Replacing commonly used polymers with sugars in making a Solid dispersion of BCS class II drugs such as Griseofulvin by Hot Melt Extrusion

N. Rezvani¹, Smrut P. Chaudhari², R. H. Dave¹
¹Arnold And Marie Schwartz College of Pharmacy And Health Sciences, Long Island University, Brooklyn, NY
²Mayne Pharma Inc., Greenville, NC

INTRODUCTION:
Improving oral bioavailability of poorly water-soluble drugs is one of the most familiar challenges of the pharmaceutical industry. Several strategies such as solid dispersions, nanocrystals, cyclodextrin complexes and lipid formulations have been designed to improving drug solubility and increasing oral bioavailability. Making a solid dispersion of a poorly water-soluble drug using Hot melt Extrusion is one of the latest strategies for increasing the solubility of the drug and thereby improving its physicochemical properties such as its dissolution rate.

METHODS:
- Physical mixtures of Griseofulvin, Polyethylene Glycol 3350 (30%), with various percent by weight of each of the sugars; Mannitol, Sorbitol, and Xylitol were prepared using a V-blender, making a total of three different formulations.
- Solid dispersion of each of the formulations was made by Hot Melt Extrusion. A thermal analysis of Griseofulvin, Mannitol, Sorbitol and Xylitol, Polyethylene Glycol 3350, as well as the physical mixture and solid dispersion of each formulation was performed by Differential Scanning Calorimetry (DSC).
- Ultraviolet (UV) Spectroscopy was the analytical method used to measure the drug release.
- Furthermore, X-Ray Powder diffraction (XRPD), Fourier Transform Infrared Spectrometry (FTIR) and Dissolution were done to support claims regarding the improvement drug solubility, and drug release profile.

RESULTS:
- Most sugars can be used instead of other polymers in making the solid dispersion of Griseofulvin by Hot Melt Extrusion.
- However, different sugars behave differently. The proportion of sugar to drug needed to make the optimum formulation varies among sugars. Use of plasticizers such as PEG3350 facilitates the process of hot melt extrusion with sugars and prevents them from burning.
- While the drug is always rendered amorphous in the formulation to increase its solubility, sugars may remain crystalline or become amorphous. All three dispersion formulations made here, showed improved solubility and dissolution compared to the pure drug.

CONCLUSION:
Sugars are relatively more safe, economic and convenient excipients which can be used instead of commonly used polymers to increase the solubility of poorly water-soluble drugs (BCS II drugs), which eventually leads to increased bioavailability. Some of the sugars may enhance drug solubility by forming a crystalline solid dispersion whereas others may form an amorphous solid dispersion or solid solution. The use of the plasticizer (PEG3350) reduces the glass transition temperature of the mixture and resulting mixture can be extruded at lower temperatures which help avoid the degradation of either drug or sugar due to elevated temperatures.