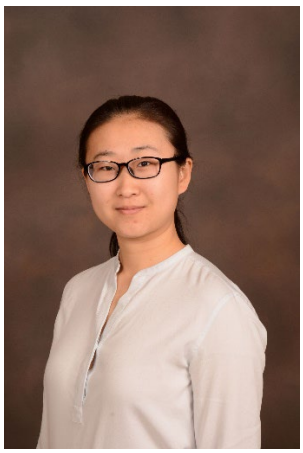
COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Department of Pharmaceutical Sciences
Ph.D. Dissertation Defense Seminar

Monday, October 3, 2022
1:00 PM Eastern Time
Hybrid
NCRC Building 10 –G065
Zoom Link
Passcode: 020113

"Development and Analytical Characterization of Lipid-Based Nanoparticles"

Presented by:



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Abstract: Lipid-based nanoparticles are highly versatile platforms with extensive therapeutic applications. Successful clinical translation of lipid nanoparticles requires lipid nanoparticle candidates to be optimized for therapeutic efficacy as well as reliable analytical methods to confirm nanoparticle quality.

Our studies are focused on the optimization of synthetic high-density lipoprotein (sHDL) nanoparticles used to treat cardiovascular diseases (CVD). In the first project, a VCAM-1 specific ligand was introduced to sHDLs to achieve the activated-endothelium-targeted delivery. The active targeting sHDLs showed enhanced binding on activated endothelium and inhibition of inflammatory response, showing their potential as a stand-alone therapy or drug delivery carrier for CVD treatment. To further enhance the functionality of sHDLs, we have incorporated phosphatidylserine (PS), a bioactive lipid with intrinsic anti-inflammatory effects. The incorporation of PS into sHDLs improved the particle stability and anti-inflammatory effects without impairing the cholesterol efflux capacity and pharmacokinetic profiles of sHDLs.

To enable the analytical characterization of lipid nanoparticles, we examined the methodology of dialysis-based drug release test (IVRT) for lipid nanoparticle drug delivery systems. Although dialysis-based methods are commonly used to evaluate the *in vitro* drug release profiles, the barrier effects of the dialysis membrane can lead to an underestimated drug release rate. To address this problem, a two-step approach was proposed. First, the barrier effect of the dialysis membrane was determined by a calibration experiment. Then, a mathematical model was applied to find the actual drug release kinetics from the apparent drug release data. The model was tested on Doxil® (doxorubicin liposomes), and a good agreement was found between the experimental data and the predicted value. The proposed model would help the methodological evaluation and proper data interpretation of drug release data for nanoparticle products.