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Fe(II) Complexes Containing Bioactive Ligands: Synthesis, DNA Binding, and Cleavage Studies

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The two Fe(II) complexes of fused aromatic N and S containing ligands of the type $[Fe(HMq)_3](PF_6)_2$ [complex (1)] and $[Fe(HSeq)_3](PF_6)_2$ [complex (2)] (where HMq = 2-mercapto-4-methylquinoline and HSeq = 2-seleno-4-methylquinoline) were synthesized and structurally characterized. The DNA binding property of the complexes with calf thymus DNA has been investigated using absorption spectra, viscosity measurements, as well as thermal denaturation experiments. Intrinsic binding constant K_b has been estimated at room temperature. The absorption spectral studies indicate that the complexes intercalate between the base pairs of the CT-DNA tightly with intrinsic DNA binding constant of 1.9×10^6 M^{-1} for complex (1) and 2.5×10^6 M^{-1} for complex (2) in 5 mM Tris-HCl/50 mM NaCl buffer at pH 7.2, respectively. Detailed analysis revealed that the metal complexes intercalates into the DNA base stack as intercalator. The oxidative cleavage activity of the complexes (1) and (2) were studied by using gel electrophoresis and the results show that complexes have potent nuclease activity.

Keywords cleavage studies, DNA binding, Fe(II) complexes

INTRODUCTION

The transition metal complexes of ruthenium, rhodium, palladium, copper, nickel, and cobalt have shown DNA (deoxyribonucleic acid) binding and cleavage activities.[1−7,51−53] In addition, these metal complexes have been found to be useful for design and development of synthetic restriction enzymes, new drugs, DNA footprinting agents, etc. [8−16] because of their potential to bind DNA via a multitude of interactions and to cleave the duplex by virtue of their intrinsic chemical, electrochemical, and photochemical reactivities. The literature survey reveals that when a photosensitizing ligand and a DNA binder are covalently bonded to a metal center, the complex becomes cleavage-active.[17] Chakravarty et al.[18] reported that DNA binding and cleavage activity of metal complexes containing sulphur ligands act as photosensitizers. They found that the photosensitizing effect is greater when the sulphur is bound to the metal center and the concerned moiety lacks π-conjugation. The choice of sulphur-containing ligand[19−21] is based on the fact that thio or thione moieties are known to show efficient intersystem crossing to the triplet state.

From a chemical point of view, selenium (Se) resembles sulfur (S) in many of its properties.[22,23] Thus, Se and S may be considered to be isosteric, as originally defined by Langmuir in 1919. Studies examining the relationship between the intake of dietary selenium and the risk of various cancers have shown that low selenium intake is associated with higher cancer rates, including liver cancer. In addition, the naturally occurring selenium-containing amino acids and fused synthetic organoselenium compounds shows anticancer, anti-inflammatory, antitumor activities, and other medicinal applications.[24−26] It also plays an important role in decreasing oxidative stress in HIV-infected cells and possibly suppressing the rate of HIV replication.[27]

The DNA cleavage reactions are generally targeted towards its basic constituents, viz.heterocyclic base, sugar and phosphate, where the reactions are targeted to the phosphodiester linkage proceed via hydrolytic cleavage pathways leading to the formation of fragments that could be regulated through enzymatic processes. The DNA cleavage by nucleobase oxidation or degradation of sugar by abstraction of sugar hydrogen atom(s) follows oxidative reaction pathway.[28]

The development of organoselenium compounds with higher anticarcinogenic efficacy, but better tolerance, continues to be a priority in chemotherapy research. In this view, our research

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