PURDUE UNIVERSITY | Department of Industrial and Physical Pharmacy

Industrial & Physical Pharmacy Seminar

IPPH 69600

Monday, October 2, 2023
3:30 PM in RHPH 164

"Orthogonal analytical methods to elucidate how low levels of residual crystallinity in posaconazole amorphous solid dispersions impact phase behavior during release"

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Last Seminar

For successful bioperformance, the drug in an amorphous solid dispersion (ASD) should not undergo crystallization in the solid dosage form during storage, or from the supersaturated solution generated upon dissolution. Incomplete processing during hot melt extrusion (HME) can lead to residual crystallinity. Commonly, residual crystallinity is evaluated using techniques such as powder X-ray diffraction (pXRD). However, residual crystallinity at levels below the detection limit of pXRD can be detrimental to ASD performance. The goal of this study was to evaluate the impact of different levels of residual crystallinity in an ASD containing the fast-crystallizing drug, posaconazole (PCZ), and hydroxypropyl methylcellulose acetate succinate (HPMCAS) on dissolution and additional crystallization. ASDs with and without residual crystallinity at 10, 25, and 50 wt.% drug loadings were prepared using HME, processing at temperatures below and above the critical temperature, which was calculated using Flory–Huggins theory. Some of the ASDs contained levels of residual crystallinity that were below the quantification limit of pXRD, requiring the use of second harmonic generation (SHG). The impact of residual crystallinity on dissolution was studied using two-stage dissolution. Additional characterization in support of dissolution measurements included SHG analysis and particle evolution with focused beam reflectance measurement (FBRM), using pH shift experiments. The 10 wt.% ASD processed below the critical solution temperature contained residual crystallinity of < 1% which promoted rapid crystallization when the ASD was in a solution environment. Real time monitoring of both the solid and solution phases revealed that PCZ in ASDs containing residual crystals underwent crystallization both in the matrix and from solution. The study supports the need to select a sufficiently sensitive crystallinity quantification technique, a suitable discriminatory dissolution technique, and appropriate HME processing conditions in order to optimize and achieve successful performance of ASDs of fast-crystallizing drugs.