The Green Research Group works at the interface of Chemistry, Biology and Physics and thereby provides extensive training and collaborative opportunities for students in our program. Our research team employs organic and inorganic synthetic methods along with spectroscopic and analytical techniques (electrochemistry, XRD, NMR, UV-Vis and others) to target current challenges in biomedicine and chemical industry. We complement our synthetic work with cellular biology, physical inorganic methods (EPR, advanced NMR, determination of binding constants, and computational methods), and studies carried out with animal models (murine to date). Our current research foci include the development of small molecules that can target diseases involving oxidative stress and/or metal-ion mis-regulation, such as Alzheimer’s. We are also working toward the development of responsive electrochemical biosensors for biomarkers associated with cancer and MRI contrast agents for diseases such as cancer, Alzheimer’s and others. Finally, we are developing a new class of metal-based complexes that can be used to study and ultimately optimize C-C and C-H transformations in organic chemistry. We work collaboratively with TCU Biology and Physics, UNT Health Science Center, UT Southwestern Medical Center, Oklahoma Southwest State University, The Max Planck Institute, and others to carry out thorough studies related to our goals.

Coordination Chemistry and Catalysis Polyaza macrocycles represent a versatile family of ligands used across a wide variety of fields thanks to the ability to form stable complexes with both transition metal and lanthanide metal cations. Nature exploits tetraza-macrocycles for a range of chemical processes including oxygen transport (Hb/Mb), organic transformations (CyP 450), and radical chemistry (B12). The promiscuous metal-binding nature of the cyclic aza backbone is largely responsible for the adaptable reactivity observed in this class of molecules. The specific chemical reactivity of a macrocyclic complex can be dictated by the metal-ion bound and whether or not the metal center is redox active. The geometry of the metal coordination sphere and corresponding redox activity can be modulated by the cavity size, denticity, flexibility, and the presence of substituents on the macrocyclic ligand. Our team uses these observations to make manipulations to ligands to provide desired activities.

The Green Research Group is interested in producing new N-heterocyclic amine systems, such as L2 and L3, as a means of exploring fundamental inorganic coordination chemistry as well as exciting applications of these ligand sets. To date we have explored a range of transition metal derivatives of L2 and L3 to understand how the electronic nature of the metal center is altered by a subtle change in the structure of the pyridine ring. We have also observed interesting electrochemistry, novel structural motifs and catalytic C-C coupling activity within the series studied to date. We are currently focused on novel ligands, new catalytic reactions, and transitioning these ligands to be used as MRI contrast agents.
Therapeutics for Neurodegenerative Disorders

Alzheimer’s disease and other neurodegenerative disorders are known to develop as a product of unregulated levels of reactive oxygen species (ROS). Therapeutics providing more than only symptom relief by targeting the molecular features of these diseases are currently not available. Therefore, there is an immediate need to develop molecules that can cross the blood brain barrier and serve as antioxidant components to halt the oxidative damage responsible for neuronal death and neurodegeneration. Our group has utilized the pyridol backbone which has long been known to possess antioxidant capacity and is used ubiquitously by nature (tannins) for these purposes. Pyridine and pyridol moieties can quench multiple ROS species, with the former being able to isolate oxygen containing molecules and the later also being able to serve as a radical scavenger. We have synthetically combined this pyridol moiety with amine ligands having affinity for metal ions known to cause ROS.

Our small molecules to date are capable of both disrupting and preventing the metal(II)-induced formation of beta-amyloid plaques in vitro by binding metal ions. In addition, the N-heterocyclic backbones possess antioxidant and radical scavenging properties, and demonstrate the ability to protect cells (FRDA, HT-22 Neuronal) against death induced by reactive oxygen species and/or amyloid. We also use animal models to explore the impact of our molecules on the cognitive and physical features of disease.

Development of Electrochemical Biosensors

Imaging modalities such as MRI are excellent for studying the structure of cancer and other diseases. However, they do not provide molecular information regarding the metabolic activity of the disease which could prove invaluable in evaluating therapeutic strategies for patients. The Green Group is developing small molecule, electrochemical sensors to evaluate molecular features of disease. To date, a library of biotin-ferrocene bioconjugates has been produced as a model for the electrochemical detection of biomolecules. The results show an interesting response in current, specific for avidin-biotin interactions and indicate that nM levels of analyte can be detected using square wave techniques. We are now focusing on the development and optimization of responsive bioconjugates for the detection of biomarkers associated with cancer, specifically enzyme responsive devices. To do this we use solid-phase peptide synthesis methods to produce our bioconjugates and evaluate the systems via electrochemistry and electron microscopy.

Selected Publications and Patents


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