COLLEGE OF PHARMACY
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Pharmaceutical Sciences Seminar

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https://umich-health.zoom.us/j/94653885917
4:00-5:00 pm

"Characterize Peptide-Poly(lactic-*co*-glycolic acid) Binding by Nano Isothermal Titration Calorimetry"

Presented by:

King Yeung (Justin) Hong
Ph.D. Candidate
Department of Pharmaceutical Sciences

Abstract: A significant challenge to develop poly(D,L-lactic-co-glycolic acid) (PLGA)-based controlled release systems for peptide therapeutics is understanding controlled release and drug stability. Cationic peptides are well known to readily bind poly(lactic-co-glycolic acids) (PLGAs) with carboxylic acid (-COOH) end-group. This binding has been considered as a critical step leading to the peptide degradation via acylation within PLGA-based long-acting formulations. The binding has also been known to affect microencapsulation and release. Herein, we utilized nano isothermal titration calorimetry (NanoITC) to investigate the thermodynamics of peptide−PLGA binding in dimethyl sulfoxide (DMSO) using a model cationic octapeptide, octreotide, which contains two primary amino groups located at its N-terminus and lysine side chain at position five. ITC results of PLGAs with different lactic acid to glycolic acid ratios (50:50 to 100:0) revealed that the extent of the interaction with the octreotide was solely dependent on the availability of the acid end group of the PLGA. The binding constants (K_a) at 37 °C were determined in a narrow range from 1.33 to 1.72 × 10^4 M^{-1} with 0.59 to 0.66 binding stoichiometries irrespective of the lactic/glycolic acid ratio in the PLGA-COOH. Over 25−65 °C, octreotide−PLGA- COOH interactions were found to be enthalpically favored ($\Delta H < 0$) and entropically unfavorable ($\Delta S < 0$). Hence, the interactions were characterized as enthalpically driven. At different sodium chloride (NaCl) levels, the sensitivity of thermodynamics of the interactions to the charge screening effect contributed by the NaCl unveiled the actual driving force of the octreotide−PLGA- COOH interactions is simple ion-pairing.

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