CHAPTER - I

INTRODUCTION
Introduction

"If you think that biochemistry is the organic chemistry of living systems then you are misled, biochemistry is the co-ordination chemistry of living systems". This comment of Wood is based on the fact that without the participation of metallic elements, life would not exist.¹⁴

About thirty three elements have been recognised to be the most essential for living systems³. Copper is the third most abundant transition metal in the body following Iron and Zinc. All animals as well as human beings posses homeostatic mechanism for absorption utilization, transportation and excretion of copper³. Most of the copper in normal human serum is bound to ceruloplasmin. It has been shown that human albumin forms a ternary complex with copper-histidine, such as copper-albumin-histidine⁵⁶. It was postulated that the ternary complex may play an important role in regulation and control of copper transport across the cell membrane⁶⁻⁷. The co-ordination compounds in living systems act as a catalyst in several metabolic processes which involve reactions in which a metal can combine with a substrate to accelerate the reaction and redox reactions in which there is change of valency of the metal in the complex. These co-ordination compounds can serve the purpose of storage and transfer of either metal ion or donor molecules³. Hence the importance of copper (II) amino acids complexes in biological activities, is well established⁸.
A large number of metallo enzymes containing copper have been identified. Cytochrome oxidase, Ascorbate-oxidase, Ceruloplasmin oxidase, Hemocyanines, Galactose oxides etc., are the examples. These are the respiratory proteins in the blood of certain animals. Cytochrome oxidase is the most important metallo enzyme in the respiratory system of man. The mixed ligand complexes may be considered as models for enzyme-metal ion substrate complexes. These complexes may also occur in biological fluids that contain several ligands as well as different metal ions.

The area of co-ordination chemistry has been widely developed in the last five decades. Complexes are playing increasingly important roles in industry ranging from anticorrosion agents and soil treatment agents to medicinal agents, which certainly testify for their importance in contemporary life. The biologically important complexes such as chlorophyll, hemoglobin and Vitamin B suggest a need of study of the principles of co-ordination chemistry by all chemists.

According to Rossotti and Rossotti a complex may be defined as a species formed by the association of two or more simple species each capable of independent existence with one of the simple species is a metal ion. The formation of a complex is the result of Lewis acid-base type of interaction, in which one atom with a vacant orbital (generally the metal) attracts the electron pair of another atom (generally a non-metal). As a
result of such an interaction bonding may occur only when metal has vacant orbitals which are symmetrically correct, sterically available and of reasonably low energy. Transition metal ions meet these requirements best, hence they form complexes readily. Nature of the metal ligand bond may be essentially ionic or essentially covalent depending upon the nature of the metal ion and the donor atoms of the ligands corresponding to the metal ion.

From a critical literature survey it is evident that complexes are formed by nearly all the metals and the donor atoms are generally the non-metallic elements, oxygen, nitrogen, sulphur, phosphorous are the common examples. When the metal ion or atom has two or more different types of ligands in its co-ordination sphere, then the complex is known as mixed ligand complex.$^{13-20}$

There are two types of reactions leading to the formation of different ligand complexes. In the first case, mixed ligand complex is formed when one ligand does not occupy all the co-ordination places on the central metal ion, the second ligand then be incorporated to occupy some or all the remaining co-ordination places on metal ion. In the second case the metal forms co-ordinately saturated complex but in the process, the valencies of inorganic ion are not compensated. Thus the mixed ligand complexes is formed due to association of the ions of the second charged ligand and the first binary complex. Mixed ligand complexes
of one ligand with two different metals have been also studied. Formation of a complex between one central ion and two or more different ligands increases the selectivity of the reaction.

Various methods are available for confirmation of the presence of mixed ligand complexes and chelates. The isolation purification and analysis of a crystalline compound is most widely used method for study of the structure of the compound. The compound is isolated, purified, recrystallised and then elemental analysis is carried out. Percentage of C, H, N and Metal is calculated from proposed formula of the complex and then the observed percentage is compared with calculated one. If calculated value and observed percentage are almost same then the proposed stoichiometry is assumed to be correct.

Infrared spectral studies are of much help in the study of the complexes, particularly for deciding the mode of co-ordination and also structures. In actual practice, the molecular vibrations in complex compounds are in abundance hence precise interpretation of spectra are usually impossible, and only conclusion of a general nature are feasible with respect to ligand, presence or absence of certain functional groups, multiple bonding, isomerism, and degree of molecular symmetry. The basic fundamental principle of infrared spectroscopy is that on co-ordination, the absorption frequencies of ligand bands shift to
higher or lower frequencies along with the variation in intensity. With the help of infrared spectroscopy the nature of bond and isomerism in co-ordination compound can be determined.

Electronic spectroscopy has also been used to demonstrate the formation of mixed complexes in solution from the shift in the maximum absorption band in various mixed ligand system. All the complexes and chelates have the distinguishing features, ie they have characteristic colour. This is used for the detection of complex formation. With the help of spectral studies, possible transitions of electrons between different energy levels can be assigned along with the stoichiometry of the complexes. The spectral studies have now been demonstrated with certainty that in the study of lingad field transitions in 'd' block metal complexes $\Delta_0/\beta$ is an important factor, $\Delta_0$ is crystal field splitting parameter and $\beta$ is Racah parameter.

Thermal analysis is a general term covering a group of related techniques where by the dependence of the parameters of any physical property of a substance on temperature is measured.

With the development of each new instrumental technique, the chemist has a new tool with which to attack and solve chemical problems. However some times there is a fairly long interval between the date the technique is developed and the time it is applied en masse to chemical problems. Such has been the case with many of the Thermal methods discussed. The first
thermoblance was developed by Honda in 1915, yet it was not until 1947 that Duval called attention to its applications to the field of inorganic gravimetric analysis. A similar situation is noted with differential thermal analysis (DTA), which was originally conceived by Roberts-Austen in 1899. For many years DTA was an invaluable technique for the identification of minerals, clays, metallic alloys and so on, but was virtually ignored by the chemists. In recent years, however, DTA has been successfully applied, either by itself or in conjunction with other thermal techniques, to the elucidation of problems of chemical interest.

The principal techniques of thermal analysis are dynamic thermogravimetry, (TG) and differential thermal analysis (DTA). Other less widely employed but useful techniques include evolved gas detection or analysis (EGD), thermo mechanical analysis (TMA), dynamic reflectance spectroscopy (DRS), electrical conductivity (EC) and photothermal analysis (PTA).

There are several monograph in the literature on the historical development, theoretical, principles, apparatus, and number of applications of the methods of thermal analysis. Although thermal analytical techniques originated much earlier, only in last four decades progress has been accelerared in this field. A number of excellent designes of advanced thermal instruments can be found in the world market and new models appearing all the time. A complex thermoanalytical equipment called Devitograph has been developed for the simultaneous
recording TG, DTG, and DTA of a sample.

Among the various analytical techniques TGA and DTA are used in present investigation.

It should be pointed out that, in many cases the use of only single thermal analysis technique may not provide sufficient information about a given system. As with many other analytical methods, complimentary or supplementary information, as can be furnished. For example, it is fairly common to complement all DTA or DSC data with thermogravimetry, if a gaseous products are evolved gas analysis may prove useful in solving the problem at hand. Simultaneous thermal techniques are useful in this respect in that several types of data are obtained from the same sample under identical pyrolysis conditions.

Dynamic thermogravimetry has been widely used during the past years to study the kinetics of thermal decomposition reactions. As pointed out by Doyle\textsuperscript{33}, one mass-loss curve is equivalent to a large number of isothermal mass-loss curves. As a general rule, definitive kinetic parameters can be derived from mass-loss data only in the light of a large amount of additional evidence.

The advantages of determining kinetic parameters by non-isothermal methods rather than by conventional isothermal studies are
(i) that considerably fewer data are required.

(ii) that the kinetics can be calculated over an entire temperature range in a continuous manner.

(iii) that when a sample undergoes considerable reaction is being raised to the required temperature, the results obtained by an isothermal method are often questionable and

(iv) that only a single sample is required.

The use of thermogravimetric data to evaluate kinetic parameters of solid state reactions involving weight loss (or gain) has been investigated by a number of workers. Freeman and Carroll\textsuperscript{31} have stated some of the advantages of this method over conventional isothermal studies. To these reasons may be added the advantage of using one single sample for investigation. However, the importance of procedural details, such as crucible geometry, heating rate, pre-history of sample, and particle size, on the parameters has yet to be fully investigated. It is also necessary to ensure accurate temperature measurements, both for precision and also to detect any departure from a linear heating rate due to endothermic or exothermic reactions. Although several methods have been developed to allow kinetic analysis of thermogravimetric data, but few attempts have been made to compare them critically. A critical comparison discussed by Sharp and Wentworth\textsuperscript{38} and concluded that the methods, those due to Coats & Redfern\textsuperscript{40} and to Achar et-al\textsuperscript{41} can lead to
satisfactory kinetic analysis, provided that the experimental conditions are such to minimise temperature gradients within the reactant. Horowitz and Metzer\textsuperscript{37} gave a sufficiently accurate and convenient method of calculating $E$, but this required the order of reaction to be determined, first. The method of Ployan-Novikova\textsuperscript{42} shows the possibility of determining the activation energy from the loss in mass curve or from $\Delta_t$ curve without first determining the reaction order.

Wendlandt \textsuperscript{39} indicated relationship between thermal stability of metal chelates and structure of the chelating agents. Liptay\textsuperscript{43} showed that thermal stability depends on the structure of the Chelate but Botei and Green\textsuperscript{44} revealed that thermal stability does not depend on the structure of the chelate.

Sheshagri and Rao\textsuperscript{45} showed that thermal stability can be increased by introduction of an extra electron releasing group in the reagent.

Coats Redfern and Ployan Novikova methods have been applied to evaluate kinetic parameters of the newly synthesized complexes in present investigation.
Literature Survey

A detailed literature survey shows that studies on ternary complexes of copper (II) with amino acids\textsuperscript{46-50} have been isolated in the solid state by various workers. These complexes are characterised on the basis of elemental, IR and electronic spectral studies.

Freeman et al\textsuperscript{51} studied the equilibria in aqueous solution between copper (II) ions and L or D histidine and L-threonine and showed the presence of one additional mixed ligand species and found the stability constant of the ternary species to be greater than that of binary one.

Singh and shrivastava\textsuperscript{52} have proved that the mixed ligand complexes of Copper (II) and nickel (II) with aspartic acid as a primary ligand and glycine, alanine, valine or lucine as a secondary ligands are less stable than binary complexes.

Ablov et al\textsuperscript{53-56} isolated certain mixed ligand complexes of copper (II) using any two among glycine, alanine and serine. These were characterised to be of the type (Cu (AB)] . X H\textsubscript{2}O on the basis of elemental analysis, I.R. and 'X' ray diffraction studies.

Bhattacharya et-al.\textsuperscript{57} investigated mixed ligand complexes using histidine and iminodiacetic acid as primary ligands and some aminoacids as secondary ligands using Irving and Rossotti's method's.
Yamauchi et-al \textsuperscript{58} isolated and characterised the mixed ligand complexes of the type [Cu (Hist) (AA)] where Hist = histidine and AA is L or D - asparagine, L-serine, L-glutamine, L-homoserine, successful isolation of the ternary complexes of histidine has been interpreted in terms of solubility differences and intramolecular hydrogen bond between carboxylate oxygen of histidine and amide of hydroxyl group of AA.\textsuperscript{58} Assuming terdentate behavior of histidine and its intramolecular interaction, a possible structure of ternary complexes in aqueous solution had been given.

The ternary complexes containing one five membered ring and one six membered ring have been observed \textsuperscript{59} to be more stable than two six membered or two five membered rings only. In the system [Cu (AB) H\textsubscript{2}], the possibility for the attachment of one proton to histamine (A) and the other to ligand (B) was predicted.

There was marked steroisoselectivity in the complexes of histidine. This was confirmed by the formation of complexes containing different optically active amino acids, copper (II), nickel (II) showed a marked difference in behaviour towards second amino acids or dipeptide ligand.

Tursunova et-al \textsuperscript{60} studied the system of the type [Cu (AB)], where A is glutamic acid, cystein, valine arginine, serine, methionine, leucine glycine, alanine and B is nicotinic acid, nicotinamide, pyridoxine folic acid and thiomine in aqueous
dioxane and ethenol media and calculated stability constant data.

Mishra et-al\textsuperscript{61} prepared copper (II) complexes in polycrystalline form by using different acids and measured their static magnetic susceptibility at room temperature by Farady's method and found relatively less values for mixed ligand complexes.

Sakuri Takashi et-al\textsuperscript{62} isolated and crystallised the ternary complexes [ Cu (II) L- asparaginate L- histidinate ] in two different forms from aqueous solutions containing Cu (ClO\textsubscript{4})\textsubscript{2}, H\textsuperscript{I}stidine and L-asparagine in the molar ratio 1:1:1 and having used D-L histidine in place of L-histidine, it was shown that L-histidine was preferentially incorporated in ternary complex formation. D'yakon et-al\textsuperscript{63} determined the structure of [Cu(L-ala)(L-Ser)] by electron diffraction techniques and found that N-atoms of amino acids are trans to each other in an octahedraon. A comparison has also been made between the crystal structure of [Cu (L-Ser \textsubscript{2})] and [Cu (L-ala)\textsubscript{2}] with that of ternary complexes. The studies of mixed ligand complexes of copper (II) with orthophenanthroline and \textsuperscript{2,2'} bipyridyl in presence of some amino acids by pH metric method of analysis revealed\textsuperscript{64} that simultaneous addition of the ligand resulted in the formation of 1:1:1 ternary complexes. The stability of the ternary complexes was found to decrease with the secondary ligand in the order phenylalanine > alanine > glycine > norleucine. Investigation of Donide et-al. on ternary complexes of Copper ( II), nickel (II),
Zinc (II) of the type $[M \text{ (Hist) (hm)}]^2$ and $[M \text{ (Hist) (hm)}]^+$ in aqueous solution resulted in comparable data to the previous data.

Sigel et-al. attempted to investigate the intramolecular ligand-ligand interaction in mixed ligand complex involving α amino acids. Sawhery et-al studied mixed ligand chelates of Cu (II) with quinolic acid as a primary ligand and some amino acids as secondary ligands and showed that 1:1 complex formation of the type $[\text{Cu (II) quinolic acid}]$ takes at lower pH only while at higher pH 1:1:1 ternary complex formation is favourable. The stability sequence of the ternary complexes decreases with respect to secondary ligands in the order gly > alanine > valine. The trend at $\log k$ values has been explained in terms of $L \rightarrow M$ and $M \rightarrow L$ bondings.

Freeman et-al isolated and characterised the ternary complex $[\text{Cu (hist) (Threo) H}_2\text{O}] \cdot \text{H}_2\text{O}$ and the structure was supported by 'X' ray crystallographic data also. Dutta et-al have prepared ternary complexes of copper (II) with bipyridyl or ortho phenanthroline and iminodiacetic and studied their spectral, magnetic properties. These complexes have been shown to have distorted octahedral structure.

The complexes of the type $[M \text{ (dipy)(catechol)}]$ where $M = \text{copper (II)}, \text{nickel (II)}$ have been prepared by Bhattacharya et-al. These complexes are characterised on the basis of analytical, magnetic and spectral data. The data suggest a square planar and distorted octahedral structure Ni (II) and
Cu (II) complexes.

A review\textsuperscript{70} regarding synthesis, characterization and structural studies of mixed ligand complexes of Ni(II) and Zn(II) with phenols and amino acids have been prepared and characterised by Bhattacharya et-al\textsuperscript{69-70}

Yukawa, Yasuhiko\textsuperscript{71} synthesised the (L-prolinato) Copper (II) complexes prepared from different solvent. He found that in aqueous medium, 1 carboxylate o-atom is co-ordinated to 2 Cu atoms and the other is co-ordinated to 1 of these Cu atoms, forming a four membered chelate ring. Each Cu atom in the complex is surrounded by 6 atoms, forming an distorted octahedron. The IR and electronic spectra, magnetic moments and simultaneous TGA and DTA are described.

Nair, et-al\textsuperscript{72} studied, the structural influence on the stability of mixed ligand complexes of Copper (II) with aliphatic diamines and amino acids, by computer based analysis of the \( p^H \)-metric data at 37°C and \( I = 0.5 \) mol. dm\(^{-3} \) (NaClO\(_4\)). In the Cu(II) -dp/tp(A) - ahba(B) system, only Cu(AB) type of ternary species has been detected. In this species abha(B) ligand binds the metal in a bidentate manner though it is tridentate in its binary species with Cu(II).

Nath et-al\textsuperscript{73} studies the spectral and thermal studies of Co(II), Ni(II) and Cu(II) complexes of shiff bases and amino acids. They showed that the mass considerations at the main decomposition
stages indicate conversion of the complex to metal oxides. Coats-
Redfern, Horowitz-Metzger equation, and the Fuoss Method
showed that the first order kinetics are applicable.

Non-isothermal kinetics of thermal decomposition reactions
of shiff base complexes of amino acids with transition metals
were determined from TGA by Li, Shu-lan et-al\textsuperscript{74}.

The above survey make it clear that very few studies
have been done in the field of copper (II) complexes with two
different amino acids. The geometry of the complex plays an
important role in the enzymatic reactions it was proposed to
synthesize some ternary complexes of copper (II) using different
amino acids and characterise them on the basis of elemental
analysis, UV, IR, TGA, DTA etc.

This thesis consists of four chapters. First part of
Chapter I describes object, scope and main features of the work
done and conclusions there from . Second part deals with the
literature survey on the ternary complexes of copper (II) with
amino acids.

The Chapter II describes the synthesis of copper (II)
complexes, using methionine as primary ligand and other amino
acids-like, alanine, proline, serine, leucine and tryptophan as
secondary ligands. The analytical data are in good agreement with
theoretical values for the proposed formula Cu[\text{AB}].2H\textsubscript{2}O of the
complexes.
In Chapter III, the IR and Electronic Spectra are discussed. The IR spectra of synthesised complexes have been compared with the IR spectra of the free ligands. In free amino acids $\tilde{\nu}$-NH$_3^+$ frequencies which are observed at $\sim$ 3100 cm$^{-1}$, $\sim$ 2900 cm$^{-1}$ and $\sim$ 1640 cm$^{-1}$ are completely absent in IR-spectra of their complexes, and appearance of $\tilde{\nu}$-NH$_2$ characteristic bands in the region of 3392 cm$^{-1}$ to 3223 cm$^{-1}$ confirms the involvement of -NH$_2$ group of amino acid in bonding. The IR - spectral shifting of $\tilde{\nu}$ ( -COO$^-$)$_{asym}$ and $\tilde{\nu}$ ( -COO$^-$)$_{sym}$ frequencies are the strong evidence of bonding through this group. Other low intensity bands observed in far IR-region $\sim$ 600 - 400 cm$^{-1}$ are due to $\tilde{\nu}$(M - N) and $\tilde{\nu}$(M-O) strech. as these bands are observed in the region at $\sim$ 592 - 380 cm$^{-1}$, which is also supported by the Nakamoto's assignments. In all the complexes the spectra show a weak band $\sim$ 800 cm$^{-1}$ due to the rocking mode of the coordinated water molecule. Hence it is confirmed that water molecules are present in co-ordination sphere of the complexes, but are not tightly bound due to Jahn Teller distortion.

The Electronic Spectral studies of newly synthesised complexes in water were recorded to evaluate geometry of the complex. All complexes show one asymmetric absorption band around 16,000 cm$^{-1}$, which may be assigned to the transition $^2$Eg $\rightarrow$ $^2$T$_2g$ a single broad band observed in all Cu (II) complexes suggests tetragonally distored octahedral trans geometry. The visible absorption maxima at $\sim$ 16,000 cm$^{-1}$ and molar extinction coefficient not change on further dilution. This confirms that
complexes are neither associated nor dissociated. Ternary complexes are generally more stable than binary complexes. On this basis the $\bar{\mu}_{\text{max}}$ values of ternary complexes with the average values of $\bar{\mu}_{\text{max}}$ for parent binary (1:2) complexes were compared. Almost in all the cases the values of $\bar{\mu}_{\text{max}}$ of ternary complexes are more than the average values of binary complexes.

Magnetic susceptibility measurements were made using Faraday's method. The positive values of $\chi_m$ confirm that the complexes are paramagnetic and $\mu_{\text{eff}}$ values correspond to the presence of one unpaired electron in the complexes.

Chapter IV describes the thermal studies of synthesised complexes. In present investigation a perusal of the thermograms indicates that the nature of the decomposition of the complexes are comparable. The data obtained have been used to evaluate kinetic parameters of decomposition of solid complexes. Order of reaction, activation energy, frequency factor, entropy of activation have been calculated.
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