

American Chemical Society-South Florida Section



SoFlacs



CH_{emical Sciences Symposium}

Elements of Life-II

Atomic masses in parentheses are those of the most stable or common isotope.

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ABSTRACTS

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South Florida Section American Chemical Society

Chemical Sciences Symposium

8:30 AM to 3:30 PM, Saturday, March 14, 2009

**Nova Southeastern University, Ft. Lauderdale
Health Professions Division, Terry Building, Auditorium-A**

Theme: Elements of Life-II

8:30-9:30 AM: Registration, Putting up Posters (**coffee and donuts: Courtesy of NSU**)

9:30-10:00 AM: Introductions

Invocation of the Symposium: Dr. Ronald Block (Professor and Chair, Department of Biochemistry, College of Medical Sciences, NSU)

Welcoming by SoFL-ACS Chair, Dr. Rose Mary Stiffin

Poster judging and awards, Symposium Co-Organizer, Professor of Chemistry, Dr. George Fisher

Introductions to Elements of Life-II, Symposium Organizer, Professor, Dr. K.V. Venkatachalam

Symposium Speakers:

10:00-10:45 AM: **Iron, Dr. Jaroslava Miksovská**, Assistant Professor, Department of Chemistry and Biochemistry, Florida International University, Miami, FL, on **“Iron Metabolism in relation to myoglobin/hemoglobin”**

10.45-11.30 AM: **Copper, Darryl Horn** (student) and **Dr. Anthony Barientos**, Associate Professor, Department of Neurology and Biochemistry and Molecularbiology, University of Miami Miller School of Medicine, University of Miami, Miami, FL, on **“Role of Copper in mitochondrial metabolism”**

11:30 AM-1:30 PM: **Poster Session along with Lunch (pizza, soda, snacks: courtesy of NSU)**

1:30-2:15 PM: **Selenium, Dr. William T. Self**, Assistant Professor, Department of Molecular Biology and Microbiology, Burnett School of Biomedical Sciences, College of Medicine, University of Central Florida, Orlando, FL, on **“Se nutrition and its role in mammalian cells”**

2:15-3:00 PM: Scientific Social: question/answers, net working, future ideas, suggestions.

3:00-3:30 PM: **Awards Ceremony - awards for student posters and appreciation to speakers**

Iron Metabolism in Relation to Myoglobin/Hemoglobin

Jaroslava Miksovska

Department of Chemistry and Biochemistry
Florida International University

Heme proteins are one of the most widely distributed metalloproteins in nature that are able to participate in the wide range of the biochemical reactions in the cell including catalytic reaction, signal detection, electron transport, gas storage and transport, and storage of small gaseous molecules. Such versatility is accomplished through a structure nature of protein matrix including variation in the heme iron ligation and fine-tuning of the polarity and/or accessibility of the heme-binding pocket. Recently, several approaches have been adopted to understand the structure-function relationship in heme proteins including computational, spectroscopic and site-directed mutagenesis techniques. Here, I will present the application of the photothermal techniques, photoacoustic calorimetry and photothermal beam deflection, to probe the conformational dynamics association with the ligand dissociation/binding to the heme proteins in term of time-resolved volume and enthalpy changes. Specifically, the thermodynamic profiles for structural changes associated with ligand dissociation/rebinding the to active center will be presented for oxygen storage proteins, oxygen sensors and peroxidases family and discuss in term of the relationship between the dynamic transitions in proteins and their function.

Mitochondrial copper metabolism and delivery to cytochrome c oxidase

Darryl Horn¹ and Antoni Barrientos^{1,2}

Department of Biochemistry & Molecular Biology¹, Department of Neurology², University of Miami Miller School of Medicine, Miami, FL 33136, USA.

Metals are essential elements of all living organisms. Among them, copper is required for a multiplicity of functions conserved from yeast to humans including mitochondrial oxidative phosphorylation and protection against oxidative stress. A network of transporters strictly controls the trafficking of copper in living systems. Once within the cell, copper is sequestered by metallothioneins (such as Cup1p and Crs5p), directed for proper copper detoxification, or delivered to the sites of its utilization, such as cytochrome *c* oxidase (COX), by specialized proteins called copper chaperones. COX is a mitochondrial metalloenzyme acting as the terminal enzyme of the mitochondrial respiratory chain. The catalytic core of COX is formed by three mitochondria-encoded subunits and contains three copper atoms. Two copper atoms bound to subunit 2 constitute the Cu_A site, the primary acceptor of electrons from ferrocycytochrome *c*. The third copper, Cu_B, is associated with the high-spin heme *a*₃ group of subunit 1. Recent studies, mostly performed in the yeast *Saccharomyces cerevisiae*, have provided new clues about 1) the source of the copper used for COX metallation; 2) the roles of Sco1p and Cox11p, the proteins involved in the direct delivery of copper to the Cu_A and Cu_B sites, respectively; 3) the action mechanism of Cox17p, a copper chaperone that provides copper to Sco1p and Cox11p; and 4) the existence of at least four Cox17p homologues carrying a similar twin CX₉C domain suggestive of metal binding, Cox19p, Cox23p, Pet191p and Cmc1p, that could be part of the same pathway. The different pathways are reviewed and discussed in the context of both mitochondrial COX assembly and copper homeostasis.

Targeting Selenium Metabolism for Novel Drug Discovery

Sarah Jackson-Rosario, Sarah Meno, Dennis Ganyc and William T. Self

Burnett School of Biomedical Science, College of Medicine, University of Central Florida,
Orlando, Florida, 32816. Email:wself@mail.ucf.edu

Selenium is a required micronutrient for mammals, as it plays an important role at the catalytic centers of several enzymes important for defense against reactive oxygen species. As such, the efficient uptake and metabolism of selenium for synthesis of selenoenzymes is critical to oxidative stress defense. In bacteria, selenoproteins can play a critical role in energy metabolism, and this role may allow for novel drug discovery to target selenium-dependent pathogens such as *Clostridium difficile*. In the post-genomic era we now have a better understanding for the diversity of selenoproteins, both in prokaryotic and eukaryotic systems, yet the role of several selenoproteins is still unknown. Intracellular selenium is most often found in the conjugated form selenocysteine (regarded as the 21st amino acid), incorporated during translation in bacteria, archeabacteria or eukaryotes. This incorporation is tightly regulated, and currently being studied in several model systems. The metabolic precursor for this pathway is hydrogen selenide (HSe⁻), an unstable and oxygen sensitive form of selenium. Our work has focused on the metabolism of selenium upstream of the pathway for incorporation of selenium into selenoproteins, since the uptake and reduction of selenium is poorly understood. Moreover, evidence has accumulated that other metalloids (arsenic) and metals (lead, mercury, cadmium) can alter the metabolism and nutrition of selenium in animal models. We have studied recently the impact of arsenicals on selenium metabolism and these results will be presented and discussed. By serendipity, we found a novel compound that efficiently blocks the metabolism of selenium in several model organisms, and this finding has led to a drug discovery effort to target selenium dependent pathogens. The central theme of this work is the metabolism of selenium, and the potential ramifications in arenas of nutrition, toxicology and antimicrobial drug development will be discussed.

Characterization of Ca^{2+} Photorelease from DM-Nitrophen Using Photothermal Beam Deflection

Gangadhar Dhulipala and Jaroslava Miksovska
Department of Biochemistry, Florida International University, Miami, FL

DM-nitrophen is one of the important caged calcium compounds which is generally used in time resolved physiological studies for systematic manipulation of calcium and are capable of raising calcium from 100nM to levels in the range of 50-100 μM . Here we studied the rate of decay of acinitro intermediates from Dm-nitrophen in the presence of calcium using photo thermal beam deflection. Photo-dissociation of DM-nitrophen results in a fast phase associated with the formation of the acinitro intermediates and a slow phase associated with decay of acinitro intermediates. Appearance of acinitro intermediates resulted in a volume contraction of $-7.6 \text{ mL mole}^{-1}$ and an enthalpy change of $65.6 \pm 9.2 \text{ k.cal mole}^{-1}$ whereas the decay of acinitro intermediates resulted in a volume expansion of $7.1 \pm 0.09 \text{ mL mole}^{-1}$ and an enthalpy change of $-18.8 \pm 10 \text{ k cal mole}^{-1}$. We determined the rate constants at different temperatures for the decay of acinitro intermediates, which are in the range of $5.2 \times 10^3 \text{ s}^{-1}$ at 16°C to $13.8 \times 10^3 \text{ s}^{-1}$ at 35°C and the corresponding activation energy is found to be $36.1 \text{ k.joule.mole}^{-1}$. In contrast to the conventional methods used to determine the rate of decay of acinitro intermediates, with our technique we are also able to measure the volume and enthalpy changes associated with formation and decay of acinitro intermediates.

“Identification of the Microorganisms by Attenuated Total Reflection Second Derivative Infrared Spectroscopy”

Michele Gonsalves, Katerina Jiskrova, Frank Amiama, Earl Sealy and Khalique Ahmed,
Department of Science, Lynn University, 3601 North Military Trail, Boca Raton, FL, 33431

The identification of micro-organisms is important in the monitoring of the infectious diseases and in the understanding of the changes in the resistance patterns of the known microorganisms. The traditional method of microorganism identification involves inspection of colony morphology of the cells cultured on the solid media followed by the microscopy of the Gram-stained preparations. This method is time consuming and may take up to 2 to 3 days for completion. In an effort to develop a simple and efficient physical method for the identification of the microorganisms we have studied the Fourier transform attenuated total reflection (FT-ATRIR) spectra of six microorganisms namely: *Serratia marcescens*, *Proteus mirabilis*, *Corynebacterium xerosis*, *Bacillus subtilis*, *Mycobacterium smegmatis* and *Saccharomyces cerevisiae*. The absorbance spectra of the thin films of the microorganisms display fingerprint peaks due to the cell constituents (RNA/DNA, protein, cell wall components etc.). The spectral differences between the microorganisms were more pronounced in the second derivative spectra. Notable spectral differences were noted in the peptide linkage peaks of proteins, CH stretching peaks of the lipids and NH stretching peaks of the proteins. Future studies involving FT-ATRIR spectra of a large number of microorganisms combined with data analysis techniques of cluster and multivariate analysis may lead to an alternative method for the identification of the microorganisms of biomedical interest.

Dynamics and Energetics Associated with Ligand photodissociation from CO Bound Chloroperoxidase

Simona Horsa, Jaroslava Miksovska, Xiaotang Wang, Lin Jiang
Department of Biochemistry, Florida International University, Miami, FL

Chloroperoxidase is the most versatile heme peroxidase that can function as peroxidase, catalase, halogenase and monooxygenase. The active site of the protein strongly resembles to cytochrome P₄₅₀ since the heme iron in chloroperoxidase is five-coordinated with Cys 29 in the position of the axial ligand. Two hydrophobic channels that connect the heme binding cavity with the surrounding are likely to provide ligand access into the active site. At alkaline pH the protein undergoes conformational transition resulting in the population of six coordinated heme iron with the histidine residue in the position of the sixth ligand. Here we report the results of the photoacoustic study of the ligand dissociation from the chloroperoxidase. The ligand photodissociation and migration out of the protein matrix occurs within 50ns and no additional kinetics were determined between 50 ns and 5 μ s. At acidic pH ligand dissociation is associated with a positive volume change ($\Phi\Delta V = 10.9 \pm 0.9 \text{ mL mol}^{-1}$) and enthalpy change $\Phi\Delta H = 24 \pm 5 \text{ kcal mol}^{-1}$, strongly indicating that the ligand release from the protein does not result in significant changes in protein structure and the ligand likely migrate through one of the hydrophobic channels. On the other hand, the thermodynamic parameters associated with CO photorelease at pH 10 are significantly smaller than those determined at acidic pH ($\Phi\Delta V = 3.2 \pm 1.1 \text{ mL mol}^{-1}$ and $\Phi\Delta H = -12.1 \pm 5.3 \text{ kcal mol}^{-1}$) due to the changes in heme coordination upon CO dissociation.

“The Green Synthesis of a Family of Potential Anti-HIV Drugs: (2Z) – 2 – [(Dimethoxyphenyl) methylidene] – 3H – Inden – 1 – ones”

Ana Major and Oluwasimidele Okanlami, Rose Mary Stiffin, PhD.,
Florida Memorial University, Miami Gardens, FL

The purpose of this study was to synthesize a series of compounds that may serve to target the HIV-1 protease enzyme, which processes most of the proteins in the HIV genome. These compounds, synthesized by a solventless, based catalyzed condensation between different dimethoxybenzaldehydes and 1 – indanone, were characterized based on melting point, chromatographic methods, and mass spectrometry. They were prepared by aldol condensation, a hallmark of organic chemistry synthesis. The route of synthesis, purification, and characterization of each drug will be presented. The compounds will be tested as potential antiviral drugs by The Scripps Research Institute of Florida.