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Project Title: A Comparative assessment of Nanocomposites versus Amorphous Solid Dispersions for Dissolution Enhancement
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Problem Statement: For bioavailability enhancement of poorly water-soluble drugs, nanoparticle formulations such as drug nanocomposites are highly desirable because of their excellent physical stability and their capability to provide high drug surface area available for dissolution. On the other hand, despite being metastable, amorphous solid dispersions (ASDs) can provide higher supersaturation solubility and accommodate higher drug dose. Unfortunately, it is challenging to compare the respective approaches head-to-head with proper controls because of differences in processing, formulations, matrix size effects, etc. A scientific methodology for comparison of dissolution performance of drug nanocomposites vs. ASDs is needed toward developing a decision-tree for proper selection of a process that enhances the bioavailability of poorly soluble drugs.

Objectives: The objectives of this project are to develop a nanoextrusion process platform for preparation of drug nanocomposites and ASDs, generate the knowledge base for the impact of various formulation (drug–polymer) properties on the drug dissolution from nanocomposites vs. ASDs, study the impact of matrix (extrudate) particle size, and prepare guidance for proper selection of solubilization technology for a given drug at low dose (emulating potent drugs) and high dose. Another objective is to assess the physical stability of the extrudates.

Methods and Materials: As a major novelty, both the drug nanocomposites and the drug ASDs will be prepared using the same continuous manufacturing process, i.e., nanoextrusion, which allows a head-to-head comparison of nanocomposites vs. ASDs. Nanoextrusion uses a drug nanosuspensions prepared by wet stirred media milling as feed with various polymers (typically HPC, Soluplus, PVP, etc.) in comparison to traditional hot melt extrusion (HME) process. In proposed work, polymers will be selected based on their solubility parameters in comparison to drugs and solvent casting/drying of drug–polymer solutions. Two model generic drugs or drugs that are of interest to the company will be formulated with polymers, and their nanosuspensions will be prepared via wet stirred media milling. There will be two major continuous processing routes: (1) melt-extrusion of polymer with drug nanosuspensions (nanoextrusion) and (2) melt-extrusion of dry-blend of as-received drug–polymer (standard HME). Depending on the polymer–drug interactions, extrudates in the form of drug nanocomposites or ASDs can be prepared using the same nanoextrusion process in comparison to the standard HME process. The extrudates will be milled and sieved into few size fractions to study the matrix (extrudate particle) size effects. Content uniformity and drug content of the formulations will be determined via assays, while the crystallinity of the drug will be determined by XRD/DSC. The dissolution performance of the extrudate powders will be investigated at low drug dose (emulating potent drugs) and high drug dose under non-supersaturating and supersaturating conditions. The same will be studied for aged samples to assess physical stability along with the use of XRD/DSC. The drug release mechanisms will be identified and modulated by using surfactants and various extrudate particle sizes.

Anticipated Impact: The project will allow for development of a methodology, knowledge base, and basic elements of a decision-tree in formulation development of drug nanoparticle-based formulations/dosages vs. ASDs at low–high drug doses. Such knowledge and tools will allow formulators to select proper formulation–processes very early on, which will prevent costly mistakes and allow for development of an optimal approach for a given drug in bioavailability enhancement.