COLLEGE OF PHARMACY
PHARMACEUTICAL SCIENCES
UNIVERSITY OF MICHIGAN

Pharmaceutical Sciences Seminar Series

Wednesday, March 6, 2024
4:00pm
2548 North University Building
Zoom

"Development of inhaled niclosamide-colistin particles for treatment of multi-drug resistant pulmonary bacterial infections"

Presented by:

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Abstract: Antimicrobial resistance has emerged as a critical global health threat. Recurrent bacterial lung infections are typical in diseases in which mucociliary clearance is impaired (e.g., cystic fibrosis and chronic obstructive pulmonary disease). The repeated use of antibiotics in this population coupled with suboptimal levels of drugs at the infection site has led to the emergence of multi-drug resistant (MDR) bacterial strains. One mechanism to address this problem is the use of additive or synergistic antibiotic combinations. A promising example of this is the combination of colistin, an antibiotic of "last-resort" commonly used to treat gram-negative infections, and niclosamide, an off-patent anthelminthic drug. The addition of niclosamide restores colistin susceptibility in resistant strains while also enabling synergistic activity and lowering the dose in susceptible strains. However, traditional *in vitro* synergy assays have proven to be unsuccessful in predicting *in vivo* synergy. Niclosamide and colistin exhibit vastly different physicochemical properties and are expected to exhibit differences in distribution and clearance upon administration. To address this problem, I propose to develop an inhaled fixed-dose combination product of niclosamide and colistin. Both niclosamide and colistin have been successfully administered via the inhalation route in humans, thus demonstrating the safety of this targeted approach. However, successful at-site antimicrobial activity that replicates synergy observed *in vitro* requires understanding and overcoming differences in niclosamide and colistin distribution and clearance from the airways and this has not been addressed with current treatment regimen approaches. Here, I will present my most recent data on the understanding of the antimicrobial killing pattern of niclosamide and colistin against clinically relevant gram-negatives as well as on the development of multicomponent particles of niclosamide and colistin for the fine-tuned drug release of drugs for matching such killing pattern.