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STUDIES ON THE DNA BINDING ACTIVITY OF SCHIFF BASE DERIVED COMPOUNDS

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ABSTRACT

In the present investigation an attempt was made to investigate the DNA cleavage activity of some newly synthesized Metal based Ruthenium and Copper complex Schiff base compounds using calf thymus DNA by gel electrophoresis method.

KEYWORDS: Ruthenium and Copper complex Schiff.

INTRODUCTION

Nucleic acid chemistry related to cleavage and synthesis of DNA and RNA has received considerable attention in the field of recombinant DNA technology and medicinal chemistry. Nucleases and polymerase are enzymes that play an important role in these fields. Nucleases are enzymes/biocatalysts that specifically act on nucleic acids (DNA/RNA). These catalysts require specific and accurate conditions like pH, concentration of substrate or catalyst, temperature etc. and are also depends on redox reactions. Cleavage and ligation of nucleic acids (especially in DNA) play an important role in gene regulation and disease/pathogen control. The cleavage of nucleic acids can be achieved through both chemical and enzymatic methods, of which second one is more accurate, site specific and frequently used method. But now a day's use of metal based drugs that having nucleic acid binding and cleavage activity and also gene regulation activity are gaining more importance (100) as most of them are having potent biochemical and biomedical applications.

In the field of medicinal inorganic chemistry there is increasing prominence of metal base compounds offer possibilities for the design of the therapeutic agents not readily available to organic compounds. The intrinsic properties of the cationic metal ion and ligand itself offer the medicinal chemist a wide spectrum of relativities that can be exploited in a wide range of coordination number, geometries, accessible redox states thermodynamic name and kinetic characteristics. In a more or less empirical fashion metals have long been used for medicinal purposes.[2]

These include metal complexes of Ru (II).[3-4] Rh III[5-6] and Ni (II)[7] complexes that cleave DNA by the effect of light on the interaction of chromium[8] cobalt[9,10] rhodium[11] and ruthenium[12-13], were investigated.

Covalent interactions of ruthenium (II) complexes is with DNA were studied using $Ru(NH_3)_2^{2+}$ fragments coordinated gaunosine derivatives.[14]

DNA interactions by Ruthenium complexes

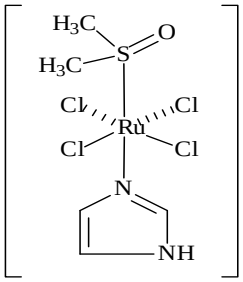
For designing and developing better probes for disguises and drugs for cancer therapy the studies of the interactions of small molecules with DNA are essential. Ruthenium complexes shown potential utility in chemotherapy.[15-17]

Ruthenium complexes generally have lower toxicity compared to cisplatin attributed to their Specific accumulation in cancer tissues.[18-20]

Ruthenium complexes in vitro and in vivo studies show high anticancer activity and some of them are currently undergoing clinical trials.[21-22]

It has been reported that trans is active against tumour metastases although this compound has a low cytotoxicity against cancer cells.[23]

Ru (II) complex is coordinated by arene ligands also exhibit promising anticancer activity Thought to be due to the hydrophobic arene ligand which enhances the biomolecular recognition processes and transport of ruthenium through cell membrane. The cytotoxicity of chair octahedral polypyridine ruthenium (II) complexes has been focused. It has been reported that polypyridine ruthenium (II) complexes with enlarged aromatic ring system can bind to double stand heliz in intercalating, groove binding and electrostatic binding modes[24-25] to make a change on conformation of DNA molecules.[26]



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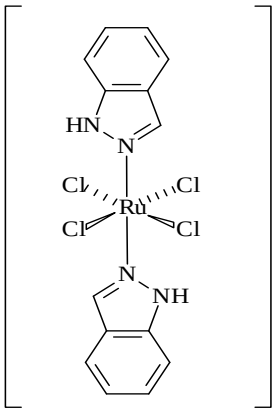

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They are ideally suited for application as sensitive non covalent probes for polymer structure since ruthenium complexes are H_2O soluble coordinatively saturated and inert substitution moreover polypyridyl complexes of ruthenium are intensely coloured due to localized metal to ligand charge transfer transition (MLCT). This MLCT transition is particular important as it is perturbed when the complex interacts with DNA providing a spectroscopic probe. However the DNA strand break via electron transfer was shown by some ruthenium complexes in their excited states.[26]

Hence in the present investigation an attempt was made to investigate the DNA cleavage activity of some newly synthesized compounds using calf thymus DNA.

MATERIALS AND METHOD

Schiff bases are synthesized in the Department of Chemistry, Kakatiya University, Warangal were primarily tested for DNA binding studies.

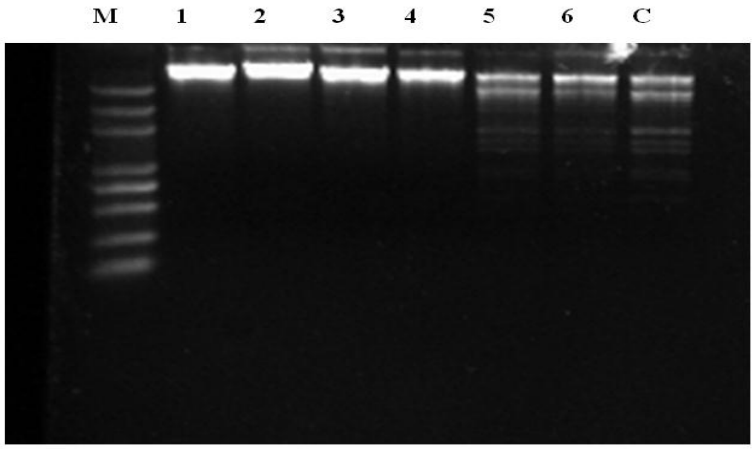
Experimental

Add 15ml of lambda DNA and 10ml each sample collected from rats serum (for –ve control no sample is added and for control 10ml cisplatin is added) separately in an eppendorff. Incubate at $37^{O}C$ for 8 hrs. Then add 10ml enzyme buffer +5ml of Ecor1 & third III enzyme + 25ml distilled H_20 then incubate at $37^{O}c$ for 12 hrs.

After incubation terminate the reaction by incubating the sample at $65^{0}C$ then mix the content with Bromophenol dye and separate through electrophoresis and the gel was documented by gel documentation system.

RESULTS AND DISCUSSION

The interaction of these compounds with CT-DNA was investigated by gel electrophoresis as shown in the figure 1. From the observation Cu(II) and Ru(II) complexes can effectively cleave the DNA when compared to the ligands in the presence of an oxidizing agent H_2O_2. This result indicates that, these metal complexes are having potent DNA cleavage activity and can be used in drug preparation.



M = Molecular Weight, 1 = $RuSP_1$, 2 = $RuSP_2$, 3 = $RuSP_3$ 4 = $CuAL_7$, 5 = $CuAL_5$, 6 = $CuAL_6$,

Fig. 1: Gel electrophoresis of schiffs bases.

CONCLUSION

Cu(II) and Ru(II) complexes can effectively cleave DNA when compared to the ligands. Schiff base derivatives of Ru and Cu compounds showed good anticancer activity. These metal complexes can be used as anticancer agents in future.

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