DREXEL UNIVERSITY
Materials Science and Engineering
College of Engineering

Department of Materials Science and Engineering,

PhD Defense

May 30th, 2019 at 9 AM
MEM Conference Room (Curtis 162)

Mechanical Properties of Compacted Powder Mixtures: General Ideas and Special Cases

Name: Jovana Radojevic

Advisor: Dr. Antonios Zavaliangos

Pharmaceutical formulations are multicomponent powder mixtures that consist of an active pharmaceutical ingredient (API) and various excipients. There has always been a desire to understand their behavior from that of individual components to increase efficiency of R&D efforts. Prior work on this topic aimed on deriving the properties of the mixtures based on interpolation of the properties of the components. Although this is tempting, there are many mixtures that defy such simple approaches. In this work sodium chloride (NaCl) and starch were used as a model mixture, which has been shown to exhibit a mechanical strength well below the interpolated strengths of its components. The evolution of mechanical behavior of starch and sodium chloride (NaCl) mixture tablets after compaction and its interaction with moisture was studied in detail. It was shown experimentally that the strengths of NaCl-starch mixtures and NaCl tablets evolved in an opposite way after compaction. When stored at a relative humidity (RH) of 60%, NaCl tablets strengthened with time, while NaCl-starch mixtures weakened. A mechanistic understanding of this effect was validated using discrete element modeling (DEM) and a novel experimental approach was developed based on the insight from DEM simulations. This knowledge was applied on the optimization of strength of NaCl-X mixtures and

it was demonstrated experimentally that the strength of various NaCl-X mixtures increases with progressively lower differences in the elastic modulus between the two components.

In addition, results from a special case of NaCl-starch mixtures are presented. This mixture, due to the processing conditions, exhibited superior mechanical strengths compared to the individual components. We report on several characterization efforts of the microstructure of this mixture despite that a full explanation of this behavior is still lacking.

This thesis highlights some of the complexities that characterize the development of the properties of powder mixtures and demonstrates that mechanistic understanding of the underlying phenomena is crucial for optimization of formulations.