Satellite Minisymposium: Metal Ions – Health and Food

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Changes of Biological Significance Induced by Metal Ions in the Structure of Nucleic Acids and Nucleotides

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We have previously shown that the action of metal ions on nucleic acids leads to a variety of perturbations in secondary structure, including crosslinking, mispairing, and degradation. We have demonstrated that metal ions also have a profound effect on the way in which nucleic acid molecules are packed together into highly organized aggregates [1]. These studies, along with those that reveal that metals also influence the enzymes that act on nucleic acids (such as cleavage enzymes and RNA polymerase) indicate how changes in cellular concentrations of metal ions can impact on cellular processes that depend on genetic information transfer.

Many of the effects of metals on nucleic acids or other biomacromolecules involve conformational changes. We have recently been concerned with the ability of metal ions or complexes to induce interconversions among at least four nucleic acid conformers [2]. These studies were carried out with poly(dGdC)·poly(dGdC), which can exist in the Z-conformation, and we have discovered that conversion to Z-DNA can lead to further conversions to other DNA structures. These structures are all in equilibrium with each other, but each can be stabilized under appropriate conditions of nucleic acid and metal concentration. These conformational transitions are important because the biological activity of nucleic acids depends on their conformation. We have shown that different conformations of DNA have different activities as template for RNA synthesis.

It has been reported that the progress of Alzheimer's disease, the most prevalent form of senile dementia, is associated with the accumulation of aluminum in the chromatin of the brain [3, 4]. We have found that Al forms crosslinks between DNA strands and that Al binding to DNA in chromatin can be monitored by nuclear magnetic resonance (NMR). Al has also been implicated in dialysis dementia [5] through binding to ATP [6]. We have found by multinuclear NMR studies that Al forms four different complexes [7] with ATP. ^{27}Al NMR is very sensitive to the chemical environment of Al and can be used in the identification of Al complexes in equilibrium with each other in a variety of systems of biological interest [8].

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Nickel Carcinogenesis

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Increased incidences of cancers of the lung, nasal sinus, larynx, and possibly kidney have occurred among workers in nickel refineries: the identity of the nickel compounds that produce cancers in nickel workers remains uncertain, although principal attention is focused on (a) insoluble dusts of nickel subsulfide (Ni_3S_2) and nickel oxide (NiO), (b) the vapor of nickel carbonyl ($Ni(CO)_4$), and (c) soluble aerosols of nickel sulfate ($NiSO_4$) or nickel chloride ($NiCl_2$). Cancers have been induced in experimental animals by several nickel compounds by a variety of routes, including (a) lung cancers by inhalation of $Ni(CO)_4$ and Ni_3S_2 in rats, (b) sinus cancers by implantation of Ni_3S_2 in cats, (c) renal cancers by implantation of Ni_3S_2 in rats, and (d) sarcomas by im injection of Ni_3S_2 in mice, rats, hamsters, and rabbits. In the author's laboratory, 18 nickel compounds have been tested for carcinogenicity in male Fischer rats by a single im injection at equivalent dosages (14 mg Ni/rat). Within two years, the following incidences of sarcomas developed at the injection site: Ni_3S_2, 100%; crystalline NiS, 100%; Ni_4FeS_4, 100%; NiO,