CHAPTER I
1. INTRODUCTION

In recent years, there has been considerable interest in the synthesis and use of coordination compounds due to their practical convenience, operational flexibility and interesting structural features. Modern coordination compounds play a crucial role in biological and other systems. For educational, economic, environmental and social reasons, the trend towards the design, synthesis, characterization and application of coordination compounds is undoubtedly increasing. Especially, the synthesis of biologically active compounds such as pharmaceuticals, agrochemicals, flavours and fragrances as well as creation of advanced materials has got great attention. Coordination compounds with bonds between a central metal atom and surrounding ligands, play critical roles in biology, biochemistry and medicine, controlling the structure and function of many enzymes and their metabolism. Though most of the coordination compounds formed by the organic ligands accounting more than fifty percent of carbon, they are included under inorganic chemistry, may be due to the fact that the central metal ion is responsible for their reactivity. Complexation with metals is mainly due to the presence of donor atoms.

Several studies have linked the concentrations of specific transition metal ions to various diseases. Low serum copper level is used as a marker for Wilson’s disease. Serum copper levels are high in a large number of chronic and acute illnesses such as Hodgkin’s disease, Leukemia and many other malignancies[1]. Zinc is an important nutritive factor as well as a cofactor for many metalloenzymes. Zinc is necessary for the growth and division of cells, especially during the stages of life when growth rates are high. Zinc deficiency is associated with syndromes that cause short structure and dwarfism. Also, iron and cobalt are all trace essential elements for human bodies. Lack of these essential elements can induce some diseases, while it is harmful and deleterious if overtaken. Iron is the fourth most
abundant element in the earth’s crust occurring in nearly all types of rock and soil minerals as both $\text{Fe}^{2+}$ and $\text{Fe}^{3+}$ ions. Iron plays a central role in the biosphere, serving as the active center of proteins responsible for $\text{O}_2$ and electron transfer and of metalloenzymes such as oxidases, reductases and dehydrases. Coordination metal complexes that incorporate Schiff bases as ligands have been playing an important part in the development of coordination chemistry as a whole.

The wide use of antibiotics in man and animals and their extensive use in areas other than the treatment and prophylaxis of disease have resulted in a serious problem of drug resistance. Many of the well-known antibiotics, penicillin, streptomycin, tetracycline etc are chelating agents, their action is improved by the presence of small amounts of metal ions. The antimicrobial activity of the ligands and their transition metal complexes against different bacteria are also reported. Copper complexes have more antibacterial activity against the bacteria Staphylococcus aureus and Klebsiella pneumonia.

Nowadays, the research field dealing with the transition metal complexes of Schiff bases has expanded enormously and embraces very wide and diversified subjects comprising vast areas of organometallic compounds and various aspects of bioinorganic chemistry. This is due to the fact that Schiff bases offer opportunities for inducing substrate chirality, tuning the metal centered electronic factor and enhancing the solubility and stability of either homogenous or heterogenous catalyst. The transition metal complexes having oxygen and nitrogen donor Schiff bases possess unusual configuration of structural liability and are sensitive to molecular environment. The environment around the metal center as coordination geometry, number of coordinated ligands and their donor groups are the keyfactors for metallo-proteins to carry out specific psychological functions. Moreover, the presence of donor atoms in the coordination sphere leads to their biological activity. Investigations on the Schiff base metal complexes cover a full gamut of areas ranging from
general academic interest to a wide spectrum of biological activity and practical applications in diverse areas viz., in medicine, in agriculture, in trace metal determination, in pharmaceutical products and in ion selective electrodes.

Schiff base can be used in dyestuff production, liquid crystal industries and also in pharmacology. They are synthetic oxygen carriers and they have been produced from intermediate products in enzymatic reactions and are used as antitumour agents. Therefore it is very important to prepare its transition metal complexes. Studies on the transition metal Schiff base complexes derived from amino acids continue to draw the attention for quite a long time.\cite{4,5}

### 1.1 SCHIFF BASES

The great potential for producing novel materials with interesting useful functions (with desirable properties) has led to the rational design and synthesis of metal-organic polymeric networks which has become an intensely studied subject. The rational construction of metal-organic supramolecular frameworks involves a cooperation between the metal first-coordination sphere and the second-sphere non-covalent active sites. Enantioselective synthesis has gained importance in the last few years, and the development of the chiral ligands has become an important field. Hence chiral coordination polymers have received much attention because of their wide application in enantioselective synthesis, asymmetric catalysis, assembly of chiral supermolecular structure, and advanced material preparation. Schiff bases have been, for decades, among the most fundamental chelating systems in coordination chemistry, and exploitation of this group of compounds in material science is currently a rapidly developing field.

Hugo Schiff, a German Chemist described the condensation between a carbonyl compound and an amine leading to a Schiff base, in 1864. He also worked in the field of
amino acids and the Biuret reagent. Schiff base contains the azomethine group, -CH=N- and is obtained as per scheme 1

\[
R\text{-NH}_2 + R_1 - C - R_2 \rightarrow C\equiv N - R + H_2O
\]

Scheme 1

Where R, R\textsubscript{1} and R\textsubscript{2} may be alkyl or aryl groups. If the reactant is an aldehyde, the group R\textsubscript{2} will be hydrogen. They are often referred to as anils, imines or azomethines. The presence of a lone pair of electron in the sp\textsuperscript{2} hybridized orbital on the imino nitrogen atom makes the azomethine group more significant, chemically and biologically. Schiff bases with additional donor atom are closer to the imino nitrogen to form stable chelate with many metal ions.

The formation of a Schiff base, from an aldehyde or ketone is a reversible reaction and generally takes place under acid or base catalysis, or upon heating (Scheme 2).

\[
R\text{-NH}_2 + R - C - R \rightleftharpoons R - C - R + H_2O
\]

Scheme 2

The formation is generally driven to the completion by separation of the product or removal of water, or both. Many Schiff bases can be hydrolysed back to their aldehydes or ketones and amines by aqueous acid or base.

The mechanism of Schiff base formation is another variation on the theme of nucleophilic addition to the carbonyl group. In this case, the nucleophile is the amine. In the
first part of the mechanism, the amine reacts with the aldehyde or ketone to give an unstable addition compound called carbinolamine.

The carbinolamine loses water by either acid or base-catalysed pathways. Since the carbinolamine is an alcohol, it undergoes acid-catalyzed dehydration.

Typically the dehydration of the carbinolamine is the rate determining step of Schiff base formation and that is why the reaction is catalyzed by acids. Yet the acid concentration cannot be too high because amines are basic compounds. If the amine is protonated and becomes non-nucleophilic, equilibrium is pulled to the left and carbinolamine formation cannot occur. Therefore, many Schiff base synthesis are best carried out at mildly acidic pH. The dehydration of carbinolamines is also catalysed by base. This reaction is somewhat analogous to the E$_2$ elimination of alkyl halides except that it is not a concerted reaction. It proceeds in two steps through an anionic intermediate.

1.2 BIOLOGICAL IMPORTANCE OF SCHIFF BASES

Schiff base ligands are able to coordinate metals through imine nitrogen and another group, usually linked to the aldehyde/ketone. A large number of Schiff bases and their complexes have been investigated for their interesting and important properties, such as their ability to reversibly bind oxygen, their catalytic activity in the hydrogenation of olefins, their photochromic properties and their complexing ability towards some toxic metals$^{[6]}$. Complexes of Schiff bases have shown promising applications in biological activity and biological modelling applications$^{[7]}$. It is well known that Schiff base derivatives possess antifungal and antibacterial activity$^{[8]}$. In particular, amino acid Schiff bases are active against a wide range of organisms since they play an important role in living organisms, such as the carboxylation, transamination and C-C bond cleavage$^{[9]}$. Furthermore, Schiff bases are known to have slight antitumour activities; a large number of these compounds have been synthesized in order to find compounds with greater antitumour activities.
Schiff bases are important in enzyme catalysis, as they maintain the oxidation state of the carbonyl group. They also form a covalent bond with the substrate, so that the substrate cannot diffuse away in the middle of the reaction and they act as electron sinks. Many Schiff bases are known to be medicinally important and are used to design medicinal compounds. Schiff bases appear to be important intermediates in a number of enzymatic reactions involving interaction of the amino group of an enzyme, with a carbonyl group of the substrate\(^\text{[10]}\).

Stereochemical investigations carried out with the aid of molecular models showed that Schiff bases formed between methylglyoxal and the amino group of the lysine side chains of proteins can bend back in such a way towards the N atom of peptide groups that a charge transfer can occur between these groups and the oxygen atoms of the Schiff bases.

Schiff bases derived from pyridoxal and amino acids are considered as very important ligands from biological point of view. Transition metal complexes of such ligands are important enzyme models. The rapid development of these ligands have resulted in an enhanced research activity in the field of coordination chemistry leading to very interesting conclusions. Many biologically important Schiff bases have been reported in literature possessing, antibacterial\(^\text{[11-16]}\), antifungal\(^\text{[17]}\), antimicrobial\(^\text{[18-20]}\), anticonvulsant\(^\text{[21]}\) and antitumour\(^\text{[22,23]}\) activities. Also certain polymeric Schiff bases have also been found to possess antitumour activity. The Schiff bases have the highest degree of hydrolysis at pH 5 and the solubility in water is also highest at this pH. The antitumour activity of the Schiff bases towards ascetic tumours increases considerably with the slight increase in water solubility. Another important role of Schiff base structure is in transamination\(^\text{[24]}\). Transamination reactions are catalyzed by a class of enzymes called transaminases or aminotransferases. Transaminases are found in mitochondria and cytosal of eukaryotic cells. All the transaminases appear to have the same prosthetic group, i.e
pyridoxal phosphate, which is covalently attached to them via, an imine or Schiff base. Schiff base formation is also involved in the chemistry of vision, where the reaction occurs between the aldehyde function of 11-cis-retinal and amino group of the protein (opsin)\textsuperscript{[25]}.

Schiff bases have been reported to have pharmacological effect which is considerably enhanced by the presence of metal ions\textsuperscript{[26]}. Consequently, Schiff base metal complexes and chelates are widely studied as model systems of biological interest\textsuperscript{[27]}.

1.3 METALLO-ELEMENTS IN BIOLOGICAL SYSTEMS

The study of the biological role of metal ions has a long history in medicine, in pharmacology and in toxicology, but is only recently that the extent and variety of metal ion involvement has been appreciated. The metalloelements, which are present in trace and ultra-trace quantities play vital roles at the molecular level in a living system. For example, among the transition metals, the elements V, Cr, Mn, Fe, Co, Ni, Cu, Zn and Mo have been shown to be essential to life and the elements Au, Ag, Pt, Pd, Ir, Os, Ti and others have either been used in therapy or claimed to be of therapeutic values. The transition metal ions are responsible for the proper functioning of different enzymes. Metal ions play essential roles in about one third of enzymes. These ions can modify electron flow in a substrate or enzyme, thus effectively controlling an enzyme-catalyzed reaction. They can serve to bind and orient substrate with respect to functional groups in the active site, and they can provide a site for redox activity if the metal has several valence states. Without the appropriate metal ion, a biochemical reaction catalyzed by a particular metalloenzyme would proceed very slowly. If their concentration exceeds certain level, the toxic effects are evident. It has been found that the biological activity of the transition metals is mainly due to the formation of complexes with different bioligands.

The mode of biological action of the complexes are governed by the thermodynamic and kinetic properties of the complexes. Sometimes, the permeability, ie., lipophilicity of
drugs is increased through the formation of chelates in vivo and the drug action is significantly increased due to much more effective penetration of the drug into the site of action. Further, the correct metal ion balance in various in vivo compartments is important for the functioning of specific metal containing sites in many enzymes and proteins. For example, if the concentrations of some metal ions are raised considerably above the norm, blocking of transport sites can occur and symptoms more normally attributed to depletion of metal ions can appear. In absolutely metal free conditions, they are inactive. The toxicity of heavy metal ions is partly due to their binding with the nucleic acids. In addition to this, in designing efficient anticancer drugs, the knowledge of binding of metal ions is helpful. Metal ion distribution can be effected by alterations in the in vivo concentration of naturally occurring low molecular weight ligands or of complexing sites of proteins. In case of diabetes, chromium metabolism plays an important role. A number of diseases and their remedies are dependent of the metabolism of inorganic constituents.

In considering in vivo activities, even if the most likely complex species can be predicted in terms of concentration and the relative abundance of these species can be determined, this information may or may not directly relate to physiological activity. A wide range of microenvironments are present in vivo and each would be expected to affect the chemistry of the metal in much the same way as would a change in the solvent or the absorption of the metal ions on a surface. In discussing the in vivo chemistry, the metal ions are classified into the class I (hard) and class II (soft) acids based on their in vitro reactions.

‘Hard’ metal ions are small, and are either not easily oxidized or reduced, or have a relatively high positive charge, e.g., Na⁺, K⁺, Mg²⁺. On the other hand, ‘Soft’ metal ions are large with a low positive charge, e.g., Cu⁺, Au⁺, Hg⁺, Cd²⁺, Pt²⁺. Divalent first-row transition-metal ions lie intermediate between those extremes. In general, ‘hard’ metal ions favour complexing with oxygen and nitrogen donors and ‘Soft’ metal ions with sulphur and
phosphorus donors. This concept is difficult to apply absolutely, but it is useful in a relative sense. The transition metal ions are good Lewis acids forming wide ranges of complexes with nitrogen, oxygen and sulphur donor ligands.

In recent years, considerable interest has been developed in copper complexes with Schiff base ligands as structural models for active site of copper proteins. Copper is a bioelement and an active site in several metalloenzymes and proteins\[30\]. Copper ions are found in the active sites of a large number of metalloproteins such as haemocyanin, tyrosinase, cytochrome C oxidase, and ascorbate oxidase. Copper can exist under normal conditions in four oxidation states 0, 1, 2, 3. These copper proteins are involved in various biological processes such as biological electron-transfer reaction, oxygen atom insertion into substrates, dioxygen reduction to hydrogen peroxide or water and hydrolytic reactions. The blue copper proteins have received considerable interest because of their unusual spectral and structural properties. Among all the transition metal complexes, copper (II) Schiff base complexes are well known for their preparational accessibilities, exhibiting the flexibility of the coordination geometry around the metal center. Azide copper (II) complexes are also of great interest for bioinorganic chemists to explore the structure and role of active sites in copper proteins such as metazido haemocyanins and tryosinases\[31\]. Copper Schiff-base complexes act as key intermediates in some pyridoxal dependent enzyme processes and possibly in the cross linking of collagen by lysyl oxidase\[32\]. Amine oxidase is a copper protein which catalyzes the oxidation of amine to aldehydes using molecular oxygen as oxidant. In this reaction, pyridoxal phosphate acts as a cofactor. In mammalian liver, a type II copper protein is found which catalyzes the oxidation of uric acid to allentrin haemocyanin. In lower invertebrate organisms of the class mollusks, arthropods and annelids, this type of copper protein is responsible for oxygen transport.
In the blood plasma of the vertebrates, Ceruloplasmin, an intensely blue coloured copper protein is present. In medicine, ligands specifically designed to complex and to remove copper in Wilson’s disease, a condition involving the accumulation of excess copper, have been synthesized and the discovery that copper aspirinate is a more effective and less ulcerogenic anti-inflammatory agent has led to the reinvestigation and extension of the chemistry of complexes of this type\[33\].

Nickel is an essential component in at least four types of enzymes: urease, carbon monoxide dehydrogenase (CODH), hydrogenase and methyl-S-coenzyme M reductase. Morrow and Kolasa reported the cleavage of plasmid DNA by square planar nickel-salen in presence of oxidizing agents\[34\]. Urease catalyzes the hydrolysis of urea to ammonium and carbamate (H₂NCO₂⁻) ions; it appears to contain a redox-inactive Ni²⁺ unit in which the nickel atom is octahedrally coordinated and probably act as lewis acid for substrate binding. Nickel Iron hydrogenase is an enzyme which catalyzes hydrogen uptake or liberation of hydrogen in some bacteria. Nickel containing enzymes of certain methanogenic organism also catalyzes the synthesis of acetyl-coenzyme A. Methyl-coenzyme M reductase contains a prosthetic group consisting of a redox active NiN₄ macrocycle (factor F₄₃₀)\[35\].

Although cobalt occurs in only a limited number of metal containing proteins, its role in vitamin B₁₂ is vital for a wide range of life forms from micro-organisms to man\[36\]. Cobalt forms stable complexes with nitrogen donor ligands, both in the di- and trivalent states, and both are thought to be implicated in the catalytic action of the vitamin. The cobalt (III) corrin complex bound to blood plasma protein fractions is carried to the tissue, where it is bound to a variety of proteins receptors which are essential for the synthesis of haemoglobin\[37,38\]. Two of the main catalytic reactions associated with vitamin B₁₂ enzymes are hydrogen and methyl transfers. Vitamin B₁₂ enzymes can cause deamination reactions converting amino alcohols into aldehydes.
1.4 EFFECT OF METAL COMPLEXATION ON BIOLOGICAL ACTIVITY

Metal complexes with nitrogenous Schiff bases are becoming increasingly relevant for their biochemical, analytical and antimicrobial activities. On viewing the metallo-elements, there are certain metallo-elements without which the normal functioning of the living organism is inconceivable. Of these metallo-elements, the so called ‘metals of life’, four members form an ‘island’. These are Na, Mg, K and Ca, amongst the transition elements V, Cr, Mn, Fe, Co, Ni, Cu, and Zn. These elements are present in trace or ultra-trace quantities and known to form Schiff base complexes. It has been found that the activity of the bio-metals is attained through the formation of complexes with different bio-ligands. Certain drugs play a vital role as bio-ligands in the biological systems. Similarly, nitrogen containing bases such as derivative of pyrrole, pyridine, pyrimidine, pyrazine and purine amines such as histamine, carbohydrates such as glucose, and different vitamins such as ascorbic acid are well recognized-bioligands. The role of metal ions in the virus replication process is extremely important. A virus can penetrate into the host’s cell only when it is mediated by some suitable metal ions. As a matter of fact, for virus replication, copper and zinc are essentially required, hence by increasing or decreasing their concentration, viral growth may be controlled. Interaction of various metal ions with antibiotics may enhance or suppress their antimicrobial activity but usually in many cases, the pharmacological activity of antibiotics, after complexation with metals, is enhanced as compared to that of the free ligands. Many of the well-known antibiotics, penicillin, streptomycin, bacitracin, tetracycline etc are chelating agents and their action is improved by the presence of small amount of metal ions. In chelates, metal is firmly held by a number of ligand atoms usually nitrogen, oxygen or sulphur through co-ordinate covalent bonds. Some of the chelates are model analogues of certain metallo-enzymes. Further, some of the chelates develop considerable antimicrobial activity. The biological activity of chelating compounds is enhanced on
chelating with a metal atom. The antitumour activity of some Schiff bases has been attributed to their ability to chelate with trace transition metal. Generally, it has been observed that transition metal complexes have greater activity and less toxic effects.

1.5 METALLO-ELEMENTS UNDER INVESTIGATION

Copper is a member of the group IB elements along with gold and silver. Thus, although in some ways a typical transition metal, it is distinct in its properties. Copper can exist under normal conditions in four oxidation states 0, 1, 2, 3. The most common oxidation state is +2. The cuprous compounds easily get oxidized to cupric state. Cupric ion (Cu$^{+2}$) is characterized by 3d$^9$ configuration. Its complexes are often distorted resulting in unequal bond lengths, inter bond angles and a large variety of possible geometries. When Cu$^{+2}$ is placed in an octahedral or tetrahedral environment, Jahn-Teller distortion is possible. The extent of Jahn-Teller distortion affects the stereochemistry of the complex. All the octahedral complexes are tetragonally distorted. As the distortion becomes maximum, the configuration becomes square planar.

Complexes of the type M$_2$CuX$_4$ are examples of tetrahedral complexes which are distorted [M = Univalent cation, X = Cl$^-$ or Br$^-$. Distorted tetrahedral and trigonal bipyramidal structures are also reported for Cu$^{+2}$ complexes. Only in few cases, the symmetry is D$_{3h}$, while in most cases, the structure is distorted. Waters et al studied the absorption spectra of a variety of complexes of copper (II). Almost all complexes were found to be either green or blue. In some cases, the complex was brown or red due to the interference of the charge transfer band in the visible region. Cu(II) ion subjected to Jahn-Teller distortion is never expected to form a regular octahedral complex. This fact is highly reflected in spectral and magnetic properties. The energy level diagram for ligand fields of D$_{4h}$ symmetry predicts three transitions, $^2$B$_{1g}$ → $^2$A$_{1g}$, $^2$B$_{1g}$ → $^2$B$_{2g}$ and $^2$B$_{1g}$ → $^2$E$_g$. But, due to the overlap of these bands, only one band is observed in a number of cases. The magnetic
moments of simple Cu(II) complexes are generally in the range of 1.8 - 2.20 BM, irrespective of the stereochemistry. Copper (II) forms a number of polynuclear compounds with magnetic anomalies. In these compounds, the magnetic moments indicate significant interaction between two adjacent copper atoms. As a result, the magnetic moment will be lowered and the value is temperature dependant. Detailed studies were carried out with Copper(II) carboxylates to interpret these magnetic anomalies.

Copper (II) also forms dimeric species. The classic example of this type is Copper acetate, a dimer with bridging carboxylate groups but dimeric complexes also occur in nature. For example, in haemocyanin, oxygen is carried as a bridged species between two copper ions and not by a haem group as the name would imply. True square planar coordination is observed in the Cu(II) complexes of pthalocyanines, but in some square planar complexes, the molecules are stacked, so that there is a weak interaction between the Cu(II) and the middle carbon atom of the neighbouring molecule.

The trend towards decreased stability of higher oxidation states continues with nickel, so that only Ni(II) occurs in the ordinary chemistry of the element. However, there is a complex array of stereochemistries associated with this species. The usual coordination numbers reported for Ni are 4, 5 and 6. The geometries encountered in these complexes are octahedral, trigonal bipyramidal and square pyramidal, square planar and tetrahedral. The highest coordination number of nickel is six. The electronic absorption spectra of octahedral complexes of Ni(II) are characterized by three transitions which are due to $^3A_{2g} \rightarrow ^3T_{2g}$, $^3A_{2g} \rightarrow ^3T_{1g}(F)$ and $^3A_{2g} \rightarrow ^3T_{1g}(P)$, all the three being allowed transitions. Octahedral complexes of Ni(II) have two unpaired electrons and show magnetic moments ranging from 2.9 to 3.4 BM, depending on the magnitude of orbital contribution. Square pyramidal and trigonal bipyramidal five coordinate complexes of Ni(II) have been reported with high spin and low spin magnetic moments. For a true trigonal bipyramidal structure the symmetry must be...
D_{3h}, but in many complexes of Ni(II), the symmetry lowers to C_{3v} as is supported by electronic spectra. The stereochemistry of the other five-coordinated complexes which do not contain “tripod” ligands is trigonal bipyramidal. A few square pyramidal complexes are also possible.

Tetrahedral complexes of Ni(II) with stoichiometries \([\text{NiX}_4]^{2-}\), \([\text{Ni X}_3L]^-\), \([\text{NiL}_2\text{X}_2]\) and \([\text{Ni}(\text{L-L})_2]\) (X = halogen, L-L bidendate ligand) are possible. However, strict tetrahedral symmetry is expected only in the complexes \([\text{NiX}_4]^{2-}\). In many cases, the dihedral angle differs from 90º, so that the resultant geometry is between tetrahedral and square planar. The extent of distortion will be reflected in the magnetic properties, as tetrahedral complexes are paramagnetic and square planar complexes are diamagnetic.

For tetrahedral Ni(II) complexes, the ground state is \(^3T_1(F)\) and the electronic absorption spectrum is characterized by the transition, \(^3T_1(F) \rightarrow ^3T_1(P)\), which falls in the visible region. A strictly tetrahedral Ni (II) complex should have a magnetic moment of about 4.2 BM. The deviations from tetrahedral symmetry is common which leads to a decrease in magnetic moment. Magnetic moments in the range of 3.5 to 4 BM have been reported for irregular tetrahedral complexes. The magnetic moment even drops to 3.0 BM, if the distortion is severe. Ni (II) prefers to have planar geometry in a vast majority of four coordinate complexes. This is because of the vacant strongly antibonding \(d_{x^2-y^2}\) orbital. But in tetrahedral configuration, the occupancy of the antibonding orbital is unavoidable. The planar complexes of Ni (II) are diamagnetic. They will be usually red or reddish brown in colour. The study of both Ni(I) and Ni(II) species is being studied increasing because of the possible involvement of these oxidation states in nickel containing metalloenzymes.

The common oxidation states of Cobalt are +2 and +3 Cobalt (II) forms very large number of complexes. Octahedral and tetrahedral complexes are more common among them. Tetrahedral complexes of Co(II) are more common than for other transition metal ions, for
the small difference in the ligand field stabilization energy between octahedral and tetrahedral configurations. For the free Co(II) ion, the ground state corresponds to $^4F$. An additional quartet state, $^4P$ of higher energy is also possible for the free ion. Octahedral complexes are pale red or purple, whereas tetrahedral complexes are blue in colour. The allowed transitions for octahedral complexes are $^4T_{1g}(F) \rightarrow ^4T_{1g}(P)$, $^4T_{1g}(F) \rightarrow ^4A_{2g}$ and $^4T_{1g}(F) \rightarrow ^4T_{2g}$. For tetrahedral complexes the allowed transitions are $^4A_2 \rightarrow ^4T_1(P)$, $^4A_2 \rightarrow ^4T_1(F)$ and $^4A_2 \rightarrow ^4T_2$.

Octahedral and tetrahedral complexes differ in their magnetic properties also. For the high spin complexes of Co(II), the ground state of $^4T_{1g}$ provides an unquenched orbital contribution to the magnetic moment. For octahedral complexes, the effective magnetic moments at room temperature are in the range, 4.7-5.2 BM. This value is much higher than the spin only value. For tetrahedral complexes of Cobalt (II), the value of the magnetic moment ranges from 4.3 to 4.7 BM.

Low spin Co(II) octahedral complexes are rare. In this case, the electronic configuration is $t_{2g}^6e_g^1$, predicting the possibility of Jahn-Teller distortion. Consequently, perfectly octahedral low spin Co(II) complexes are rare and such systems have a tendency to lose ligands so that low spin five or four coordinate complexes result. The square planar complexes of Co(II) have magnetic moments in the range, 2.2-2.7 BM. The stereochemistry of five coordinate complexes will be either square pyramidal or trigonal bipyramidal. High spin complexes having three unpaired electrons and low spin complexes with one unpaired electron are known for both these geometries. Co(III) also forms numerous complexes, most of which are octahedral[62]. In the presence of an octahedral field, the free cobalt (III) ion having the $d^6$ configuration will have the lowest energy state $^5T_{2g}$. But the $^1A_{1g}$ state originating from one of the high energy singlet states of the free ion drops very rapidly.

As a result, most of the Co(III) octahedral complexes are low spin and diamagnetic. The synthesis of some binuclear cobalt (IV) phthalocyanines has also been reported[63].
1.6 REVIEW OF THE LIGANDS

Ligands play a prominent role in the synthesis of complexes. The neutral molecule or ions which are attached with the central metal ion are called ligands. In a co-ordination compound, the ligands act as lewis bases whereas the central metal ion act as lewis acid. The number of ligand atoms arranged in a definite geometry and directly bonded to a central metal ion is called the coordination number of that ion. Depending upon the coordination number of the central metal ion, the ligands adopt a definite geometry. The common geometries are linear (Coordination number = 2), equilateral triangular (Coordination number = 3), tetrahedral or square planar (Coordination number = 4), Square pyramidal (Coordination number = 5) and octahedral (Coordination number = 6).

Depending upon the number of atoms per ligand, that are attached to the central metal ion, ligands are classified as monodentate, bidentate, tridentate ligands etc. Ligands other than monodentate are chelating ligands. If the different groups belonging to different types of ligands are bonded to the central metal ion, such complexes are termed as ‘Mixed Ligand Complexes’. In the present study glutaraldehyde and amino acids such as L-Leucine(leu), L-Valine(val), L-Alanine(ala), L-Histidine(his) and L-Glutamine(gln) are used as ligands.

1.6.1 Amino acids

Amino acids, a significant class of organic based compounds, contain potential donor sites such as COOH (an acidic group) and NH₂ (a basic group) which have a good ability to coordinate with metal ions. In biochemistry, this term refers to α-amino acids with the general formula NH₂CHRCOOH.
These are molecules where the amino and carboxylate groups are attached to the same carbon, which is called the $\alpha$-carbon. It is well known that the human body contains essential amino acids which play important roles and interact with many biological molecules.

Amino acids are the chemical units or “building blocks” of the body that make up proteins. Protein substances make up the muscles, tendons, organs, glands, nails, and hair. Growth, repair and maintenance of all cells are dependent upon them. Next to water, protein makes up the greatest portion of our body weight. Amino acids that must be obtained from the diet are called “Essential Amino acids”, and other amino acids that the body can manufacture from other sources are called “Non Essential Amino acids”.

The molecular formula and molar mass of L-Leucine(leu) is $\text{C}_6\text{H}_{13}\text{NO}_2$ and 131.17 g mol$^{-1}$ respectively. It works with Isoleucine and Valine to promote healing of muscle tissues, skin and bones; recommended for those recovering from surgery, lowers blood sugar levels and aids in increasing growth hormone production.

The molecular formula and molar mass of L-Valine(val) is $\text{C}_5\text{H}_{11}\text{NO}_2$ and 117.15 g mol$^{-1}$ respectively. It is needed for muscle metabolism and coordination, tissue repair, and for the maintenance of proper nitrogen balance in the body. It is used as an energy source by muscle tissue, helpful in treating liver and gallbladder disease, promotes mental vigor and calms emotions.

L-Alanine is an $\alpha$-amino acid which is abbreviated as ala, with the chemical formula $\text{CH}_3\text{CH(NH}_2\text{)COOH}$. It molar mass is 89.09 g mol$^{-1}$. It occurs in bacterial cell walls and in some peptide antibiotics. It is found in wide variety of foods, but is particularly concentrated in meats. It plays a key role in glucose-alanine cycle between tissues and liver.

The molecular formula of L-Histidine is $\text{C}_6\text{H}_9\text{N}_3\text{O}_2$ and is abbreviated as his. Its molar mass is 155.15 g mol$^{-1}$. It is an amino acid with an imidazole functional group.
It is found abundantly in haemoglobin; has been used in the treatment of rheumatoid arthritis, allergies, ulcers and anemia; is essential for the growth and repair of tissues; important for the maintenance of the myelin sheaths, which protect nerve cells; is needed for the production of both red and white blood cells; protects the body from radiation damage; lowers blood pressure and aids in the removal of heavy metals from the body.

L-Glutamine is an $\alpha$-amino acid which is abbreviated as gln, with the molecular formula $C_5H_{10}N_2O_3$. In human blood, glutamine is the most abundant free amino acid, with a concentration of about 500-900 umol/1. Glutamine plays a role in a variety of biochemical functions including protein synthesis, regulation of acid-base balance in the kidney etc. It also acts as a source of cellular energy and carbon donation. Dietary sources of glutamine include beef, chicken, fish, eggs, milk and vegetables.

1.6.2 Properties of amino acids

A tetrahedral carbon atom with four distinct constituents is said to be chiral. The only one amino acid not exhibiting chirality is glycine since its “R-group” is a hydrogen atom. Chirality describes the handedness of a molecule that is observable by the ability of a molecule to rotate the plane of polarized light either to the right (dextrorotatory) or to the left (laevorotatory). The two optical isomers are called D and L. The L-amino acids represent the vast majority of amino acids found in proteins. D-amino acids are found in some proteins produced by exotic sea-dwelling organisms.

Amino acids contain both a basic group (-NH$_2$) and an acidic group (COOH). In the dry solid state, amino acids exist as dipolar ions, a form in which the carboxyl group is present as a carboxylate ion – CO$_2^-$, and the amino group is present as an aminium ion, -NH$_3^+$ (dipolar ions are called Zwitterions).
In aqueous solution, an equilibrium exists between the dipolar ion and anionic and cationic forms of an amino acid (Scheme 3).

The predominant form of the amino acid present in a solution depends on the pH of the solution and on the nature of the amino acid. In strongly acidic solutions, all amino acids are present primarily as cations; in strongly basic solutions they are present as anions. At some intermediate pH, called the isoelectric point, the concentration of the dipolar ion is at its minimum and the concentrations of the anions and cations are equal. Each amino acid has a particular isoelectric point.

1.6.3 Glutaraldehyde

A clear, colourless to pale straw-coloured pungent oily liquid with molecular formula C₅H₈O₂ and molar mass 100.12 g mol⁻¹ is glutaraldehyde (glu). It is a clear liquid with 1.06 g/ml density. It melts at -14°C and it is soluble in all proportions in water and alcohol, as well as in organic solvents. Its boiling point is 187 °C. It is mainly available as acidic aqueous solutions (pH 3.0-4.0), ranging in concentration from less than 2% to 10%. It is a useful tissue and molecular fixing reagent. The aldehyde moiety reacts mainly with primary amino groups to form Schiff’s base, which is reversible but reasonably stable at pH 7. The bifunctional glutaraldehyde, (CHO – (CH₂)₃ – CHO), successfully stabilizes protein molecules due to generally plentiful amines on their surface. A glutaraldehyde solution of
0.1% to 1.0% concentration may be used for system disinfection and as a preservative for long term storage. Glutaraldehyde is used in biological electron microscopy as a fixative. Another example of an application for treatment of proteins with glutaraldehyde is the inactivation of bacterial toxins to create toxoid vaccines, e.g., the pertussis (whooping cough) toxoid component in the Boostrix Tdap vaccine produced by GlaxoSmithkline. In a related application, glutaraldehyde is employed in the tanning of leather. Glutaraldehyde is frequently used in biochemistry applications as an amine-reactive homobifunctional crosslinker. Glutaraldehyde is also used in SDS – PAGE to fix proteins and peptides prior to staining.

The literature on the reaction of glutaraldehyde with biological systems is extensive. Hopwood[64] has reviewed its application in fixation. Many authors have described its use for the preparation of insoluble protein aggregates and insoluble derivatives of certain enzymes[65,66]. Glutaraldehyde can react with several functional groups of proteins, such as amine, thiol, phenol and imidazole because the most reactive amino acid side-chains are nucleophiles. Various data on aldehyde reactivity with the following amino acids have been reported in the literature: lysine, tyrosine, tryptophan, and phenylalanine, histidine, cysteine, proline, serine, glycine, glycylglycine and arginine. Glutaraldehyde has undoubtedly found the widest application in various fields such as cytochemistry[67], histochemistry[68], microscopy[69], leather tanning industry, enzyme technology, chemical sterilization and biomedical and pharmaceutical sciences[70].

1.7 Review of Schiff Base Metal Complexes

The great potential for producing novel materials with interesting useful functions and desirable properties has led to the rational design and synthesis of metallo-organic molecules which has become an intensely studied subject.
Schiff bases have for decades been among the most fundamental systems in coordination chemistry. Schiff bases possess delocalized $\pi$ orbitals, flexible behaviour and multi functional ligating sites. Schiff bases function as ligands of higher denticity than the components from which they are formed. Thus the metal ions form highly stable Schiff base complexes. Schiff base complexes can be classified in a number of ways as mononuclear, binuclear and polynuclear on the basis of number of metal atoms present and as monodentate, bidentate and polydentate depending on the number of binding sites present in the ligands.

Protonation constants of the Schiff bases and stability constants of the Schiff base complexes derived from furfural and DL-alanine, DL-valine and DL-phenylalanine have been determined potentiometrically in water and characterized by analytical, spectroscopic techniques, molar conductivity, magnetic and thermal measurements. Solid-state conductivities of the synthesized substances were measured using the four-probe technique on a compressed pellet at room temperature by Nursen Sari et al\textsuperscript{[71]}. In a separate work, the relationship between antimicrobial activities and the formation constants of amino acid-Schiff bases and their Cu(II) and Ni(II) complexes have recently been studied by Gurkan et al\textsuperscript{[72]}. For this purpose, a series of Schiff bases were prepared from DL-amino acids (DL-glycine, DL-alanine) and haloaldehydes (5-chloro-2-hydroxybenzaldehyde, 5-bromo-2- hydroxybenzaldehyde). The Schiff bases and their Cu(II) and Ni(II) complexes were characterized by elemental analysis, spectral analysis, magnetic moment, molar conductivity and thermal analysis data. The protonation constants of the Schiff bases and stability constants of the complexes were determined potentiometrically in a dioxane -water solution at 25°C and 0.1M KCl ionic strength. Antimicrobial activities of the Schiff bases and their complexes were estimated against various bacteria.

The antimicrobial activity assessment revealed that the bromo-substituted complexes of the Ni$^{2+}$ ion are generally more active than their chlorine-substituted analogs. The
lipophilicity of complexes increase due to the delocalization of \( \pi \)-electrons in the chelate ring with an increase in the stability constants. In general, the activity of the complexes depended on the chain length of the amino acid-Schiff bases ligand.

In another recent investigation, the inhibitory bioactivity of six new transition metal complexes against urease and Xanthine oxidase (XO) was studied. The new compounds were complexes (M = Cu(II), Ni (II) and Mn(III) of tridentate (H\(_2\)L\(_1\),HL\(_2\)) and /or bidentate (HL\(_3\),HL\(_4\)) Schiff- base ligands, obtained from the condensation of salicylaldehyde with glycine, N-(2-aminoethyl) morpholine, 4-(2-aminoethyl) phenyllic acid and 4-(2-aminoethyl) benz sulfamide, respectively. They were synthesized and structurally determined by single-crystal X-ray analysis. Copper (II) complexes showed potent inhibitory action against jack bean urease, comparable with acetohydroxamic acid, which is a positive reference. In addition, these copper (II) complexes also exhibited a strong ability to inhibit activity of XO, comparable to allopurinol which was used as a positive reference. Nickel (II) and Manganese (II) complexes showed a weak inhibitory activity to jack bean urease and no ability to inhibit XO.

In 2007, a series of 20 complexes (M=Co(II), Cu(II), Ni(II), Zn(II) of Schiff bases derived from Salicylaldehyde and 5 amino acids were reported. First, the Schiff bases were isolated as solids by reflux in an ethanol/water solution followed by concentration of the solution under vacuum. The complexes were prepared by addition of KOH and metal(II) salt in ethanol/water and were found to have the general formula K\(_2\)[ML\(_2\)].[K:potassium, M:metal and L:ligand]. The magnetic moments and electronic spectral data suggested that all have an octahedral geometry.

Elemental analyses and NMR spectral data of the ligands and their Zn(II) complexes agree with their proposed structures. The synthesized ligands, along with their metal complexes, were screened for their in vitro antibacterial activity and in vitro antifungal
activity against various bacteria and fungi. The results of these studies show the metal complexes have great antimicrobial activity against the various species as compared with the uncomplexed Schiff base ligands. All the complexes were intensely coloured, air and moisture stable amorphous solid which decompose without melting. They were insoluble in water, DMF and DMSO.

Copper(II) complexes of Schiff bases formed between pyridoxal and various biogenic amines\textsuperscript{73} have been prepared and studied by spectroscopic and magnetic measurements.

Copper(II) complexes of chloramphenical Schiff bases were reported\textsuperscript{74}. Panova et al\textsuperscript{75} discussed the formation mechanism, structure and stereochemistry of four coordinate Schiff base chelate compounds and their analogues. The configuration of the chelate group in the four coordinate complexes may be square-planar tetrahedral, distorted tetrahedral or distorted pyramidal with the metal atom at the apex. The configuration depends primarily on the nature of the metal atom and also on the magnitude and symmetry of the ligand field. Schiff base complexes of copper(II) are believed to be key intermediate of pyridoxal dependent enzymes. Consequently, a number of studies of the Schiff bases derived from amino acids and pyridoxal have been reported\textsuperscript{76}. Kwik et al\textsuperscript{77} prepared and characterized a series of mixed ligand complexes of copper (II) containing a mono condensed Schiff base and an amino acid. Ternary complexes incorporating the toxicity studies against Drosophila malanogaster has been worked out by Raso et al\textsuperscript{78}. Jesierska\textsuperscript{79} discussed the synthesis and structural aspects of Copper(II) complexes derived from tricoordinate Schiff bases involving amino acids.

Mohamed N. Ibrahim and Salah E\textsuperscript{80} have reported many Schiff bases which were prepared by condensation reaction of certain aromatic amines with aromatic aldehydes derivatives, then the fluorescence properties of these Schiff bases were examined in acidic and basic media. It shows that these compounds can be used for spectrofluorimetric
monitoring of small pH changes. Hai Jain YANG, Wen Hua SUN et al[81] have described that a microwave-assisted preparation of a series of Schiff-base via efficient condensation of salicylaldehyde and aryl amines without solvent is in high yield as well as environmental friendship reaction in organic synthesis. Khalil R A, Jalil Alt and Abd-Alrazzak AY[82] have reported about the possibility of using a Schiff base as an acid-base indicator. This surprising phenomenon can be considered as an interest due to the fact that Schiff bases are usually unstable in solutions and definitely undergo hydrolysis. It was found that such a specific observation depends merely upon the chemical structure and type of the substitute of amine that reacts with aldehyde to give the Schiff base. Shreenivas MT, Chetan BP and Bhat AR[83] have reported many Schiff bases and they were prepared by condensation reaction of nitro compound containing biphenyl ether amines with aromatic aldehydes and ketone derivatives and thiazolidines.

The influence of solvent medium of the formation, hydrolysis and equilibrium constant of the Schiff base formed with 5-pyridoxal phosphate was discussed by Gorostidi et al[84]. Five coordinated copper (II) complexes with reduced Schiff base ligands of amino acids possessing non polar side chains with salicylaldehyde have been synthesized and their ternary complexation behaviour with imidazole, 1, 10-phenanthroline and pyridine were studied by Roh et al[85]. Ternary Copper (II) complexes containing reduced Schiff base N-(2- hydroxybenzyl) -α- amino acids and 1,10-phenanthroline was synthesized and characterized by Yang et al[86].

Alkoxo-phenoxo bridged tetranuclear Copper(II) complexes containing pentadentate Schiff base ligand N, N-(2-hydroxypropane-1,3-diyl) bis (salicylaldimine) were prepared and characterized by Mukherjee et al[87]. Reddy et al[88] investigated the light induced DNA cleavage activity of copper(II) Schiff base complexes containing NSO donor Schiff bases. Some mononuclear nickel(II) and copper(II) complexes of the Schiff base derived from 2,6-
diformyl-4-methyl phenol and S-methylisothiosemicarbazones were synthesized and characterized by Gradinaru et al.\cite{89} ESR and magnetic measurements confirm the square planar structure of these complexes. Patel et al\cite{90} reported the synthesis, characterization and biocidal evaluation of nickel(II), copper(II) manganese(II), cobalt(II) and cadmium(II) complexes with bis (acetophenone) ethylene diamine and 5-chlorosalicylideneaniline or 5-bromosalicylideneaniline. Morad et al\cite{91} prepared, characterized and evaluated the antibacterial activity of square planar nickel (II) Schiff base complex derived from salicylaldehyde and o-amino benzoic acid. Arshi N et al\cite{92} reported Non–Classical methods for the preparation of Schiff bases from 3-chloro-4-fluoro aniline and several benzaldehydes. These methodologies constitute an energy-efficient and environmentally Benign greener chemistry version of the classical condensation reactions for Schiff bases formation. Lei Wang, Yaquing Feng, Jinqiang Xue, Yukun Li\cite{93} reported some novel porphyrin Schiff bases. The synthesis of Schiff bases were characterized on the basis of chemical properties and spectral data. G. Rossi\cite{94} reported certain aromatic aldehydes on reacting with aromatic amines give rise to Schiff bases. Venugopal KN, Jayashree BS\cite{95} reported a fast and highly efficient method for the synthesis of some of the Schiff bases of bromo coumarins by microwave irradiation. The resulting products were evaluated for the qualitative and quantitative antibacterial activity.

Chantarasiri et al\cite{96} analyzed the structure and physicochemical properties of zinc (II) complexes of hexadentate Schiff base derived from salicylaldehyde and o-vanillin with triethylenetetramine. The stability constant values of these complexes were determined by potentiometric titration method. Temel et al\cite{97} reported the synthesis of novel quadridentate N$_2$O$_2$ type Schiff base complexes of transition metals. Kaya et al\cite{98} studied the oxidative polycondensation reaction conditions of 2-(p-tolylazomethine) phenol with air/oxygen and sodium hypochlorite in aqueous alkaline medium and reported that a part of the azomethine
group is oxidized to carboxylic group during the polycondensation reaction. The oligomer metal complexes of cobalt (II), copper (II), zinc (II) and promethium (II) were synthesized and the antimicrobial activities of the complexes as well as the oligomer were examined.

\(\mu\)-phenoxo bridged polynuclear complexes of cobalt(II), nickel(II), copper(II) and zinc(II) with their self assembling behaviour was explained by San Martin et al\(^{[99]}\). The rate of formation and hydrolysis of the Schiff base formed by pyridoxal -5'-phosphate with L-tryptophan and its methyl and n-butyl esters were investigated by Gorostidi et al\(^{[100]}\). Novel amino acid Schiff base iron(II) complexes were synthesized and characterized by Shaker et al\(^{[101]}\). Parikh et al\(^{[102]}\) reported the synthesis of Schiff base complexes by the template reaction of metal-diamine complexes with salicylaldehyde. Catalytic activity of Cobalt(II) Schiff base complexes were discussed by Nishinaga et al\(^{[103]}\).

The electro chemical properties of Vanadium(IV) derivatives of Salen Schiff bases were investigated by Kianfar et al\(^{[104]}\). The electronic and steric effect of equatorial Schiff base ligands affect the oxidation potentials via interaction with the d-orbitals of the metal ion was explained. The formation constant of Schiff base metal complexes involving o-vanillin with amino acids and their biological activity were investigated by Nair et al\(^{[105]}\).

The biological properties of some Schiff base complexes on the activity of some neutral, acidic and basic amino peptidases were assayed by Zeng et al\(^{[106]}\) and demonstrated generally an inhibitory effect. Neelakantan et al\(^{[107]}\) reported the synthesis, characterization and biological activities of transition metal complexes containing monobasic Schiff base derived from o-vanillin and 2-aminobenzothiazole.

Indrasenan et al\(^{[108]}\) reported the antibacterial activity of Schiff bases from heterocyclic aldehydes such as furan-2-aldehyde and pyridine-2-aldehyde. The antimicrobial properties of Ni(II) and Cu(II) complexes with Schiff bases furfurylidene isoniazide,
furufurylidene-4-aminoantipyrine and furufurylidene-2- amino pyridine have been reported by Mishra\cite{109}. Schiff bases of bis phenol-C synthesized by reacting substituted benzaldehyde (ortnonitro, p-nitro and p- methoxy) and amino-bisphenol-C in DMF were screened for their activity and found that they possess antibacterial and antifungal activities\cite{110}. Dioxouranium (VI) complexes of Schiff bases 2-N-(benzalidene) amino pyridine were proved to be antifungal by Kishor Arora et al\cite{111}. Schiff base ligands derived from vanillin, 4-dimethyl aminobenzaldehyde and 3,5 di-t-butyl-4- hydroxybenzaldehyde with N-(pyridyl)-3-methoxy-4-hydroxy-5-aminobenzylamine and their complexes with Cu(II), Co(II), Ni(II) Vo(IV) and Zn(II) were synthesized and characterized by Tumer et al\cite{112}. Pulimamidi Saritha Reddy\cite{113} discussed the synthesis and structural studies of first row transition metal complexes with pentadentate ONNO donor Schiff Base derived from 5-Acetyl 2,4-Dihydroxy Acetophenone and Diethylene Triamine. The synthesized complexes were assigned to have octahedral stereochemistry. Sheeja Lovely et al\cite{114} studied the DNA cleavage and antimicrobial studies of Cu(II), Ni(II), Zn(II) and Co(II) complexes of Schiff base derived from 4-pyridine carboxaldehyde with Tryptophan and revealed that all complexes showed enhanced nuclease activity.

Shivaraj et al\cite{115} reported the formation constants and thermodynamic parameters of bivalent metal ion complexes with 3-amino-5- methyl isoxazole Schiff bases and N,N; N,O and O,O donor ligands in solution. The order of stability constants with respect to metal ions was found to be in accordance with Irving-Williams natural order. From the positive $\Delta \log K$ values, it was observed that the ternary complexes were more stable than 1:1 binary complex of secondary ligand. Ali Javadi Zare et al\cite{116} synthesized and characterized complexes of tetradeutate Schiff base derived from 2,3- diaminopyridine and salicylaldehyde and reported that the synthesized compounds can be used as catalysts in redox reactions. K. Krishnankutty et al\cite{117} studied the metal complexes of Schiff bases derived from dicinnamoylmethane and
ortho-substituted aromatic amines and discussed the formation of their complexes with Ni(II), Cu(II) and Zn(II) and their nature of bonding on the basis of analytical and spectral data. Billman JH et al[118] reported the preparation and antitumour activity of some Schiff bases of 2-Amino-4,5-dichlorobenzenesulfonanilide and 2-Amino-p-toluenesulfonanilide. Rehman W et al[119] investigated Diorganotin (IV) complexes derived from 5,5-Diethyl Sodium Barbital and explained its enhanced activity of the complexes towards various microorganisms. N. Raman et al[120] performed the synthesis, structural characterization and antimicrobial studies of five novel copper (II) complexes using Schiff base ligands synthesized by the condensation reaction of anthranilic acid and knoevenagel β-ketoanilide condensates. It represented a novel class of metal-based antimicrobial agents which provide opportunities for a large number of synthetic variations for the modulation of the activities. Sunil S. Patil et al[121] reported the synthesis and biological studies of mixed ligand Ni(II) complexes of the type [M(Q)(L). 2H₂O] by using 8-hydroxyquinoline as a primary ligand and N-and/or O-donor amino acid such as L-serine, L-isoleucine, L-proline, 4-hydroxy-L-proline and L-threonine as secondary ligands.

Munde et al[122] discussed the synthesis and characterization of some transition metal complexes of an asymmetrical tetradeinate Schiff base ligand derived from dehydroacetic acid, 4-methyl-o-phenylenediamine and Salicylaldehyde. He assumed that the ligand behaved as dibasic, ONNO tetradeinate coordinating via the phenolic oxygen and the imino nitrogen and the complexes were found to be biologically active and thermally stable. Mohamed et al[123] reported the synthesis and characterization of metal complexes of Schiff bases derived from 2-furancarboxaldehyde and 2-aminothiophenol. Gupta et al[124] described the behaviour of the bidentate aromatic Schiff base ligand prepared by the condensation of 2-Pyridyl carboxylaldehyde and ethylene diamine and screened the synthesized compounds for their physiological activities against various microorganisms.
Ahmed et al\textsuperscript{[125]} described the synthesis and characterization of neutral tetradeinate \(N_2O_2\) type complexes of vanadium (IV) using a Schiff base formed by \(o\)-aminobenzoic acid, \(o\)-aminophenol, Benzidin and 1,4-phenylene diamine with Benzil, salicylaldehyde and 2-methylcyclo-pentane-1,3-dione in alcohol medium and proposed these vanadyl complexes to function as potent insulin-mimetic and antidiabetic agents. Stanila A et al\textsuperscript{[126]} reported the antibacterial activity of copper and cobalt amino acid complexes using methionine, phenylalanine, valine, leucine and lysine as ligands and suggested these complexes to have antibacterial activity and their potential application as antibacterial agents.

1.8 SCOPE OF THE PRESENT INVESTIGATION

The relationship between metal ions and biological activity of certain systems is obvious and a subject of great interest. It has been demonstrated through several studies that biologically inactive compounds become active and less biologically active compounds become more active upon coordination with the metal ions.

The apparent role played by metal ions in the induction or enhancement of biological activity of the organic compounds or ligands are therefore definite, but how, is still a matter of conjecture. In order to get an insight into this role, the behaviour of Schiff bases have gained a great deal of attraction. The azomethine linkage (-N=CH-) is a significant feature that makes Schiff base ligands the interesting candidates for biological activities as well as coordination with the metal ions. The interaction between metal ions and such biologically active ligands represents an important route in designing new metal-based antibacterial, antifungal and anticancer therapies against different kinds of bacteria, fungi and cancer-associated viruses that become resistant to the use of conventional drugs. So it is worthwhile to synthesize some Schiff bases and study their biological behaviour via coordination to metal ions with the expectation that these studies may result in achieving new targets in synthesizing metal based compounds that could fight more aggressively against bacterial and
fungal strains which become resistant to certain presently available and commonly used antimicrobial agents.

Glutaraldehyde, which has been chosen as primary ligand in the synthesis of Schiff base is of biological importance. It is used as a tissue and molecular fixing reagent. It has been used as a disinfectant and chemical preservative. Various works have been done which explain the effective protein cross-linking ability\textsuperscript{[127]}. It has also been used in the preparation of bioprotheses such as heart values, vascular grafts, conjugation of enzymes to carrier systems etc. The dialdehyde has the tendency to react with the protein in collagen fibres and undergo the formation of Schiff base\textsuperscript{[128]}. This demonstrates the wide range of roles of aldehyde in biomedical field. Habeeb et al\textsuperscript{[129]} reported the reaction of proteins in tissues with glutaraldehyde leading to the formation of Schiff bases. Avrameas et al\textsuperscript{[130]} studied the cross-linking of proteins with glutaraldehyde and its use for the preparation of immunoadsorbents.

Amino acids constitute the building blocks of proteins and are chemical species indispensable for performing a huge number of biological functions as exemplified by the role of enzymes\textsuperscript{[131]}. The amino acid Schiff base metal complexes have received considerable attention because of the interests in the biological field\textsuperscript{[132,133]}. Investigations performed on amino acid Schiff base metal complexes can be used to elucidate the poisoning role of certain metallic elements in living organisms as well as to clarify the action of drugs\textsuperscript{[134]}. Hence, the studies presented in this thesis is concerned with synthesis, characterization and antimicrobial activities of some transition metal Schiff base complexes.

The amino acids used in the present investigation can be classified into four groups.

a. Alanine and Valine are potentially bidentate amino acids with aliphatic side chain

b. Histidine is a basic amino acid with imidazole nitrogen as a third donor site.

c. Leucine is a hydrophobic amino acid due to its aliphatic isobutyl side chain.
d. Glutamine is an essential amino acid with amide side-chain formed by replacing the side-chain hydroxyl of glutamic acid with an amine functional group. The solid complexes of these ligands with Co(II), Ni(II) and Cu(II) were isolated and characterized using various physico-chemical techniques.

The present study is organized under five chapters. A general introduction to the chemistry of coordination compounds and a review of Schiff base and its complexes are given in chapter I.

The second chapter presents the study of synthesis of various Schiff bases and its complexes with metal (II) ions such as Cu(II) ion, Ni(II) ion and Co(II) ion, and also various characterization techniques used for the study.

The third chapter deals with results and discussion. It describes the various results obtained by undergoing spectral studies, elemental analysis, conductance measurement, magnetic susceptibility measurement, x-ray diffraction and thermal studies.

Chapter four deals with the study of antimicrobial activity of the synthesized Schiff bases and its complexes. Chapter five gives the summary and conclusion of the presented work and scope for future work and at last the references are listed.

The present investigation leads to important conclusions such as the following.

1. The mode of coordination of the Schiff base ligand with the metal ions.
2. The geometry around the metal ions in the solid state of the complexes.
3. Thermal stability of the synthesized complexes.
4. Crystalline or amorphous nature of the complex.
5. The antibacterial and antifungal activities of complexes.