FURMAN

Chemistry Department
2020 Summer Research Program

Research Group of John and Sandy Wheeler

The Wheeler group is active in three areas of research: (1) investigating the ability of select compounds to protect against (S, Se) OR initiate (Cr^{3+}) DNA damage in cancer prevention and treatment; (2) developing novel strategies for characterizing the properties of commercial biocides; and (3) developing and understanding the capacity of mushrooms to bioremediate pesticides and other organic contaminants contained in polluted soils.

(1) Oxidative DNA damage is one of the leading causes of cancer and other degenerative diseases, and Reactive Oxygen Species (ROS) (e.g., hydroxyl radical) are well associated with the formation of DNA damage. One avenue through which ROS may be prevented is through the availability of antioxidants. In collaboration with Dr. Julia Brumaghim at Clemson University, we are exploring the application of complexes of S and Se as potential antioxidants by investigating a mechanism of protection in which the antioxidant of interest (i.e., a **S or Se-containing compound**) coordinates with a metal of interest in the body (e.g., Fe^{2+}), **thereby preventing the ROS formation**. As model systems, we are investigating compounds *N,N'*-dimethylimidazole thione (*dmit*) and selone (*dmise*), as well as methimazole (*MetIm*). Our results to date using PCR and gel electrophoresis demonstrate that these compounds protect DNA, evidenced by continued successful replication of DNA after exposure to ROS. This summer we will focus on the development of new assays using UPLC-MS and RT-PCR.

We have collaborated with Dr. Noel Kane-Maguire, Professor Emeritus, to show that in addition to preventing damage, complexes like $[Cr(diimine)_2DPPZ]^{3+}$ (where DPPZ = dipyridophenazine) can intercalate with B-DNA, with significant binding affinities ($K_{DNA} > 10^5$). When excited by UV light, **these complexes have demonstrated they can induce DNA damage and thus have promise as chemotherapeutic agents**. In some cases, monodentate ligands (i.e., 1-methylimidazole) have been substituted, and following excitation by UV light, permanent DNA adducts to DNA have formed. We use a various bioanalytical techniques to characterize the nature of the Cr(III)/DNA interactions including isothermal titration calorimetry, PCR, capillary electrophoresis, and UPLC-MS.

(2) Complex biocide formulations including agents such as polyhexamethylbiguanide (PHMB) are routinely used in contact lens solutions (MPS) and other personal care products to prevent bacterial infections. The concentrations required to be effective are quite small, however, and the majority of these agents do not absorb UV light well, creating a challenging problem for quantitation. We work with the U.S. Food and Drug Administration (FDA) and a private manufacturer of PHMB **to develop novel strategies for analysis of commercial PHMB formulations,** including studies of efficacy, adsorption, and release related to sterile materials using a variety of methods including solid phase extraction (SPE), size-exclusion chromatography (SEC), and UPLC-MS. Improving our understanding of how the structure of these biocides affects their effectiveness is critical to designing safe and effective treatments for the future.

(3) In our most recent project, we are working with a local company to explore the potential application of mushrooms to **bioremediate** soils rendered toxic by the over-application of certain pesticides (e.g., atrazine and diuron) or other organic contaminants which could affect human health. Mycologists are working directly with students in the Wheeler lab to develop analytical strategies aimed at isolating, identifying, and quantifying these compounds and then subsequently **examining uptake/bioaccumulation, metabolism, and the potential for remediation using these natural fungi**. This is possible because fungi do not rely on photosynthesis for energy; thus, pesticides that work by interfering with photosynthesis have little toxic effect on mushrooms. To this point, we have characterized the enzymatically-produced breakdown products of pesticides using three mushroom species and are working to gain an increased understanding of the relationship of fungal growth cycle to maximum rate of remediation.