Time & Location: June 30, 2020 at 1:00 PM in Virtual Defense
https://us02web.zoom.us/j/89930288200?pwd=d2lRU2NKbm1INEjJNzdxFVJ0OFY5QT09
Title: NON-LINEAR INVERSE LIQUID-SOLID CHROMATOGRAPHY AS A METHODOLOGY TO CHARACTERIZE DRUG CONCENTRATION LOSSES TO POLYMERIC MATERIALS USED IN BODY-ON-A-CHIP DEVICES FOR DRUG DISCOVERY

Body-on-a-chip and human-on-a-chip systems are currently being used to augment and could eventually replace animal models in drug discovery and basic biological research. However, hydrophobic molecules, especially therapeutic compounds, tend to adsorb to the polymer materials used to create these microfluidic platforms, which may distort the dose-response curves that feed into Pharmacokinetic/Pharmacodynamic (PK/PD) models which translate preclinical data into predictions of clinical outcomes. Adsorption of hydrophobic molecules to these polymer materials needs better characterization.

Inverse Liquid-Solid Chromatography paired with a numerical optimization based on the Langmuir model of adsorption was used to characterize the adsorption isotherm parameters of selected drugs to polydimethylsiloxane (PDMS) and polymethylmethacrylate (PMMA), polymers commonly used in these platforms after extensive modification to an existing HPLC-MS instrument.

Surface modification by organosilanes is one method being explored to modify PDMS, but the effect of organosilanes on drug adsorption isotherms are not well characterized. We utilized Inverse Liquid-Solid Chromatography (ILC) to characterize the adsorption parameters of the selected drugs with native PDMS and organosilane-modified (fluoropolymer (13F) and polyethylene glycol (PEG)) PDMS surfaces to correlate the modifications to changes in drug adsorption. We found that the organosilane modifications significantly changed the energy of adsorption.

The adsorption isotherms were then compared against concentration measurements of drugs recirculated in these platforms. It was found that the adsorption alone does not account for the drug concentration losses, which was expected as the drugs will diffuse into the bulk of the material. Organosilane surface modifications were successfully made to PDMS parts but were not fully adequate in preventing concentration losses, also due to diffusion into the bulk. Future work will characterize the diffusion and be integrated with the work presented in this dissertation to create a larger model of drug adsorption and diffusion which drives the concentration losses.

This research establishes a foundation for a new approach whereby quantifying drug or drug candidate interactions before system dosing and including this data in the PK/PD models, that polymers used in these platforms need not be limited to “less-adsorbing” materials.

Major: Materials Science and Engineering

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Bachelor’s of Chemistry, BA, 2008, Whitman College
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Approved for distribution by James J. Hickman, Committee Chair, on June 16, 2020.

The public is welcome to attend.