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Project Title: Mathematical model development and experimental studies of hot melt extrusion (HME)
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Problem Statement: HME is a highly promising technique in pharmaceutical manufacturing for abuse deterrence and for the preparation for poorly soluble and high drug loading solid dosage forms. The challenges are that the quality of the extrudates are highly dependent on several factors such as the extent of API/polymer mixing and the shear/temperature profiles in the extruder as well as the pressure profile at the dye.

Objectives: The overall objective of this multi-year project is to develop a more mechanistic understanding of the HME process via an integrated mathematical modeling and experimental program and to subsequently physically integrate the HME equipment in the Rutgers pilot-plant CM line. The specific objectives for Year 1 are to better understand the effect of extruder process parameters (RPM, flowrate) and drug loading on API dispersion and distributive mixing, temperature, shear and pressure profiles.

Methods and Materials: The choice of an adequate polymer as a matrix to form stable solid solutions is crucial in HME. We will use PEG and/or PVP. We will work with our industrial partners to select a suitable API candidate and the drug loading(s). The equipment to be used is the ThermoScientific Pharma 11 twin screw extruder located at Rutgers, where we will work with Thermo to characterize and then finalize the best design of the extruder for HME. NIR, HPLC and/or imaging will be used to study the content uniformity and uniformity of solid dispersion in the extrudates. Residence time distribution (RTD) studies (both experimental and mathematical) will be performed to quantify and optimize the mixing in the extruder. CFD studies will be performed to quantify the profiles of temperature, shear and pressure across the extruder and dye. We will also validate models by RTD experimental measurement and the use of temperature probes at different locations and torque measurements. Rheometry will be used to characterize the physical transformations of the melt to better understand the mixing efficiency of the extrusion process by applying similar shear and temperature processing parameters as extrusion.

Anticipated Impact: We fully expect to move toward a more optimal operation (as a standalone and in an integrated CM line) of the HME process to obtain higher quality extrudates in terms of better API/polymer dispersions and content uniformity. The integrated modeling and experimental approach will also lead to reduced cost and labor in optimizing the process and will quantify the sensitivities and interactions of input parameters on key outputs and performance metrics.