The current work focused on the development, evaluation and understanding of objective risk assessment with an emphasis on techniques that: (a) are material sparing and (b) provide mechanistic insight to the problem as well as the determination of conditions that are required for consistent and unambiguous results. Prior work in the literature on this problem clearly indicates that the fundamentals and the mechanisms are not well understood. Our results include the evaluation of (a) a removable punch tip coupled with SEM imaging analysis and (b) an adhesion punch. The first technique is objective and material sparing, but time consuming and destructive (the punch cannot continue to be used after microscopy imaging). Also, the sensitivity of the adhered materials to interactions with the electron beam and the SEM environment need to be taken into account. For materials that are reasonably stable in the SEM environment, it provides rich insight into fundamental mechanisms. The adhesion punch is a quasi-online and nondestructive technique. And our experimental and computational work show that it is difficult to obtain objective results for the ranking of materials. Finally, a detailed examination of the effect of surface preparation on the experimental results for sticking was conducted using a laser reflection-based technique developed in our lab.

Based on the SEM imaging, we understand now that there is (a) a non-uniform sticking distribution across the punch face reflecting the non-uniformity of compaction and separation of punch from the tablet, (b) that sticking is a non-monotonic phenomenon at the local scale with deposition and removal of the material at the same time, and (c) that fragmentation and local defects may lead to cracks that promote detachment during unloading. Computational modeling of the adhesion punch led to an understanding of the non-uniform stress state leading to a non-uniform unloading which concerns the normalization of the force over an unknown area that is last in contact. DEM also showed that there is no unique relationship between powder/wall adhesion and the force required to separate the upper punch and the compact. While we addressed the weaknesses of the design, our work showed that there are ambiguities in the adhesion punch design that makes it difficult to use it for detailed work on sticking. The consistent surface preparation technique that was developed highlighted important phenomena that had not been explored before in the context of pharmaceutical engineering such as the rapid aging of the punch surface due to the interaction of the atmosphere. Our results point to the importance of the evolution of the punch surface due to continuous interaction with environment and the formulation components that may lead to sticking, and to the need to understand such interaction so that appropriate tests can be designed to provide objective information outside the production environment.