Inorganic biochemistry:
Metal complexes of proteins, peptides and ligands

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- Metal interactions with natural peptides and proteins

The research lies at the interface of inorganic chemistry and biochemistry, and is directed toward understanding the interaction of metal ions with proteins and other biological molecules. The overall goal of these studies is to determine the chemical basis (binding, reactions, structural effects) for the biological roles and physiological effects of metal ions. Much of our current research focuses on the coordination chemistry of proteins and peptides, which are potential ligands for metal ions. Our approach involves quantifying metal ion binding to a protein or selected peptide sequence, and then using spectroscopic and physical methods to characterize the resulting metal-protein/peptide complex.

- Molecular mechanisms of metal-related toxicity and carcinogenesis:

Ni(II) compounds are well known as human carcinogens, though the molecular events which are responsible for this are not yet fully understood. It has been proposed that the binding of N(II) ions within the cell nucleus is a crucial element in the mechanism of carcinogenesis. The most abundant proteins in the cell nucleus are histones, and this makes them the prime candidates for this role.

- Chelating agents for toxic metals and effect of toxic metal on biomolecules

Chelation therapy is the preferred medical treatment for reducing the toxic effects of metals. Chelating agents are capable of binding to toxic metal ions to form complex structures which are easily excreted from the body removing them from intracellular or extracellular spaces.

- Role of metal ions in biochemistry and chemistry of metal-based drugs

Metal ions are required for many critical functions in humans. Scarcity of some metal ions can lead to disease. The ability to recognize, to understand at the molecular level, and to treat diseases caused by inadequate metal-ion function constitutes an important aspect of medicinal bioinorganic chemistry.

Metal ions can also induce toxicity in humans, classic examples being heavymetal poisons such as mercury and lead. Even essential metal ions can be toxic when present in excess. Understanding the biochemistry and molecular biology of natural detoxification mechanisms, and designing and applying ion-specific chelating agents to treat metal overloads, are two components of a second major aspect of the new science that is evolving at the interface of bioinorganic chemistry and medicine.

- Metal ions in neurodegeneration

Neurodegenerative disorders include a variety of pathological conditions, which share similar critical metabolic processes such as protein aggregation and oxidative stress, both of which are associated with the involvement of metal ions.

Numerous studies have established a clear connection between neuronal oxidative stress and several neurodegenerative diseases, with consequential damages to lipids, proteins, nucleic acids, etc. In addition, several

modifications indicative of oxidative stress have been described in association with neurons, neurofibrillary tangles and senile plaques in Alzheimer's disease, including advanced glycation end products and free carbonyl oxidation. A connection between genetic and environmental causes of Parkinson's disease (PD) has been recently reported. There is considerable evidence that excess of environmental and occupational exposure to Mn(II) (i.e. in miners and welders), induces symptoms that resemble Parkinson's disease, called Parkinsonism or manganism, by attacking the central nervous system.

Methods

Peptide synthesis

Potentiometric measurements

Spectroscopic measurements: UV-Vis, NMR, EPR, CD

Computational chemistry in peptide and protein structure calculations

Publications

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