While the development of chemistry of transition elements occurred slowly throughout the 19th century, it was in the last two decades, with the work of Sophus Mads Jorgensen in Denmark and Alfred Werner in Switzerland, that the heart and soul of this discipline, namely transition metal complexes took shape. Both the chemists made massive contributions to the ‘data base’ but it was Werner, an impulsive and intuitive genius, who has been called inorganic Kekule, supplied the conceptual firepower and finally came up with secrets of coordination compounds through cobalt complex that not only made history but opened the new way to the new exiting experimental work and also provided frame work for the future developments in chemistry [1].

Coordination chemistry has always fascinated and inspired chemists all over the world. The prolificacy of research papers and diversity of application of these compounds amply support this. This has led to the emergence of wider themes and scope in coordination chemistry research. The growth of coordination chemistry has been three dimensional, encompassing breadth, depth, and applications. In a very real sense, coordination chemistry is an area that spawns fields; notable examples being transition metal organo-metallic chemistry, homogeneous catalysis, bioinorganic chemistry, medicinal chemistry etc. And equally important, it is foundational to other burgeoning fields, for e.g. Solid-state chemistry, extended and mesoscopic materials, photonic materials, model for solid surfaces, separation science, and molecular electronics, machines and devices. The enormous extensions of the field reflect its fundamental nature; the principles are so basic that they have immediate
applications as undreamed of new substances serendipitously appear in chemistry (e.g., dihydrogen complexes, metal derivatives of fullerenes, metal containing liquid crystals). The spawning of new fields is an inevitable consequence of the foundational position of coordination chemistry in the chemical sciences [2].

Coordination chemistry was not handicapped in extending its developments as application in various fields. Thus present research work in coordination chemistry around world is much more devoted towards the application of coordination compounds in various fields along with their structural diversity in various new ligand environment rather than only on theory of bonding and structure in coordination compounds that early workers were devoted. At present vast interest has been developed by bioinorganic chemists to devise small molecule models, the properties of which can be compared with different metalloproteins. The properties of a metal in a metalloprotein depend on its chemical environment, coordination geometry, number of coordinated ligands and their donor groups. These structural parameters affect the electrochemical, spectroscopic and, in multinuclear systems, magnetic characteristics of the metallobiosite. Thus, different modeling metal environments can help to build up an understanding of the effects on the physicochemical properties, and this can be used to deduce structural features of the metalloprotein. Studies on model compounds are particularly appropriate when structural details are not available or not yet unambiguous. Numerous multimetallic coordination compounds derived from multinucleating ligands have been prepared. For the
most part, the objectives of these investigations were to determine the structure and physical properties and to reproduce the coordination of multimetallic sites of metalloproteins.

Along with major advances in the chemical synthesis and coordination chemistry of new ligands and metal complexes, significant strides have been made in correlating physical characteristics of metal complexes with biological behavior. Metal complexes are currently being utilized in the diagnosis of a wide variety of disease states ranging from heart disease, brain disorders, cancer, anticonvulsant and diabetics. Metal complexes are also able to determine specific aspects of disease such as tissue hypoxia, as well as detect molecular phenomena such as multi-drug resistance. The advent of attaching metal complexes to larger biological molecules has essentially created a new realm of research in the field of bioconjugates. Metal complexes attached to biomolecules allow even more specific biological processes to be studied, including the formation of thrombi, the imaging of infection and the understanding of antigens and receptors found in certain types of cancer.

The use of metal complexes in therapy and diagnostic imaging is increasing. Throughout history ancient and modern, metal and metal compounds have been used in medicine to treat a variety of ailments. In the last century, metal complexes were used to treat diseases ranging from syphilis (organoarsenic compounds) to cancer (platinum anti-tumor drugs) to arthritis (gold compounds). The use of metal complexes as diagnostic agents is a relatively new area of medical research, and has flourished during the last 40 years.
Today, there are a wide variety of radiometals and radiometal complexes used in gamma scintigraphy and positron emission tomography (PET). An even more recent development is the use of paramagnetic metal complexes for enhancing contrast of magnetic resonance imaging (MRI) and single photon emission computed tomography (SPECT). There are now a number of non-radioactive metal complexes used as MRI contrast agents.

In this respect chemistry of transition elements have drawn much more attention of various research groups around the world because of the following facts:

➢ The transition elements typically form compounds in two or more oxidation states, and redox chemistry, including electrochemistry, is of major importance.

➢ The majority of transition element compounds have visible spectra (which is why they are colored) and the interpretation of these spectra provides a wealth of information concerning their electronic structures.

➢ A great many transition element compounds have one or more unpaired electrons and therefore have interesting and useful magnetic properties. These magnetic properties range from simple Curie paramagnetism to those associated with high-temperature superconductivity [3].

Thus these are the driving forces for the author to select for transition metals for his research work. And since the nature of the coordination compounds is governed by the controlling factors like, metal ion (nature of the metal ion), the donor atom structure of the ligand (skeleton of the ligand) and the interaction...
between the metal ion and ligand [4], the present research task is concerned with these facts towards some typically first row transition metal ion like copper, nickel, cobalt and zinc in +2 state with various ligand environments like N,S, O donor atom around the metal ion. It becomes necessary to come across the description of selected metal ions for the present work.

Cobalt with various oxidation states, -1 to +5 in that +2 and +3 as a predominant one, had attracted the coordination chemists since from 19th century. In this concern Werner occupies the top most position. It was Werner and it was cobalt complexes through which the heart and soul of transition metal complexes took shape. Thus in abroad sense one can say that coordination chemistry was started with cobalt complexes.

Such an important metal, cobalt, with its oxidation states +2 and +3 in its coordination complexes not only present in large number but also exhibit substantial variety in both nature and behavior. These facts can be observed through their oxidation state, coordination number, geometric structure, liability and stability, as well as in many other aspects of their chemistry.

There are four possible, distinct stereo chemical configurations namely, octahedral, square planar, tetrahedral, trigonal bipyramidal through which cobalt(II) complex may appear. The stereo chemical verities of cobalt (II) compounds are more often discussed in terms of magnetic and spectral data than on the basis of isomerism. And regarding biological importance of the cobalt compounds Cyanocobalmin, vitamin-B12 in which benzimidazole nucleus attached to cobalt(III) ion via its ring nitrogen is important one. Cobalt
compounds also have some synergic effects on certain antibiotics notably penicillin. Such a vital element in animal nutrition, the cobalt and its biological importance has been reviewed by Nicholls [5]. The ground state electron configuration of cobalt (27) is [Ar] 3d⁷4s². Numerous studies have been directed towards understanding and application of these important substances. The more common techniques include synthetic-, spectral-, solution-, stoichiometry-, magnetic-, kinetic-, equilibrium-, stereochemical- and X-ray investigations.

Nickel is the member of the first transition series having atomic number 28 and 1s²2s²2p⁶3s²3p⁶3d⁸4s² electronic configuration, was isolated in 1751 by A.F.Cronsted from some ores in the cobalt mines of Helsingland, Sweden. Nickel compounds have been found to occur with the metal in oxidation states ranging from -1 to +4. However, comparatively very few compounds correspond to the lowest (-1) and to the higher (+3 and +4) oxidation states. Most of the nickel compounds in the solid state and almost all in aqueous solution contain the metal in the oxidation state +2, which, by consequence, can be considered the ordinary oxidation state for the nickel in its compounds. The most stable electronic configuration of the free Ni(II) ion is [Ar] 3d⁸ which is also the ground state configuration in its complexes. The majority of nickel(II) complex have coordination number of four, five [6-9] and six. Complexes with coordination number of three, seven and eight are still quite rare [10].
Nickel is now recognized as an essential trace element for bacteria, plants, animals and humans. While the role of this metal in animal biochemistry is still not well defined, to date four bacterial enzymes have been found to be nickel dependent; Crease (also found in plants), carbon monoxide dehydrogenase (CODH), hydrogenase (H₂-ase), methyl-S-coenzyme-M methylreductase (MCR), which employs a Ni-containing prosthetic group (factor 430) [11].

Copper is one of the typical transition element, copper, occurs in a range of oxidation states and its ion undergo immediate complexation yielding variety of coordination compounds. Its electronic configuration is [Ar] 3d⁹4s². Copper exhibits more than one oxidation states covering +1 to +3, with +2 in cupric compounds as common oxidation state. With these, even though copper occurs in zero, (in metal), and +4 oxidation states, but these are limited. In 3d⁹ configuration copper(II) undergoes John-Teller distortion when placed in an environmental of cubic symmetry (i.e., regular octahedral or tetrahedral) and this has profound effects on its stereochemistries. In six coordinated octahedral geometry, octahedron is severely distorted. The typical distortion is an elongation of one four fold axis, so that there is planar array of four short Cu-L bonds and two trance long ones. The kind of distortion may lead to a situation where an octahedral geometry becomes indistinguishable from square planar coordination. Hence the case of tetragonaly distorted octahedral coordination and square coordination cannot be easily differentiated.

Regarding application of copper complexes, they occupy very top position in organic chemistry due to their important role in oxidation, coupling reactions,

Copper is also involved in many biological processes. For example, Cu(DMG)$_2$ shows some activity against cancer [14] and shows increasing life span to the extent of 200-300%. But only DMG, dimethyglyoxime is not active against cancer. This shows the necessary of complex formation in biological processes.

Zinc is the last member of the first transition series, having atomic number 30 and electronic configuration as [Ar]$^{3d^{10}}$4$s^2$ have attracted the chemists in one or the other way from last few years. Even though it exhibits two oxidation states +1 and +2, it will appear in +2 state in its coordination compounds as a predominant one and its +1 state is not possible under normal conditions except as spectroscopic species. Usually zinc(II) will form complexes with various organic ligands which are essentially diamagnetic due to completed d-orbital, i.e. $d^{10}$ configuration. But the complexes of zinc(II) may be of tetrahedral, square pyramidal or trigonal bipyramidal and octahedral when the coordination number is 4, 5 and 6 respectively. But it is invariably seen that zinc in its +2 state forms only tetrahedral complexes with coordination number 4. Many polymeric structures involving bridging group are reported. Certain complexes show even coordination number seven.

Regarding its biological aspects, zinc has roles that are second only to iron in importance [15]. One of the roles of zinc in biology is as a structural component in proteins. This role was first proposed in 1983 for the protein transcription factor IIIA, which has zinc based domains called fingers [16].
Binuclear zinc complexes with N, O as donor atoms in ligands are of current interest since such systems of two zinc atoms at a distance less than 3.4 Å are known to exist at the active site of some zinc containing enzymes such as phospholipase C from Bacillus cereus [17] and bovine lens leucine amino peptidase [18-19]. The chemistry of zinc complexes with tri-, and tetradentate N₅S₇ ligands is well developed. This fact is clear from various publications from various groups like C.Kimblin [20], P.Ghosh [21], S.J.Chiou [22], and B.S.Hammes [23] in which the design of N₂S and NS₂ ligands, Zn-complexes, and their structural models for the related zinc-enzymes have been reported.

In the last few years a variety of Zn(II) complexes with synthetic ligands have been used in biomimetic zinc [24] chemistry. Binucleating phenol based ligands are suitable to stabilize binuclear metal cores and widely used to mimic bimetallic biosites [25,26].

With this brief introduction about coordination chemistry and transition metals, selected for the present work, this paragraph starts with the aim of the present task. The present aim is to design and synthesize the ligands and their metal complexes with different donor atoms and functional groups such as O, N, S and >C=N, -OH, -NH₂, >C=S, -SH etc and investigate chemistry and bioactivity of these complexes.
Introduction

Thesis is divided into seven chapters for the convenience.

Chapter-1: Introduction

Chapter-2: This section summarizes the materials, methods and instruments used in the present research work. A brief description of the analytical methods and physicochemical measurements employed for the investigation of the free ligands and their metal complexes is discussed.

Chapter-3: This part deals with the synthesis, characterization, antibiogram and DNA binding studies of novel Co(II), Ni(II), Cu(II) and Zn(II) complexes of Schiff base ligands with quinoline core. Ligands are derived by the condensation of 2-hydroxy-3-formylquinoline with salicyloylhydrazide and 2-hydrazinobenzothiazole. Because of the anticancer property of the quinoline core and its high binding affinity towards DNA give an immense interest in the synthesis of later first row transition metal complexes.

Chapter-4: This section deals with the transition metal chemistry of ‘tritopic’ 4-aminoantipyrine scaffold based heterocycles; Efficient anticonvulsants in Wistar rats. Ligands (L^1H and L^2) were prepared by the condensation of 4-aminoantipyrine with 2-hydroxy-3-formylquinoline and isatin. So prepared ligands were used for the synthesis of transition metal complexes namely, Co(II), Ni(II), Cu(II) and Zn(II) thereafter these are characterized by the analytical and spectral techniques.
Chapter-5: This chapter is composed of study of coordinative versatility of ligands with quinoxaline core. For convenience this chapter is further divided in two sections, A and B.

Section-A: Nitrogen/Oxygen containing heterocyclic transition metal complexes are of immense interest because of their perfect biological activities which are used in the pharmaceutical industry. This part of work is mainly focused on metal complexes of quinoxaline, quinoline and coumarin derivative with their antibiogram study. Ligands were prepared by the condensation of 2-hydroxy-3-hydrazinoquinoxaline with 2-hydroxy-3-formylquinoline and 3-acetylcoumarin. They were well characterized by the physico analytical and spectral methods.

Section-B: The coordination chemistry of sulfur donor ligands are of immense interest as, these compounds mimic the cystein sulfur coordination in metalloenzymes. Furthermore these compounds show electronic and structural properties of the active sites as in blue copper proteins involving S and N-coordination. In addition to this the sulfur containing hydrazone metal complexes have found to be DNA intercalating agents. With these above mentioned activities this division explores the coordination chemistry of sulfur containing metal complexes derived from the quinoxaline derivatives. Ligands were prepared by the condensation of 2-mercapto-3-hydrazinoquinoxaline with 2-hydroxy-3-formylquinoline and 3-acetylcoumarin.

Chapter-6: In this chapter synthesis, spectral characterization and antidiabetic studies of transition metal complexes with N\textsubscript{2}O donor ligands with
benzimidazole hub, were studied. Benzimidazole nucleus is a constituent of many of the bioactive heterocyclic compounds that exhibit a large range of biological activities. Incorporation of benzimidazole nuclei is an important synthetic strategy in drug discovery program as it exerts broad-spectrum of biological activity and widely occur in nature in the form of alkaloids. The ligands were prepared by the condensation of the 2-aminomethylbenzimidazole with 2-hydroxy-3-formylquinoline and o-vanilide.

Chapter-7: This section reveals the synthesis and characterization of binuclear copper and zinc complexes with antimicrobial evaluation. Syntheses of ligands were performed by the condensation of bi-acetyl azine with thiosemicarbazide and thiocarbohydrazide.
References


