Synthetic Amphiphiles as Antibiotic Potentiators

Date: November 21, 2022  
Time: 1:00 pm to 3:00 pm  
Place: 5th-floor conference room, Benton Hall

Abstract
Antibiotic resistance has become a massive threat to modern medicine. Bacteria acquire resistance either through genetic mutations or mobile genetic elements, such as plasmids. The growing resistance crisis is aided by over-prescription of antibiotics and improper use. As antimicrobial resistance becomes more widespread, superbugs (bacteria resistant to more than one class of drug) have evolved. Since few new drugs reach clinical trials and even fewer are approved by the FDA, we must find a way to make existing drugs more potent. One technique to accomplish this is by using combination therapy. By administering two or more drugs at a time, their combined effect can be greater than that of the individual drugs.

Lariat ethers (LEs) and their salts have shown activity against a variety of bacteria, including multi-drug resistant pathogens such as *K. pneumoniae* and methicillin-resistant *S. aureus* (MRSA). LEs have also been shown to reverse resistance in tetracycline-resistant *E. coli*. Their bactericidal activity and resistance reversal is mainly thought to occur by enhanced membrane permeability and disrupted ion homeostasis. However, neutron reflectometry suggests that a supramolecular complex may form between tetracycline and the LE. In this work, a set of LEs and their salts were examined for supramolecular complexation of clinically relevant drugs using nuclear magnetic resonance (NMR) and dynamic light scattering (DLS). Additionally, the same combinations were screened for *in vitro* combination activity.

(Bis)-Tryptophans are a class of amphiphile prepared by the Gokel Lab, which are composed of an alkyl or phenylene spacer that links two terminal tryptophan residues. These compounds have shown activity against Gram +/- bacteria, as well as the eukaryote *Saccharomyces cerevisiae*, in the low micromolar range and have been demonstrated to be non-cytotoxic. For these reasons, a variety of structures have been proposed to expand the library of (Bis)-Tryptophans.

Defense of Dissertation Committee
George W. Gokel, Ph.D. Chairperson  
Michael R. Nichols, Ph.D.  
Bruce Hamper, Ph.D.  
Wendy Olivas, Ph.D.