Project #7
A Comparative Assessment of Nanocomposites vs. Amorphous Solid Dispersions for Dissolution Enhancement

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Problem Statement

- Dissolution performance of BCS Class II drugs can be improved by either increasing the surface area via nanomilling or increasing the saturation solubility through ASD (HME/SD).

- Nanocomposites are physically stable, but do not provide significant supersaturation unlike ASDs, which are metastable and may exhibit stability issues during storage/dissolution.

- Drug nanosuspensions are converted into nanocomposites via spray-drying or fluidized-bed coating/granulation. New continuous drying processes needed!

- No head-to-head comparison between drug nano-composites and ASDs on dissolution enhancement; impact of matrix (extrudate) size and drug particle size to be studied

Objectives

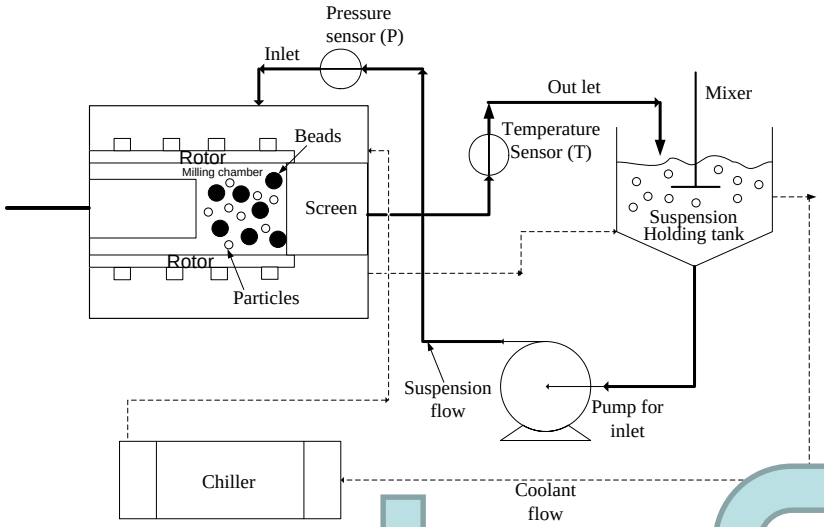
- Develop a nanoextrusion process platform for preparation of drug nanocomposites and ASDs of the same drug
- Generate the knowledge base for the impact of various formulation (drug–polymer) properties on the drug dissolution from nanocomposites vs. ASDs
- Elucidate the impact of polymeric matrix type/size on the drug dissolution performance at non/supersaturating conditions
- Assess the physical stability of the extrudates
- Prepare guidance for proper selection of solubilization technology for a given drug at low dose (emulating potent drugs) and high dose

Materials

- **Two BCS Class II drugs**
  - Generic model compounds (e.g. GF, FNB)
  - Compounds that are of interest to the company
- Polymers will be selected based on their solubility parameters in comparison to drugs and solvent casting/drying of drug–polymer solutions
- **Potential Polymers**: Soluplus, PVP, HPC, etc.
- **Surfactant:** SDS
- **Target Drug Loading:** 10-40%

Nanoextrusion Platform for Preparation of Drug Nanocomposites and ASDs

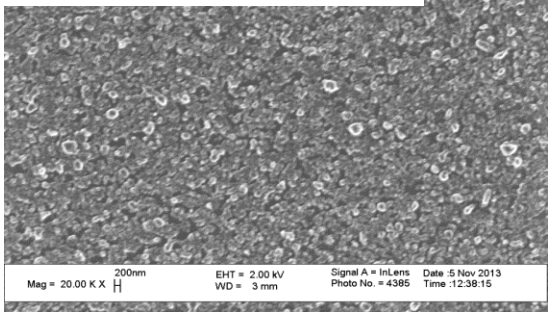
Wet stirred media mill

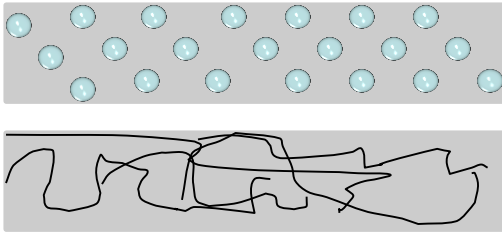


Co-rotating twin-screw extruder

Additional Polymer

Drug nanoparticles





http://www.plasticshotline.com/images/news/Leistritz/0112-4.jpg

Extrudate is milled to powder

Characterization Methods

- **Particle sizing via laser diffraction/DLS/SEM**
- **Drug content via assays**
- **Dissolution Test: USP II**
- **Ultraviolet (UV) Spectroscopy**
- **SEM, polarized light microscope**
- **Solid State Characterization: XRD, DSC**
- **Liquid Penetration Study**: drug wettability by polymer solutions

Anticipated Impact

- Nanoextrusion platform: a continuous process for preparing both nanocomposites and ASDs of the same drug; in comparison to standard HME
- 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
- Understanding of the role of matrix (extrudate) size and drug particle size on the dissolution response
- Such knowledge and tools will enable formulators to select proper formulation–processes very early on, which will prevent costly mistakes and allow for development of an optimal solubilization approach in bioavailability enhancement.

Q & A?