JMU Chemistry and Biochemistry Departmental Seminar

Friday, March 15, 2013
3:35 pm in ISAT 159

Seeking Optimal Antibacterial Products (SOAP or NO SOAP?)

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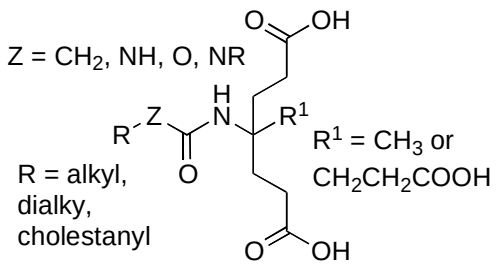
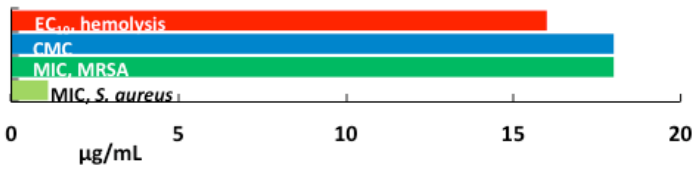
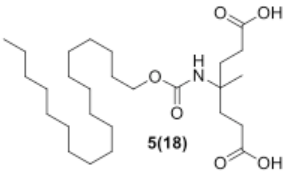
The onslaught of drug-resistant bacteria has created challenges for treating and preventing infections. Random mutations in bacteria that cause structural or metabolic changes enable cells to survive in the presence of an antibiotic. Soaps and detergents kill bacteria by disrupting cell envelopes and destroying the cellular structure. Unfortunately, these molecules cannot be used as drugs because they have the same effect on several mammalian cell types. Can these molecules be re-engineered to be safe for mammalian tissue but to remain deadly to bacteria? Detergency and membrane disruption are linked to the ability of these molecules, called amphiphiles, to self-aggregate in assemblies called micelles. Perhaps, modifying soap molecules to not form micelles can lead to safe anti-infective agents. We have developed water-soluble antimicrobial agents, called dendritic amphiphiles, which have shown excellent activity against bacteria, fungi, and mycobacteria.[1–8] The high species- and compound-selectivities suggest a specific mechanism of action for each microbe, which appears to be unrelated to membrane disruption. Our recent report[7] has established several crucial points for the continued exploration of dendritic amphiphiles as anti-infectives. Several compounds show excellent activity against methicillin-resistant *Staphylococcus aureus* (MRSA). Our methods for evaluating micellar (CMC), hemolytic (EC_{10}), and antibacterial properties (MIC) in nutrient broth, the medium for growing bacteria, enable directly comparing these three properties under identical conditions. One promising anti-Staphylococcal agent, **5(18)** has an MIC of 1.1 μg/mL, which is slightly better than that (2.2 μg/mL) of vancomycin, the drug of last resort in Staphylococcal infections. Mechanistic studies, including molecular dynamics simulations,[9] are underway to probe the activity of these amphiphiles.



Dendritic Amphiphiles





References:

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