An overview

About Coordination Chemistry

The growth of coordination chemistry is not restricted itself in a single dimension, instead of three dimensional, encompassing the breadth, depth and application. It is difficult to arrest in a single page about the developments in three-dimensional growth of coordination chemistry except some selective ones. Coordination chemistry was not handicapped in extending its developments as application in various fields. Thus present research work in coordination chemistry around the world is much more devoted towards the application of coordination compounds in various fields along with their structural diversity in various new ligand environments rather than only on theory of bonding and structure in coordination compounds that early workers were devoted. Coordination compounds are of great scientific interest and play an important role in many biological processes [1,2]. The rapidly developing field of bioinorganic chemistry is centered on the presence of coordination compounds in living systems. The rapid growth of interest in recent years in the chemistry of metal complexes (with ligands of biological origin) is due to the extremely important role which metal ions play in biological processes. Progress in coordination chemistry is concomitant with the growth in the number of complexes used in industry, agriculture, medicine, domestic life, etc. On account of the virtually limitless scope for synthesizing new compound, coordination chemistry ensures a constant improvement in the exploitable properties of the available compounds. It is probable that the trends in extensive scientific research into the use of coordination compounds and the developments in this field will continue to flourish and prosper. Progress in this direction has to go hand in hand with a much better understanding of the chemistry involved. It is clear from the above facts that the discovery of coordination compounds and their applications is only the beginning and this promises to be of great interest from many aspects.
About Transition Metal Complexes

Transition metal chemistry is an integral part of coordination chemistry and its ever growing importance and applications encompass many fields. Transition metals form an important part of bioinorganic chemistry, being essential to life, and also with the spawing of newer uses in organic synthesis. Among the transition metal ions, Co(II), Ni(II), Cu(II) and Zn(II) have drawn much more attention of various research groups around the world. Hence it becomes necessary to present a brief note about the selected metal ions which have been employed during the present work.

Cobalt occurs in the oxidation states +1 to +5 with +2 and +3 being most predominant and relevant. It is a trace element in animal nutrition. There are four possible, distinct stereo chemical configurations viz, octahedral, square planar, tetrahedral, trigonal bipyramidal or tetragonal pyramidal through which Co(II) complex may appear. Vitamin B$_{12}$ contains benzimidazole nucleus attached to Co(II) ion via ring nitrogen. Co(II) complexes with varying donors have shown to be antimicrobial by Efthimiadou [3]. Co(II) complexes also have some synergic effects on certain antibiotics notably penicillin.

Nickel occurs in the oxidation states +1 to +4 with +2 being most common and relevant biologically. It is less toxic than its soluble salts. The chronic toxicity results in degenerative changes in the heart muscles, brain, lung, liver and kidney tissue and can result in cancer [4]. The great interest in Ni(II) complexes arised from the possibility of their existence in different stereo chemical configurations, viz., square planar, tetrahedral and octahedral. These forms are capable of manifesting complicated equilibria, which are dependent on the nature of the solvent, concentration and temperature Nickel(II) chelates play its biological role in nutrition, enzyme activation, hormone action, structural stabilities of biological macromolecules and in general metabolism [5].
Copper is one of the most abundant elements on the earth and occurs in a wide range of oxidation states ranging from 0 to +4 with +2 as the common oxidation state. In 3d^9 configuration Cu(II) undergoes Jahn –Teller distortion when placed in an environment of cubic symmetry (i.e. regular octahedral or tetrahedral) and this has profound effects on its stereochemistry. In six coordination, the octahedral geometry, is severely distorted. Typical distortion is an elongation of one fourfold axis, so that there is planar array of four short Cu-L bonds and two trance long ones. This kind of distortion may lead to a situation where an octahedral geometry becomes indistinguishable from square planar coordination. Hence the case of tetragonally distorted octahedral coordination and square coordination cannot be easily differentiated. Apart from the above sterric effect in ligands is also one of the factors for the distortion. Copper is an essential component of metalloenzymes and plays a vital role in structure and functions of nervous system and maintenance of skeletal and vascular system. Copper(II) usually binds to proteins in living organisms and increases the cellular permealibility of erythrocytes, disturbing the enzyme system. This causes nausea, vomiting epigastric pain etc. in the patient [6]. Cu(II) complexes have shown promising activity such as anti-HIV and anti-cancer [7].

Zinc is the last member of the first transition series with the electronic configuration [Ar]3d^{10}4s^2. It exhibits +2 state in its coordination compounds. Zn(II) is known to form complexes, which are essentially diamagnetic due to filled d^{10} configuration. Zn(II) exhibits tetrahedral, square pyramidal or octahedral geometries with varying coordination numbers. Zinc is a constituent of enzyme carbonic anhydrase, which is involved in conversion of CO_2 to carbonic acid in plants [8]. Deficiency of zinc in animals results in stunted growth and male sexual immaturity. An important aspect of zinc is its low toxicity. Zinc containing enzymes are involved in hydrolysis reactions with the zinc ions acting as Lewis acids. Zinc ions are key structural components of a large number of proteins and are typically tetrahedral with either purely cysteine donors or with a mixture of cysteine and histidine donors [9].
About Lanthanide(III) Complexes

Coordination chemistry of lanthanides is one of the active research fields in inorganic chemistry. However, the development in this field is much less than the development in coordination chemistry of transition metals. This is due to the fact that the interactions of the lanthanide ions with most of the ligands, especially with donor atoms other than oxygen are very weak. Moreover, the isolation of lanthanide complexes is not as simple as the corresponding transition metal complexes. The coordination chemistry of lanthanides is of recent origin i.e., six decades only where as the coordination chemistry of transition metals which is about two centuries old. In spite of all these difficulties, a good number of lanthanide complexes have been isolated during the last three decades.

The metal ligand bonding in the lanthanide(III) complexes is essentially electrostatic in nature which is incorporated by magnetic, spectral and kinetic data [10]. However some evidence for, at least minor covalent interaction between the metal ion and the ligand does exists. In a given series of ligand increasing covalency is expected with decrease in size of the lanthanide ions. Further evidence for covalent interaction is shown by the study of $^1H$ NMR spectra of lanthanide(III) complexes. For diamagnetic lanthanum(III) complexes, low shifts of protons are generally observed because of the deshielding of protons due to the drainage of electron density from the ligand to the metal ion. This suggests covalent interaction in these complexes. Most of the lanthanide(III) complexes have colors resembling that of free metal ions. Since the colours of the lanthanide ions are due to the f electrons, it is reasonable to suggest that the f electrons do not participate in bonding. Perturbations in electronic spectra upon complexation are accounted for alterations in crystal field symmetry but not simply covalent interactions. The magnetic data of the complexes are also dependent upon 4f bonding. From the above observations it can be inferred that the 4f orbitals, although energetically available are spatially less available for bonding and hence, the
involvement of f orbitals in bonding in any, must be weak. Hence any covalent contribution to bonding must involve 5d or higher orbitals that are normally unoccupied in the lanthanide ions.

Lanthanides have strong preference for negatively charged donor groups, O > N > S > P > As [11]. Lanthanide(III) complexes exhibit coordination numbers ranging from six to twelve with nine and eight being very common and coordination six being rare. Coordination number eight and nine is characteristic of larger lanthanide ions, having square-antiprismatic (D_{4d}) and triangular dodecahedron (D_{2d}) geometry in case of former and symmetrical tricapped trigonalprismatic(D_{3h}) geometry in case of latter [12].

Lanthanide(III) complexes are used as in vivo diagnostic agents and therapeutic tools. Complexes of lanthanide radio nuclides such as^{158}Sm and ^{166}Ho are used for treatment of primary bone cancer lesions. Lanthanides can induce perforations in the cell membranes even in concentrations as low as 10^{-5} M, in contrast to Ca^{+2} which work only at higher concentrations causing harm to host cells. This property promotes the transformation of plasmid in bacteria, which is a desirable way to enhance secretion through membrane and better uptake of drug molecules. The intracellular accumulation of cis-platin and the transformation of plasmid pBR 322 and the PUC 18 in E.Coli has been reported, further lending credence to increase in permeability by Ln (III) [13]. Smaller doses of SmCl_{3} and PrCl_{3} (0.05mg/kg body weight) have inhibited lipid per oxidation in rat lung. High doses of Ln(III) are known to induce apoptosis in tumor cells and inhibit their growth. Apoptosis of rat skin fibroblasts and incubated macro phagocytes of rat teeth was induced by Ce^{+3} and Gd^{+3} , respectively. Lanthanides enhance pulmonary absorption of insulin and are also used in analysis of drugs. Hence the integrated effects comprising ROS scavenging effects, cell protection, cytoskeleton stabilizations and immunological enhancement together act as multiple target systems in anticancer therapy.
Nafion-based rare earth catalysts, polyacrylonitrile-based rare-earth catalysts and microencapsulated Lewis acids are a few rare earth catalysts, which have been used successfully in many reactions. Polymerization reactions involving rare-earth metals are well known. Polymerization of methylmethacrylate(MMA), alkyl acrylates, thermoplastics, elastomers, lactones, etc are all initiated by rare-earths. \([\text{La} \left( \text{CH(SiMe}_3\right)]_2 \left( \text{C}_2\text{Me}_5\right)]\) initiator was used to polymerize acrylnitrile and alkylisocyanates, and \(\text{Ln(acac)}_3/AIR/H_2O\) for oxiranes respectively.

Lanthanide complexes of two enolic B-diketones dipivaloyl methane(DPM), heptafluorodimethyl octanedione (FOD) and decafluoroheptanedi-one (FHD) are being used as shift reagents. The use of europium and other lanthanide complex as chemical shift reagents and have enabled the NMR studies of even very complex molecules [14].

Lanthanide (III) complexes of gadolinium of DTPA and DOTA are used as contrast agents. These complexes have exhibited unique contrast properties like lower toxicity, high thermodynamic stability, kinetic inertness and an inner sphere water molecule which exchanges rapidly with the bulk water in the body makes them the ideal candidates for imaging agents [15]. Their application as a diagnostic tool has opened broad possibilities for the solutions of many biological and medical problems.

Lanthanide (III) complexes are promising as efficient light conversion molecular devices having potential applications as luminescent labels in fluoroimmunoassays, light concentrators for photovoltaic devices, antennas in photosensitive bioinorganic compounds and high-technology optics [16].

During the last few years, lanthanide (III) complexes have been studied in great detail. There are however many more areas that are availing its applications and much more remains to be done in this regard.
About Schiff Bases

A Schiff base, named after Hugo Schiff, is derived from an amino and carbonyl compound are an important class of ligand that coordinate to metal ions via azomethine nitrogen and have been studied extensively [17]. It is an important intermediate for the synthesis of some bioactive compounds such as metal complexes. In azomethine derivatives, the C=N linkage is essential for biological activity, several azomethine were reported to process remarkable antibacterial, antifungal, anticancer and diuretic activities [18]. Schiff bases have wide application in food industry, dye industry, analytical chemistry, catalysis, fungicidal, agrochemical, tuberculostatic activities etc. Schiff bases act as herbicides, insecticides, nematocides, rodenticides and plant growth regulators. They exhibit spasmonolytic activity, hypertensive action and activity against leukemia, sarcomas, and other malignant neoplasm. They are also used as effective sterilants for houseflies [19]. They also possess anthelmintic activity [20]. Schiff base complexes are also considered to be among the most important stereo-chemical models in main group and inner transition metal coordination chemistry due to their preparative accessibility and structural variety [21].

About Quinolines

Quinolines are the class of organic compounds which come under heterocycles where pyridine ring is fused with benzene. They are found in nature mainly in plants. Alkaloid quinine is a traditional anti-malarial drug. The quinoline skeleton has since been used as basis for design of many synthetic anti-malarial compounds of which chloroquinoline is one such example. Simple quinoline is a stable liquid which is used in laboratory as high boiling basic solvent. Quinoline derivatives have proven to be the potential anti-inflammatory, analgesic, anti-convulsant, antibacterial, antipyretic and interferon inducing agent [22]. 3-Formyl quinoline [23] a derivative of quinoline has a wide synthetic application. Meth-cohn et al reported the
synthetic application of 2-chloro-3-formyl quinoline. Quinoline derivatives with various substitutions at C-3 position have been synthesized and reported for their analgesic, anti-inflammatory and ant-pyretic activities [24]. Many Schiff base derived from 2-chloro-3-formyl quinoline has been reported for their antifungal, anticancer and as potential biodynamic agent [25].

Recent Literature on Transition and Inner Transition Metal Complexes of Quinoline Derivatives

Although the transitional metal complexes of quinoline derivatives have been well studied, lanthanide (III) metal complexes of quinoline derivatives have rarely been reported till date.

Liu et. al [26] reported the three novel 2-oxo-quinoline-3-carbaldehyde Schiff-bases and their Cu(II) complexes. The molecular structures of Cu(II) complexes were determined by X-ray crystal diffraction. The DNA-binding modes of the complexes were also investigated by UV–vis absorption spectrum, fluorescence spectrum, viscosity measurement and EB–DNA displacement experiment. The results showed that the three Cu(II) complexes exhibited more effective cytotoxic activity against HL60 cells and HeLa cells than corresponding ligands. Also, CuL³ showed higher cytotoxic activity than CuL¹ and CuL².

Primik et. al [27] synthesized a number of indolo[3,2-c]quinolines and modified at the lactam unit to provide a peripheral binding site able to accommodate metal ions. Potentially tridentate ligands HL¹a-HL⁴a and HL¹b-HL⁴b were reacted with copper(II) chloride in isopropanol/methanol to give novel five-coordinate copper(II) complexes. All complexes were tested for cytotoxicity in the human cancer cell lines CH1 (ovarian carcinoma), A549 (non-small cell lung cancer), and SW480 (colon carcinoma). The compounds are highly cytotoxic, with IC₅₀ values ranging from nanomolar to very low micromolar concentrations. Substitution of the seven-membered azepine ring in
paullones by a pyridine ring resulted in a six- to nine-fold increase of cytotoxicity in SW480 cells.

Kulkarni et al [28] reported a series of Co(II), Ni(II), Cu(II), and Zn(II) complexes of quinoline-thiosemicarbazones. The ligands and complexes were characterized by elemental analysis, infrared, $^1$H NMR, UV-Vis, fast atom bombardment (FAB) mass spectroscopy, and electron spin resonance (ESR) spectral studies followed by magnetic susceptibility and conductivity measurements. All the complexes were found to have octahedral geometry except [CuL $^1$H(H$_2$O)Cl], which exhibits a square pyramidal structure. All the complexes are nonelectrolytic in nature and the electrochemical behaviors of complexes were briefly discussed. Further ligands and complexes were evaluated for their antimicrobial activity against bacteria Escherichia coli and Pseudomonas aeruginosa and fungi A.niger and Cladosporidium.

Zhang et al [29] reported Co(II), Cu(II), Zn(II), Cd(II) and Ag(I) complexes with the semirigid tridentate 8-(2-pyridinylmethylthio)quinoline ligand. Depending on electron configuration and size, different coordination patterns were observed.

Duraisamy et al [30] reported the reaction of 2-oxo-1,2-dihydroquinoline-3-carbaldehyde 4($N,N$)-dimethylthiosemicarbazone (HL) with copper(II) nitrate in methanol which yielded the water soluble [{Cu(L)(CH$_3$OH)}$_2$(NO$_3$)$_2$·H$_2$O complex. Structural analysis revealed that the complex consists of centrosymmetric binuclear entities containing square-pyramidal copper(II) ions bridged through the sulfur atoms. The spectroscopic experimental evidences strongly suggested that the ligand and complex could interact with calf thymus DNA (CT-DNA) through intercalation. A gel electrophoresis assay demonstrated the ability of the complex to cleave the pBR322 plasmid DNA. Further, the cytotoxic effect of the complex was examined on HeLa, Hep G2, and HEp-2, which showed that the complex exhibited substantial cytotoxic specificity on HeLa over the other two.
Kurdekar et. al [31] reported a series of Co(II), Ni(II), Cu(II), and Zn(II) complexes of Schiff base of ligands 2-hydroxy-3-formylquinoline with salicyloyldihydrazide and 2-hydrizinobenzothiazole in absolute ethanol. The prepared complexes were characterized by the analytical and spectral techniques. The stoichiometry of the complexes were found to be 1:1. The presence of coordinated and lattice water was confirmed by the TG and DTA studies. Subsequently all the prepared complexes were screened for antimicrobial activity against bacteria and fungi. The Cu(II) complexes have been found to be more active than the ligand. In addition the DNA binding/cleaving capacity of the compounds was analyzed by absorption spectroscopy, viscosity measurement, thermal denaturation, and gel electrophoresis methods.

Four isostructural lanthanide (III) complexes with 5,7-dichloro-8-quinolinol (H-ClQ) were synthesized by Zhen-Feng Chen et.al [32], in which the lanthanide was coordinated by three ClQ anions and two aqua ligands. The in vitro cytotoxicities of complexes against five human tumor cells were evaluated. They all exhibited enhanced cytotoxicity in comparison to H-ClQ. The binding properties of complexes to DNA examined by various methods indicated that complexes interacted with DNA more strongly than free quinolines.

Yan-Cheng Liu et. al reported [33] the four mononuclear and isostructural lanthanide (III) complexes with 5,7-dibromo-8-quinolinol (H-BrQ). Against BEL7404, SGC7901 and A549, complexes exhibited enhanced cytotoxicity than H-BrQ or the corresponding lanthanide salts. The binding
properties of H-BrQ with DNA were investigated by various methods. Results indicated that these lanthanide (III) complexes interacted with DNA more strongly than free quinoline.

Shikun Li et. al., [34] synthesized three novel rare earth complexes \([\text{N(CH}_3\text{)}_4][\text{Ln(NF)}_4]6\text{H}_2\text{O}(\text{Ln=Nd(III)(1), Sm(III)(2), Ho(III)(3)})\) using hydrothermal method from norfloxacin \(\text{HNF}=1\text{-ethyl-6-fluoro-1,4-dihydro-4-}
\text{oxo-7-(1-piperazinyl)-3-quinoline carboxylic acid, C}_{16}\text{H}_{18}\text{FN}_3\text{O}_3\), imidazole and rare earth nitrates. Each rare earth ion was eight-coordinated with carboxyl-O atoms and keto-O atoms from norfloxacin. Four of the norfloxacin ions acted as bidentate chelate group took part in the coordination with rare earth ion. The interaction between complex and DNA was studied by electronic absorption spectra and fluorescence spectroscopy. The binding interaction between the complex and bovine serum albumin (BSA) was studied by fluorescence spectroscopy. The complex 1 bound to DNA by the mode of partial intercalation. Gao et. al [33] synthesized a series of lanthanide binuclear complexes, \([\text{Ln}_2(L)_6(\text{H}_2\text{O})_4]\cdot2\text{H}_2\text{O} (\text{Ln=Sm(III), Gd(III), Er(III), Yb(III)}, \text{HL=4-quinolinecarboxylic acid, by reactions of corresponding rare earth salts with 4-quinolinecarboxylic acid at room temperature. The variable-temperature magnetic susceptibility showed that complex [Gd}_2(L)_6(\text{H}_2\text{O})_4]\cdot2\text{H}_2\text{O performed very weak antiferromagnetic property at low temperature and exchange was almost paramagnetic at high temperature.}

Li et. al., [36] reported the synthesis and crystal structure of tetra((8-quinolyl)-amido-N)ytterbium bi(tetrahydrofuran-O)lithium, which consists of one ytterbium atom, one lithium atom, four 8-aminoquinoline ligands and two THF molecules. The ytterbium atom was coordinated by eight nitrogen atoms of four 8-aminoquinoline ligands, forming a distorted dodecahedral geometry.
Junwei et al. [37] reported the effect of auxiliary-ligand on assembly of lanthanide(III) complexes with quinoline-2-carboxylic acid. They investigated the influence of configurations of auxiliary ligands on the coordination architectures, the 4,4’-bipyridine (4,4’-bipy), 2,2’-bipyridine (2,2’-bipy) and 1,10-phenanthroline (phen) as auxiliary ligands were introduced to form six different structures [Ln2(QUIN)6(H2O)6].3H2O (Ln = Pr (1), Nd (2), Sm (3), Eu (4)), [Pr (QUIN)3(H2O)]n (5) and [Pr2(QUIN)4(phen)2(NO3)2(H2O)2] (6). The crystal structures, thermogravimetric, photoluminescence and magnetic properties of these complexes were also presented.

Some more literatures on the quinoline Schiff bases and their metal complexes are given in the respective chapters.

Based on the above literature survey of quinoline derivatives, Schiff bases, transition metal complexes and lanthanide(III) complexes, we thought to synthesize, characterize and study the biological activity of some transition metal complexes using 3d series transition metal ions viz., Co(II), Ni(II), Cu(II) and Zn(II) and some lanthanide (III) complexes using La (III) ions viz., La(III), Pr(III), Nd(III), Sm(III), Eu(III), Gd(III), Tb(III), Dy(III) and Yb(III) with the Schiff bases of quinolines derivatives.