PURDUE UNIVERSITY | Department of Industrial and Physical Pharmacy

Industrial & Physical Pharmacy Seminar

IPPH 69600

Monday, October 31, 2022
3:30 PM in RHPH 164

"Dissolution Mechanisms of PVPVA-Based Amorphous Solid Dispersions: Role of Drug Load and Molecular Interactions"

Alexandru Deac
Purdue University, Taylor Lab

Amorphous solid dispersions (ASDs) have been used commercially to enable delivery of poorly soluble drugs. However, high drug load ASDs are a challenge to formulate because drug release is inhibited at high drug loads. The maximum drug load prior to inhibition of release has been termed the limit of congruency (LoC) for copovidone (PVPVA) based ASDs. The terminology was derived from the observation that below LoC the polymer controlled the kinetics and the drug and polymer released congruently, while above LoC the release rates diverged and were impaired. Recent studies show a correlation between the LoC value and drug-polymer interaction strength, where a lower LoC was observed for systems with stronger adhesive interactions. The aim of this study was to investigate the mechanisms responsible for the LoC. Confocal microscopy was used to monitor the ASD-solution interface during release by using molecular probes for labeling drug-rich and polymer-rich phases. Surface normalized release from the ASD was performed with an intrinsic dissolution apparatus. The drug and polymer concentrations were determined by high performance liquid chromatography (HPLC) and size exclusion chromatography (SEC). Micrographs show evidence of a gel layer at the interface of all ASDs. In addition, amorphous-amorphous phase separation (AAPS) was detected inside the gel layer. The morphology of the hydrophobic (drug-rich) phase formed following AAPS was found to correlate with the release behavior. A discrete phase resulted in good apparent drug release, where the kinetics were governed by polymer dissolution. However, when the phase formed a continuous network, it severely reduced the drug and polymer release by acting as a porous barrier on the surface of the ASD. The discrete hydrophobic phase was isolated by centrifugation and its composition and glass transition (T_g) was measured by differential scanning calorimetry (DSC) and HPLC/SEC, respectively. The continuous network was observed to form at lower drug loads for systems with strong drug-polymer interactions because the network contained a significant amount of polymer. The study highlights the complex molecular behavior at the dissolution interface of copovidone-based ASDs and provides a thermodynamic argument for qualitatively predicting the release behavior based on drug-polymer interactions.

Alex is a 5th year PhD student in Prof. Lynne Taylor's lab. He received his bachelor's degree in Chemical Engineering from the University of Illinois at Urbana-Champaign and has spent six years in the pharmaceutical industry working for AbbVie in drug development. Alex joined Dr. Taylor's lab in August 2018 and his research focuses on developing a molecular understanding of the dissolution process in amorphous solid dispersions.