CHAPTER - I

INTRODUCTION

Essential metal ions in most tissues and fluids include sodium, potassium, calcium, magnesium, manganese, iron, cobalt, copper and zinc. In addition there may be variable amounts of non-essential or even potentially toxic cations notably lead, mercury and cadmium. Complex forming organic molecules are also numerous in biological systems and include amino acids, peptides, proteins, carboxylic acids, organic phosphates and nucleic acids, together with inorganic ligands such as chloride, bicarbonate and phosphate. This alludes to the possible formation of metal complexes in biological systems. Metal ions iron, magnesium and cobalt are known to be integral components of haemoglobin, chlorophyll and vitamin B_{12}, respectively. Similarly, there are many metalloenzymes such as the iron containing peroxidases, zinc containing carbonic anhydrase, copper and molybdenum containing oxidases, in which the presence of appropriate metal ion is essential for biological activity. This clearly demonstrates an intimate linkage between inorganic chemistry and living processes.

In the mammalian body, the total ligand concentration greatly exceeds the metal content, so that living tissues and fluids have been likened to arenas in which the various complexing species compete for the different kinds of metal ions, that are present. The extent to which any ligand binds any particular metal at a particular pH depends, not only on the relative and absolute concentrations of all the kinds of metal ions and ligands that are present, but also on the basicity of the ligand and other factors affecting the strength of M-L bond.

Orgel [1] suggested that Ca(II), Mg(II) and Mn(II) ions should be bound preferentially to carboxylate groups, Cu(I) to cysteine and histidine, Cu(II) strongly to amines and carboxylates, Zn(II) to amines and thiols,

Fe(III) to carboxylates, tyrosine and amines and Fe(II) should have an increased affinity for thiol and amino group, relative to carboxylate. Williams [2] suggested that at physiological pH ($\sim$ 7.3), Mg(II), Mn(II) and Ca(II) ions are unlikely to be bound to any groups except oxyanions, Cu(II) and Zn(II) ions are likely to be held by sulphur or possibly nitrogen groups, but not by oxy-anions, whereas Co(II), Fe(II) and Ni(II) ions are likely to be bound by mixed oxyanion-nitrogen coordinating ligands.

As numerous potential ligands are likely to compete for metal ions found in vivo, mixed-ligand chelation occurs in biological fluids. Mixed -ligand formation has important biological implications in facilitating enzyme-substrate interaction through the formation of an intermediate enzyme-metal ion-substrate ternary complex [3-15]. For e.g., in the metalloenzyme carboxy peptidase A (CPA), zinc is coordinated, in a distorted tetrahedral stereochemistry to two histidine residues, one glutamic acid residue and a water molecule. The substrate dipeptide molecule displaces the water ligand and gets coordinated to zinc from the peptide oxygen site [16], thereby forming a ternary complex. Similarly in pyruvate kinase the manganese ion, already bound to an imidazole, coordinates to an oxygen in the phosphate group of the substrate forming an enzyme-metal ion-substrate complex [4]. Hence ternary complexes of bio-chemically important ligands are being considered as models for biochemical processes. However, biomolecules mainly involve O, N and S coordinating atoms and have a variety of active metal ion sites showing keen specificity and selectivity. This necessitates deeper study of the factors related to the stability of the ternary complexes.

Formation Constants of Ternary Complexes :

Ternary or mixed-ligand complexes are formed by complexation of a metal ion (M) with two different kinds of ligands (A or L). A common way to quantify the stability of such ternary complexes is by calculating the values of $\triangle$ log K (equation 1.1) [17-20].

$$\triangle \log K = \log K^{MA}_{MAL} - \log K^{M}_{ML}$$

$$= \log K^{ML}_{MLA} - \log K^{M}_{MA}$$

$$= \log \beta^{M}_{MAL} - \log K^{M}_{MA} - \log K^{M}_{ML} \qquad (1.1)$$

In accordance with the statistical considerations [19], negative values for $\triangle$log K are usually expected. In binary systems also, $K^{M}_{MA} > K^{MA}_{MA_2}$ and the difference, $K^{MA}_{MA_2} - \log K^{M}_{MA}$ is generally about - 0.5 to - 0.8 log units for monodentate ligands and about - 1 to - 2 log units for bidentate ligands [21]. Statistical values for $\triangle$ log K in ternary complexes have also been determined. In case where A and L are bidentate ligands, for a complex having regular octahedron geometry (oh) $\triangle \log K_{oh} = - 0.4$ [22]. For a square planar geometry (sp), the theoretical value of $\triangle \log K_{sp}$ should be - 0.6. For a distorted octahedron (do) ternary copper (II) complex the statistical value of $\triangle \log K_{do}$ has been calculated to be - 0.9 (or - 1.1) to - 0.3 [23]. In case of ternary copper (II) complexes of strong field ligands, the most appropriate statistical value of $\triangle \log K_{do/Cu}$ is considered

to be - 0.9 [24]. Hence, an experimentally determined value of $\triangle \log K\rangle$ - 0.9 indicates that the formation of ternary complex is favoured.

Though from statistical considerations, it is expected that $\triangle \log K$ of a ternary complex MAL should be negative, i.e. $K^{MA}_{MAL} < K^{M}_{ML}$, there are many astatistical factors that stabilize the ternary complexes. The understanding of the influence of the astatistical factors on the stability of ternary complexes [18, 24-26] has evolved through several observations. These factors are :

i) Charges on the ligands leading to electrostatic repulsion [27-29],

ii) Steric hindrance due to bulky groups on the ligands [30-34],

iii) Ring size effect [35-37],

iv) Tridentate character of one of the ligands [38],

v) Π - acid effect [39-52].

These factors are operative in metalloenzyme systems, stabilizing the intermediate enzyme-metal-substrate complexes.

However, the most predominant interaction which stabilizes the ternary complexes in biological systems is intramolecular interligand interactions. Such interactions lead to specificity and selectivity of ternary complex formation and have attracted much attention in recent years, for their relevance to biological reactions, involving metal ions at the active sites [19, 53, 54]. The hormone-receptor, enzyme-substrate and antigen - antibody interactions are among the most important in biological systems and many of them are achieved by the interaction between specific side chain groups of proteins involved [55]. These interactions are of two types [56-58] :

a) **Rigid interaction :** One of the ligands is fixed rigidly with the metal ion and the other one has a flexible non-coordinating group interacting with the rigid ligand. For e.g. a rigid interaction between a coordinated aromatic diamine and the non-coordinated base of a nucleotide as in [Cu-2, 2' - bipyridine - adenosine triphosphate] complex [59, 60].

b) **Flexible interactions :** If both the ligands have free non-coordinated group, there can exist flexible interaction between them, as between non-coordinated side group of an amino acid and free base part of ATP in [Cu-ATP-tryptophan] complex [61] or non-coordinated side groups of two amino acids as in [Cu-phenylalanine-tryptophan] complex [62]. In case of both the types of intramolecular interligand interactions the nature of forces operative may vary. They are of following types :-

i) **Hydrogen bonds :** Formation of hydrogen bonds between two different ligands already coordinated to the same metal ion is possible [63], and is also known to exist in solid mixed-ligand complexes [64]. In the crystal structure of [Cu-5'-inosine monophosphate- diethylenetriamine]Na complex, interligand hydrogen bonding between oxygen of the phosphate group of IMP and $-NH_2$ group of diethylene triamine has been observed [65].

ii) **Ionic or Electrostatic Interactions :** Intramolecular interaction may be due to electrostatic attraction between the positively charged protonated amine part of an amino acid and free negatively charged carboxylate part of another amino acid. In complexes [CuAB], A = ethylene diamine monoacetic acid, B = DL - arginine, ornithine, lysine, alanine or L-valine, enhanced CD magnitudes were inferred to be due to electrostatic interaction between charged COO^- of A and $-NH_2$ of B.

In mixed amino acid complexes [MAB], A = acidic amino acids like aspartic acid, glutamic acid, cystine, B = basic amino acid like arginine, an electrostatic interaction occurs between negative charged COO^-, SH^- of A and NH_3^+ of arginine [66-70].

iii) **Stacking Interactions :** Intramolecular aromatic ring stacking between two suitable ligands within a ternary complex was first shown to occur in the ternary Cu^{+2} complexes formed by 2,2' - bipyridine and adenosine - 5' - triphosphate or inosine - 5 - triphosphate [59, 71, 72]. The evidence came from electronic spectral, NMR spectral and stability studies. X-ray structure determinations of solids of such ternary complexes show an intramolecular stacking between the aromatic moieties of the co-ordinated ligands [73-76]. In crystals the kind of stacking is determined by the lattice, such stacking interactions contributing significantly towards the stability of crystal latticce [76, 77].

Sigel has observed intramolecular stacking interactions in mixed-ligand complexes involving ATP and tryptophan [78]. UV spectral studies show a new peak at 295 nm which can be attributed to an interaction between indole group of tryptophan and purine moiety of ATP. In ^{1}HNMR, positive shifts of the signals of H(2), H(4) and H(5,6) of tryptophan and H(2) and H(8) of ATP, compared to those of corresponding free ligand signals confirms the formation of intramolecular stack between the indole residue of tryptophan and imidazole residue of adenine moiety of ATP.

In the complexes involving Cu^{2+}, 1, 10-phenanthroline (phen) and phenyl-carboxylates ($C_6H_5 - (CH_2)_n - COO^-$; n = 0 to 5), it was observed

that the extent of intramolecular stacking depends upon the flexibility of the coordinated ligands [79]. The extent of stacking interaction was found to be maximum for phenylacetate (n=1).

In the ternary complexes with the phenylcarboxylates having a longer chain (n= 2 to 5), the increased flexibility lowers the ligand-ligand interactions. It was also observed that with the increase in size of the involved aromatic ring systems, the extent of stacking increases : the replacement of 2-phenylacetate by [2-(β -naphthyl)] acetate promotes the interaction.

Stacking interactions have also been observed in biological systems. Examples are interaction of adenine base of ATP with the protein part of the enzyme glutamate dehydrogenase [80], creatine kinase [81], octopine dehydrogenase [82] or myosin [83,84]. Stacking interactions between purine and pyrimidine bases contribute to the stability of nucleic acid helics [85]. Such interactions were also observed in models of flavin adenine dinucleotide [FAD] [86,87] or nicotinamide adenine dinucleotide [NAD] [88,89].

iv) **Hydrophobic Interactions :** Intramolecular hydrophobic interactions are closely related to the described aromatic ring stacking interactions. The first such interactions was shown to occur in the ternary Cu^{+2}, and Zn^{+2} complexes between the metal bound 2, 2' - bipyridine or 1, 10-phenanthroline and trimethylsilyl moiety of the second ligand 3 - (tri-methylsilyl) - 1 - propane sulphonate or 3-(trimethyl silyl) propionate [90,91] or alkyl groups of other aliphatic carboxylates [91,92]. The methyl resonances of trimethylsilyl groups are shifted upfield in the [Cu or Zn - 1,

10-phenanthroline - trimethylsilyl alkane carboxylates or sulphonates], compared to the free ligands, supporting interligand interactions.

Complexes of the type [MAL] where A = 2, 2' bipyridine or 1, 10-phenanthroline and L = amino acids like alaninate, 2-amino propionate, nor-valinate, nor-leucinate, valinate, leucinate or isoleucinate show hydrophobic interactions between the aliphatic side chain of the amino acid and aromatic ring of the dipyridyl or 1, 10-phenanthroline. The extent of hydrophobic interaction is dependent on the length of the aliphatic side chain of the amino acids as revealed by NMR studies [93].

In the mixed-ligand complexes of the type [M-ATP-Amino acids], it was observed that formation constants of the complexes involving amino acids with aliphatic side chains such as 2-amino propionic acid, nor valine, nor leucine, leucine, iso-leucine and amino butyric acid have a higher value compared to alanine complexes [94]. This higher formation constant is attributed to intramolecular ligand-ligand hydrophobic interactions between non-coordinating alkyl group of the amino acids and the purine moiety of ATP. The ^{1}HNMR signals of terminal methyl group(s) of amino acid side chain in (M-ATP-Amino acid with aliphatic side chain) complexes appear at higher fields than those of [M-ATP-alanine] complex, indicating hydrophobic interactions between the adenosine moiety of ATP and non-coordinating alkyl side groups of the amino acids.

The factors determining the hydrophobic ligand-ligand interactions have been studied for the complexes [M (Phen) (iAiCA)] where M = Cu or Zn; iAiCA = 2 methyl propionate, 3 methyl butyrate, 4 methyl valerate,

5 methyl hexanate and 6 methyl heptanate [95]. As in case of stacking interaction, it was observed that the number of methylene groups between the isopropyl residue and the coordinating carboxylate group influence the complex stability. Maximum stability is obtained for the complexes 5-methyl hexanate, whereas for 6-methyl heptanate the stability is lowered, because the methyl group reaches beyond the aromatic ring system.

Though weak, such hydrophobic interactions are also observed between suitable groups in the absence of the metal ions [90, 91, 93]. ^{1}HNMR studies [93] showed that the methyl resonance of leucine is increasingly .shifted upfield with increasing concentrations of 2, 2' - bipyridyl or 1, 10-phenanthroline, thus indicating that a hydrophobic adduct is formed between these aromatic systems and the isopropyl moiety of leucine. The addition of Zn^{+2} to such a system leads to a much larger upfield shift, thus giving clear evidence that the hydrophobic interaction between the isopropyl group of leucine and the aromatic ligands is significantly promoted by the formation of a metal ion bridge between these ligands.

The hydrophobic and aromatic ring stacking interactions are solvent dependent [96-98]. There is also evidence that both aromatic and aliphatic hydrocarbon portions of ligands tend to occupy space near the metal ion rather than out in solution [99,111]. This tendency is sometimes referred to as ligand-metal interaction [101] though a direct favourable hydrocarbon metal interaction, by less than van-der waals distances, has been shown only for aromatic rings, in crystal structure determinations [105].

It is evident that a possible intramolecular ligand-ligand inter-

action does not occur in hundred percent of molecules but it may occur only in a certain number of complex species present. This gives rise to two isomers of the ternary complex MAB i.e. an 'open' form, where there is no ligand-ligand interaction and a 'close' form, where ligand-ligand interaction exists. This then leads to an intramolecular equilibrium between these two isomers which may be represented as follows :

$$K_I = \frac{[\ MAB_{(closed)}\ ]}{[\ MAB_{(open)}\ ]}$$

The dimensionless constant K_I allows to calculate the individual percentage of two isomers. It has been shown that [112].

$$\%\ MAB_{(Closed)} = \frac{K_I}{1 + K_I} \times 100$$

Metal - Peptide Complexes :

Metalloproteins are known to be acting as metalloenzymes. The study of the coordination properties of simpler constituents of proteins i.e. the dipeptides gives an insight to the coordination properties of the more complex protein molecules, in the metalloproteins. The major constituent of proteins is a polypeptide chain consisting of α-amino acids, linked together by amide bonds between the α-carboxyl of one residue and α-amino group of the next.

It is generally accepted [113-122] that initial complex formation between a dipeptide and a metal ion in the binary system results in a chelate involving a terminal amino group and oxygen of the neighbouring

amide group. A variety of techniques have confirmed the presence of five membered chelate rings with N (amino) and O (peptide) donors in metal - peptide solutions. The NMR spectrum of glycylglycine in D_2O solution, for instance, has two proton resonances due to the two non-equivalent $-CH_2$ groups. The addition of Cd^{+2} ions to the solution causes a greater chemical shift in one frequency than the other. This signal belongs to $-CH_2$ group which is closest to the donor atoms i.e. $-CH_2$ between the amino and peptide groups [123]. The same observation is also made when Cu^{+2} ions are added instead of Cd^{+2} ions, thus proving that the initial sites of chelation are the same for Cd^{+2} and Cu^{+2} ions [124].

I.R. Spectra of metal-peptide complexes in D_2O also reveal the same coordination sites of the peptide. In case of glycylglycine, it is observed that the peptide C=O frequency shifts from 1645 cm^{-1} in the free ligand to 1625 cm^{-1} in copper complex, indicating that C=O group is coordinated to the metal ion [125, 126].

At higher pH values, however, the dipeptide undergoes deprotonation of the amide group and it becomes tridentate coordinating through N-amino, N-peptido and O-carboxylato groups. The N(peptide) atom binds a metal only when the process is accompanied by the dissociation of the peptide proton. Metal-binding at the N(peptide) atom would otherwise imply the formation of a fourth bond, a change from trigonal sp^2 to tetrahedral sp^3 hybridization, and the loss of the peptide group resonance. Such deprotonated peptide complexes are observed with many metal ions (Cu^{+2}, Ni^{+2}, Pt^{+2}, Pd^{+2}).

The dimensions of the peptide group are slightly but signifi-

cantly changed by coordination at the N(peptide) atom [127]. For Cu(II), the C=O bond length changes from 1.24 A° to 1.26 A° and the C-N bond length from 1.325 A° to 1.30 A°.

Electronic spectral studies also indicate the ambidentate nature of the dipeptides. For a 1:1 mixture of [Cu(II) - glycylglycine] complex [128], the absorption peak shifts from $\sim$650 nm at low pH to a shorter wave length ($\sim$625 nm) or higher energy region, at a higher pH, due to change of coordination site to strong field nitrogen donor (N^- of peptide) in place of weak field oxygen donor (C=O of the peptide).

The coordination sites of dipeptides have been confirmed by cyclic voltammetric studies [129]. At a lower pH, where the coordination is from amino nitrogen and peptide oxygen, the reduction peak observed for the CuL species is at $\sim$-0.03V. The reduction potential shifts to a higher negative value of -0.315V, at a higher pH ($\sim$7.1) due to the formation of CuL_{-H} species where the dipeptide is coordinated through a strong donor, the deprotonated peptide N^-, and the amino group.

In the biological systems there is formation of binary and ternary complexes involving peptides and proteins and hence binary metal-peptide complexes and ternary complexes involving dipeptides and other ligands of biochemical significance are of relevance.

The interaction of amino terminal tetrapeptide fragment of human fibrinopeptide A(Ala-Asp-Ser-Gly) with Copper(II) and Ni(II) was studied with the help of potentiometric and spectroscopic techniques [130]. It was observed that an unusally stable ($CuH_{-1}L$) species was formed in the pH range 4-9. Copper(II) complexes of glycyl-L-leucyl-L-tyrosine, glycyl -

L-tyrosylglycine and L-tyrosylglycylglycine were studied pH-metrically and by spectroscopic methods [131], at 25°C and ionic strength 0.2 mol dm^{-3} KCl. It was observed that the phenolic hydroxy group in the side chain does not play a direct role in coordination to metal ion.

Formation of H^+, Zn(II) and Co(II) complexes of glycys(glycyl-L-cysteine) and cysgly (L-cystylglycine) was studied by pH-metric, spectrophotometric and ^{1}HNMR methods [132]. Amide deprotonation and coordination cannot be observed below pH 10 in any of the systems studied. Pettit et al [133] studied the interaction of Copper(II) with Phe-Phe-Ser-Asp-Lys and other peptides containing the Phe-Phe subunit. The stability constants and the binding modes of the proton and Copper(II) complexes of S-tyrosyl-S-tyrosine (Tyr-Tyr) and S-tyrosyl-S-tyrosyl-S-tyrosyl (Tyr-Tyr-Tyr) were studied [134].

Copper(II) and Nickel(II) complexes of tri and tetrapeptides [Arg-Lys-Asp-Val, Arg-Lys-Asp and Arg-Lys-Arg-Asp] were studied by potentiometric, spectrophotometric, CD and EPR methods [135]. The coordination of terminal amino, 2 deprotonated amide nitrogens and the β-carboxylate of the aspartic acid residue was proved in all cases. Complexation of non-coordinating side chains of the dipeptides (Phe-Leu, Leu-Phe, Phe-Met and Met-Phe) with Cu(II), Ni(II) and Co(II) was studied by carrying out potentiometric, calorimetric and spectroscopic measurements [136]. For the species $[MH_{-1}A]$ in these systems an increase in the stability is observed w.r.t. complexes of glycylglycine or of dipeptide containing one non-glycine residue, and this effect is attributed to the hydrophobic interactions between the non-coordinating side chains. The ease of complex formation is in the order Cu(II) $>$ Ni(II) $>$ Co(II). Copper(II) dipeptide

complexes with Tyrosinate and Lysinate as bridging residues were studied by pH-metric and spectrophotometric techniques [137].

It has been observed that the dipeptides retain their coordination properties in ternary complexes also [138-141]. It was also observed that various kinds of intramolecular interligand interactions exist in mixed-ligand complexes involving dipeptides. Martin et al studied the ternary Pd(II)-peptide-amine complexes by ^{1}HNMR spectroscopic methods and revealed the hydrophobic ligand - ligand interactions between the side chains of coordinated glycyl-L-phenylalanine and a monodentate amine with a varying length aliphatic chain with or without an attached aromatic ring [101].

The Cu(II) complex formation by tyrosine containing peptides can be considered as model for endogenous peptides with morphine like analgesic activity (opioid peptides) such as enkephalin and endorphin, all of which have the essential N-terminal tyrosyl residue with a phenol group capable of binding with Copper(II) [107, 110, 142, 145] and stacking with aromatic rings [146-148]. Hence Yamauchi et al [149] made a detailed ^{1}HNMR spectral study of ternary palladium(II) complexes Pd(L)(DA), where L refers to dipeptide with the N-terminal aromatic amino acids tyrosylglutamate (Tyr-Glu), tyrosylglycinate (Tyr-Gly), tryptophylglutamate (Trp-Glu), tryptophylglycinate (Trp-Gly), Phenylalanylglutamate (Phe-Glu) and phenylalanylglycinate (Phe-Gly) and DA refers to 2, 2' - bipyridine (bpy), 4, 7 - diphenyl - 1, 10 - phenanthroline - 4', 4" - disulphonate (bphen), or ethylenediamine(en).

They observed stacking interaction in Pd(L)(DA) (DA=bpy or bphen) complexes which have been revealed by the upfield shifts of the

ring proton signals of L due to the ring current effect of DA. They also evaluated the equilibrium constant for "unstacked⇌stacked" forms.

Copper-protein Complexes :-

Since the beginning of the coordination chemistry, increasing attention is being paid to the chemistry of copper complexes [150-153]. The biochemistry of copper has been the topic of interest, since long, due to indispensable role of copper in biological systems [154]. The copper content of the normal human adult is of the order of 50 to 120 mg and this trace amount of copper is essential for life. The essentiality of copper in every form of life from plants to man, arises from its role as prosthetic group in a number of vital enzymes and proteins. This ability of copper depends on its intrinsic favourable chemical properties. As transition metal ion, the element has the capacity to complex effectively with a variety of proteins and porphyrins. Yet even when strongly chelated, copper can vary oxidation states and hence copper ions have long been known to be important redox catalysts. In biology, the copper enzymes normally are divided into three main classes :

i] electron transfer proteins

ii] Oxidases

iii] Oxygenases

Copper(II) can have three different forms in the copper proteins. Type-I Cu(II), present in so called blue proteins, is in an asymmetric site with Cu-cysteine (Cu-S) bond, leading to high absorption at 610 nm and intense deep blue colour. The electron spin resonance(esr) parameters for the copper(II) in these proteins are also unusual, especially the hyperfine

splitting constant which is approximately one-third of that for normal copper(II) complexes. The relatively high redox potentials (0.3-0.8V is attributed to Cu-S bond and asymmetry of these blue proteins. Type-II Cu(II) in square planar site, are less blue, though more intense than synthetic Cu(II) complexes. They have high molar absorbances and show considerable variability in redox behaviour. Type-III has two antiferromagnetically coupled, EPR silent Cu(II) centres, due to superexchange through bridges.

The electron transfer copper proteins like plastocyanin, Azurin and Stellacyanin have only type I Cu centre. Multicopper blue proteins have all 3 types of Cu-centres and act (i) as oxidases, transferring the electron from substrate to molecular O_2 as in laccase and ascorbate oxidase (ii) for Cu transport and Fe(II) oxidation activity as in ceruloplasmin (iii) affecting monooxygenase activity like hydroxylation of benzene as in tyrosinase and dopamine β-monooxygenase. Tyrosinase also acts as catechol oxidase.

Besides above, Cu is also present in cytochrome C oxidase (the terminal electron acceptor in respiratory system), in superoxide dismutase (decomposing toxic superoxide), in haemocyanin with Cu(I) - Cu(I) site, responsible for oxygen transport in molluscus and in metallothionines present in liver. Hence, study of copper biochemistry is significant. The present thesis comprises of the study of ternary complexes of copper(II) involving some biologically important ligands.

The second chapter of the thesis deals with the study of formation constants of the ternary complexes CuAL where A=dipeptides such as glycylglycine(gg), glycyl-L-alanine(ga) and glycyl-L-leucine(gl) and L= α-alanine (ala), phenylalanine (phe), tryptophan (trp), tyrosine (tyr),

3,4-dihydroxy phenylalanine (L-dopa) and histidine (hist).

In the third chapter, electrochemical studies of mixed ligand complexes, CuAL where A = dipeptide gg and L= ∝ alanine and tyrosine have been carried out. Electrochemical studies were also carried out for the mixed amino acid complexes, Cu hist L, where L=∝-alanine, phenyl-alanine, tyrosine and tryptophan.

The fourth chapter presents an account of the stability of ternary complexes CuAL where A = dipeptides as mentioned above and L = catechol (cat) and its derivatives such as pyrogallol (pyr), tiron and 2, 3-dihydroxy napthalene(nap).

The fifth chapter comprises of the study of ternary complexes CuAL where L=auxins such as indole acetic acid (IAA), indole propionic acid (IPA) and indole butyric acid (IBA).

In the sixth chapter of the thesis, formation constants of the mixed-ligand complexes CuAL, where L=primary and tertiary amines such as ethylenediamine (en), 1, 10 - phenanthroline (phen), 5 - nitro 1, 10-phenanthroline (Nphen), 2 (2' pyridyl) imidazoline (pyz) and 2 (2' pyridyl) benzimidazole, have been studied. Electrochemical study of the binary complex Cu-en and one of the ternary complexes copper-en-gg has also been carried out.

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