Chapter 3

SYNTHESIS AND STRUCTURAL ASSESSMENT OF NEWER MIXEDLIGAND HALO COMPLEXES OF COPPER(II) INCORPORATING BIORELEVANT COLIGANDS

3.A Introduction

Copper(II) is a biologically essential element occurring in multitude of metalloproteins. Pharmcological and potential technological applications have rendered coordination chemistry of copper(II) an actively persued area of current research **[1-5].** Structural diversity and complexity associated with synthesis offers rewarding challenges. An understanding of the nature of metal − ligand interaction is a key aspect of the coordination chemistry of the metal. Synthesis followed by isolation in solid state, is undoubtedly, the main prerequisite to gain entry into this fascinating research area of thematic importance. Mixedligand complexes containing aminoacid as coligand are potential biomimetic models for metal-enzyme interaction

[6-9]. Ternary complexes of histidine and threonine occur in significant proportion in human serum and are important in relation transport of copper in blood **[10-11].** Copper exists only in bound forms in the biological system both in metalloproteins and in low molecular weight complexes. Occurrence of copper (II) aminoacid complexes and mixed copper (II) aminoacid and the true nature of these complexes is beginning to be unfolded from the last decade or so. In light of the dual role of copper as an indispensable component of the cell metabolic machinery and a potential cytotoxic agent, compounds able to perturb intracellular copper homeostasis have been investigated as potential anticancer agents.[12,13] Copper complexes can directly interact and damage nucleic acids when ligands behaving as DNA intercalating agents are [**14-16**]. As a consequence, direct DNA damage can, therefore, be a key determinant of the cytotoxic potential mediated by copper complexes [**17-21**]. Mixed ligand complexes play an important role in biological process as exemplified by many instances in which enzymes are known to be activated by metal ions [**22-26**]. Also, amino acids as co-ligand have special importance compared to other chemical compounds in the sense that they are regarded as the foundation stones of living organisms. Fostered by the crucial role of amino acids in our life, studying their structural, chemical and physical properties becomes very necessary to explain their behavior and potential applications [**27**]. The amino acids like glycine(gly), L-alanine(ala), L-valine(val) and L-phenylalanine(phe) in the form of mixed ligand species partake well in transamination, decarboxylation and metabolism in human [**28**] and are used as reagents in biology, pharmacy, industry and laboratory [**29**]. Many drugs and drug precursors containing amino acid moieties are found to have therapeutic activities [**30**]. Mixed ligand species of amino acids are also involved in the exchange and transport mechanism of trace metal ions in the

human body **[31].** The stability of mixed ligand–amino acid species depends on the chelate formation, the size **[32]** and basicity of amino acids which in turn depend on the interactions of metal(II) ions with amino and carboxyl groups. Copper amino acid complexes in encapsulated in protein superstructure with profound effect on microenvironmental dielectric constant **[33-35]** has also been the subject of much current interest. Despite rather extensive X-ray crystallographic characterisation of a large number of copper aminoacid complexes, the binding mode of such ligand to the Cu(II) centre continues to intrigue the chemists **[36-38].**

Halide ion as ligand to copper are second only to N-or O-donors. Here again, chlorides are more common than bromide, and those with fluorides are very scant **[39].** As a part of ongoing programme of our laboratory on mixedaminoacid fluoro complexes of copper(II), complexes of the type $NH_4[CuF_3L(H_2O)_2].nH_2O$ (L = glycine, n = 1; l-alanine, n=0; l-serine, n=2) were earlier synthesised and characterised **[40].**

In tune with the objective of present research, we report herein the synthesis and characterisation of $[CuX_2(aminoacid)H_2O].nH_2O$ (X = F, Cl, or Br) and $[CuX_2(oxin)_2]$ (X = F, Cl, or Br).

3.B Experimental

Reagent used, starting materials for the synthesis, the methods of chemical analysis of the complex formed and details of the instrument used for the same are as described in **Chapter 2**. The procedures for the synthesis of different mixedligand complexes of copper(II) **(1 to 10)** are described herein**.**
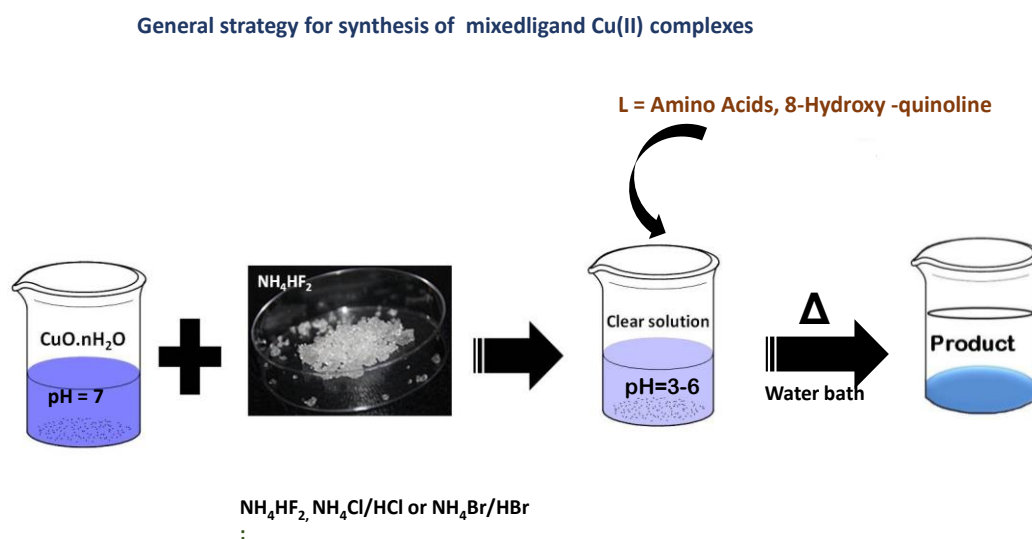
General strategy for synthesis of mixedligand Cu(II) complexes

L = Amino Acids, 8-Hydroxy -quinoline

NH$_4$HF$_2$

CuO.nH$_2$O

pH = 7

Clear solution

pH=3-6

Δ

Water bath

Product

NH$_4$HF$_2$, NH$_4$Cl/HCl or NH$_4$Br/HBr
;

Fig.3.1 : Illustartion for synthesis of Cu (II) complexes

Synthesis of [CuF$_2$(oxin)$_2$] (1)

To a freshly prepared aqueous suspension of hydrated copper (II) oxide CuO.nH$_2$O obtained from CuSO$_4$.5H$_2$O (1g, 4m mol), ammonium bifluoride, NH$_4$HF$_2$ was added about (0.41g, 7m mol) just to obtain a clear blue solution followed by 8-hydroxy quinoline (1.16g, 8m mol) in hot ethanol with constant stirring, when a sky blue product was obtained. The pH of the solution was recorded to be ca. 6. The product was separated by filtration and washed repeatedly with water and then ethanol. It was dried over fused CaCl$_2$ *in vacuuo*. The yield was about 65%.

Synthesis of [CuCl$_2$(oxin)$_2$] (2)

To a freshly prepared aqueous suspension of hydrated copper(II) oxide, CuO.nH$_2$O obtained from CuSO$_4$.5H$_2$O (1g, 4m mol), drop wise dil. HCl was added just to dissolve the suspension. The pH of the solution was recorded to be ca. 6. To this blue solution, solid NH$_4$Cl (1g, 18m mol) and then 8-hydroxyquinoline (1.16g, 8m mol) in hot ethanol was added with constant stirring when a light green product was formed. The product was filtered and repeatedly washed with water and then finally with ethanol. It was dried over fused CaCl$_2$ *in vacuuo*. The yield was 60%.

Synthesis of [CuBr$_2$(oxin)$_2$] (3)

To a freshly prepared aqueous suspension of hydrated copper (II) oxide, CuO.nH$_2$O obtained from CuSO$_4$.5H$_2$O (1g, 4m mol), drop wise dil. HBr (40% solution) was added just to dissolve the suspension. The pH of the solution was recorded to be ca. 6. To this blue solution, solid NH$_4$Br (1g, 10m mol) and then 8-hydroxyquinoline (1.16g, 8m mol) in hot ethanol was added with constant stirring when a light green product was formed. The product was filtered and repeatedly washed with water and then finally with ethanol. It was dried over fused CaCl$_2$ *in vacuuo*. The yield recorded was 60%.

Synthesis of [CuF$_2$(Hleu)(H$_2$O)] (4)

To a freshly prepared aqueous suspension of hydrated copper (II) oxide CuO.nH$_2$O obtained from (1g, 4m mol) of CuSO$_4$.5H$_2$O ,solid NH$_4$HF$_2$ (5g, 8m mol) was added to obtain a clear blue solution (pH ~ 4-5) followed by l-leucine (0.52g, 4m mol) in 25% hot ethanol. The solution was heated in a water bath for 45 min. when a sky blue product was isolated. The pH of the solution was recorded to be ca. 3-4. The product

was filtered, washed repeatedly with water and finally by ethanol. It was dried over fused $CaCl_2$ *in vacuuo*. The yield was 50%.

Synthesis of [CuBr$_2$(Hleu)(H$_2$O)] (5)

To a freshly prepared aqueous suspension of hydrated copper (II) oxide $CuO.nH_2O$ obtained from $CuSO_4.5H_2O$ (1g, 4m mol); NH_4Br (1g, 10m mol) was added. It was treated with HBr (20% in acetic acid) drop by drop with constant stirring to obtain a clear green solution (pH ~ 3-4). To this, l-leucine (0.52g, 4m mol) in 25% hot ethanol was then added and the solution was warmed in water bath for 45 min. with occasional stirring. A sky blue product was obtained which was filtered, washed repeatedly with water and finally by ethanol. The compound was dried over fused $CaCl_2$ *in vacuuo*. The yield recorded was 50%.

Synthesis of [CuF$_2$(Hmet) (H$_2$O)] (6)

Hydrated $CuO.nH_2O$ (1g, 4m mol) in ethanol is treated with   l-methionine (0.6g, 4m mol) in ethanol followed by addition of solid NH_4HF_2 (0.52g, 8m mol) with constant stirring (pH ~ 3). The resulting solution was heated in a water bath for 45 min. when a sky blue product was obtained. It was filtered and washed with water. The yield was 45%. In an alternate method, $CuO.nH_2O$ was treated with NH_4HF_2 to get a clear solution (pH ~ 6). To it (0.6g, 4m mol) methionine was added to get a sky blue compound. The compound was treated with few drops of HF (40%) just to dissolve (pH ~ 3-4) and then concentrated in a water bath when a sky blue product was obtained, it was filtered and washed with water repeatedly and finally with alcohol ,then dried over fused $CaCl_2$ in vacuuo. The former method afforded more yield than the latter (60%).

Synthesis of [CuF$_2$(Hphe)(H$_2$O)] (7)

To a freshly prepared aqueous suspension of hydrated copper (II) oxide obtained from CuSO$_4$.5H$_2$O (1g, 4m mol) solid NH$_4$HF$_2$ (0.5g, 8m mol) was added just to dissolve (pH ~ 4-5), followed by l-phenylalanine (0.66g, 4m mol) in a mixture of ethanol and water. A sky blue product was obtained (pH ~ 4-5). The whole was heated on a water bath for 45 min. and then filtered. The product was washed with water repeatedly and finally by ethanol and dried over fused CaCl$_2$ *in vacuuo* yield 55%.

Synthesis of [CuBr$_2$(Hphe) (H$_2$O)] (8)

To an aqueous suspension of CuO.nH$_2$O obtain from CuSO$_4$.5H$_2$O (1g, 4mmol) NH$_4$Br (1g, 10 mmol) was added and then drops of HBr to dissolve the suspension (pH ~ 3-4) followed by l-phenylalanine (0.66g, 4m mol) in ethanol solution (1:1). When instantly a sky blue product was formed. The whole was concentrated in water bath for 15 min and filtered, washed with water and finally by ethanol and dried over fused CaCl$_2$ *in vacuuo*. The yield was 50%.

Synthesis of [CuF$_2$(Hcys)(H$_2$O)] (9)

To a freshly prepared aqueous suspension of hydrated copper (II) oxide obtained from CuSO$_4$.5H$_2$O (1g, 4m mol) solid NH$_4$HF$_2$ (0.5g, 8m mol) was added to dissolve (pH ~ 3-4) followed by l-cystine (0.96g, 4m mol) in alcoholic suspension. The whole was then warmed on a water bath for 25 min. when a light green product was obtained. It was filtered, washed with water and finally by ethanol then dried over fused CaCl$_2$ *in vacuuo*. The yield recorded was 55%.

Synthesis of [Cu(val)$_2$(H$_2$O)] (10)

To a freshly prepared aqueous suspension of hydrated copper (II) oxide obtained from CuSO$_4$.5H$_2$O (1g, 4m mol) an aqueous solution of l-valine, (0.938g, 8m mol) was added and stirred when a deep blue solution was obtained (pH ~ 6). To this solution an aqueous solution of NH$_4$HF$_2$, (0.52g, 8m mol) was added with constant stirring when the colour of the solution got slightly faded (pH ~ 5). The solution was concentrated on a water bath and allowed to cool to room temperature with concommitant formation of shiny blue coloured crystalline product. It was filtered and washed with ethanol and then 50% ethanol and dried over fused CaCl$_2$ *in vacuuo*. The yield recorded was 50%. The compound can also be prepared without adding the bifluoride provided the pH of the reaction solution is maintained by addition of other dilute mineral acid.

3.C Results and Discussion

The aminoacid ligands, l-leucine, l-methionine, phenyl alanine, cysteine, serine, valine and oxine chosen for the present work are known to co-ordinate to copper(II) centre. Independently halides (F⁻, Cl⁻, Br⁻) are also known for their strong affinity towards copper(II). Evaluation of appropriate condition for the coordination of both halide and the chosen aminoacid as coligand to copper(II) centre was the first prerequisite. The strategy adopted for the synthesis is based on the interaction of freshly prepared hydrated copper(II) oxide, CuO.nH$_2$O with HX (X = Cl, Br) or HF$_2$⁻ in the presence of coligand aminoacid   **(Scheme 3.1).** The compounds formed were characterized to be of the type [CuX$_2$L(H$_2$O)].nH$_2$O. For the complex **(10)** with valine as coligand, the order of addition of reagent was different (l-valine first followed by fluoride) from the rest of the syntheses   (compounds **1 – 9**). However the compound

[Cu(val)$_2$(H$_2$O)] can also be prepared without adding NH$_4$HF$_2$ but only to maintain the pH of the solution (pH~6).

This account for somewhat different composition of this complex [Cu(val)$_2$(H$_2$O)] . Interestingly, the cysteine complex, [CuF$_2$(cys)(H$_2$O)] (**7**) reported herein is different from the one ([Cu(cys)(Hcys)F].$_2$H$_2$O) prepared earlier in our laboratory under rather similar condition [20]. A minor difference in the preparative procedure (i.e. use of Cu : F as 1 :2 in the present case as against 1 : 4 in the earlier case) led to such compositional variation. Under rather similar condition but longer reaction time (> 12h), the composition of the complexes formed with glycine, alanine or serine were of the type [CuL$_2$(H$_2$O)]. [19]. The methionine complex could be formed irrespective of the order of addition of ligands. A relatively higher pH (> 6) has been shown to be detrimental to mixedligand coordination and led to only binary products. A series of complexes with 8-hydroxoquinoline as coligand, [CuX$_2$(oxin)$_2$]   (X = F, Cl or Br) were obtained indicating the generality of the synthetic route. Analogous nickel-fluoro complex, [NiF$_2$(oxin)$_2$] has been prepared and characterized earlier in our laboratory [21]. The conducive pH at which the desired mixedligand complexes were accessed were spontaneously maintained in the range 4-6. The yields were recorded to be ~50%. The compounds (**7**) – (**9**) were sparingly water soluble thus not permitting measurements of solution electrical conductance. Except the valine complex (**10,** Λ_M = 215 s cm eq ; 2:1 electrolyte) rest were all obtained as nonionic systems. A molar conductance value of ca. 40 s cm^2 mol^{-2} for 10^{-3}M of aqueous solution of fluoro-oxine compound (**1**) was somewhat higher than that expected for a molecular complex. Presumably the complex is partly dissociated in solution. Repeated experiments on freshly prepared solution (1x10^{-3} M) did show some fluctuation (±10) in Λ_M value. The solution electrical conductance measurements   for complex   (**2**) – (**6**)

revealed Λ_M to be $< \sim 12$ S cm^2 mol^{-1} thus clearly suggesting the ionic nature of the complexes. The compounds **(1-10)** were all obtained as stable microcrystalline coloured solids. The effective magnetic moment values **(Table 3.1)** of the molecular complexes are in the range 1.88 – 1.94 BM concordant with mononuclear d^9 (S = ½) copper(II) system. The analytical data **(Table 3.1)** are consistent with the proposed formulation.

The vibrational spectroscopy has been very useful for elucidating structural motifs. The structurally significant I.R. features are presented in **Table 3.2.**

Complexes **(1)**, **(2)** and **(3)**, [CuX$_2$L$_2$] (X = F, Cl, or Br) incorporating oxine as coligand showed features in the range of 800 – 1500 cm^{-1} typical of phenyl ring of the oxine ligand. A band at around ~ 3400 cm^{-1} has been attributed to ν_{OH} mode of –OH group of unionised N-coordinated oxine ligand. Absence of peaks at 1635 cm^{-1} and 3450 cm^{-1} assignable to δ_{H-O-H} and ν_{OH} mode, respectively, ruled out water molecules being present. The compound **(1)** and **(3)** exhibit bands at 1400 cm^{-1} and compound **(2)** at 1375 cm^{-1} **(Table 3.2 ; fig. 3.1 - 3.3).** This is believed to have originated from a combination of -OH (oxine) bending and C–O stretching mode of the phenolic group **[41].** Since δ_{NH2} mode of NH$_4^+$ ion also show a strong ~ 1400 cm^{-1} peak, however, absence of supplementary peaks for N–H stretching at ~ 3200 cm^{-1} in complex **(1)** – **(3)** ruled out its presence as counterion or otherwise in the complex **(1)** – **(3).** The Cu-X stretch near 400cm^{-1} or so could not be located with certainty. These features compare well with analogous nickel (II) complex, [NiF$_2$(oxin)$_2$] **[42,43].** The oxine ligand occurring in its neutral form is presumed to be monodentate on copper (II) centre through the sp^2 – nitrogen. A relatively unaltered sharp ν_{OH} band at ~ 3370 cm^{-1} (c.f.: free oxine ligand, ν_{OH} : ~ 3370 cm^{-1}) ruled out coordination via

phenolic–O of oxine ligand. The copper–fluoro–oxine complex **(10),** showed a broad weak intensity absorption at ~395 nm assignable to d–d transition ($\in = 8$ dm^3 mol^{-1} cm^{-1}) and some strong bands at 210, 233 and 258 nm in the low energy region as characteristic of oxine ligand itself (π - π^*).
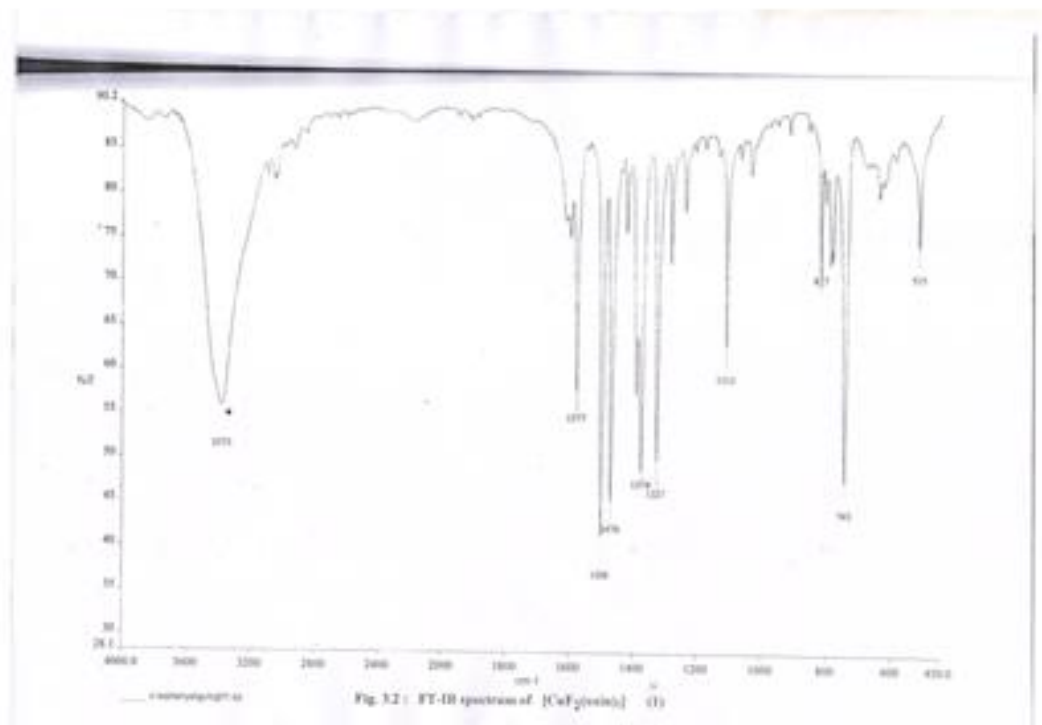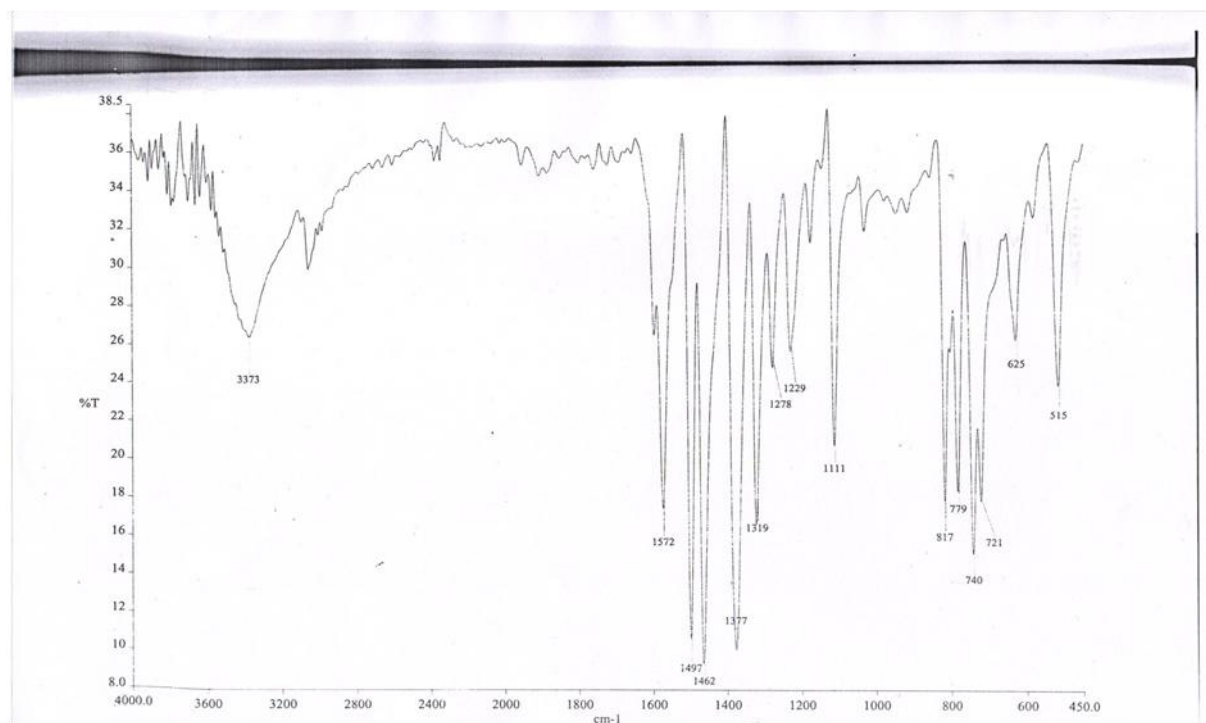
Fig.3.2 FT-IR spectrum of [CuF$_2$ (Oxin)$_2$](1)
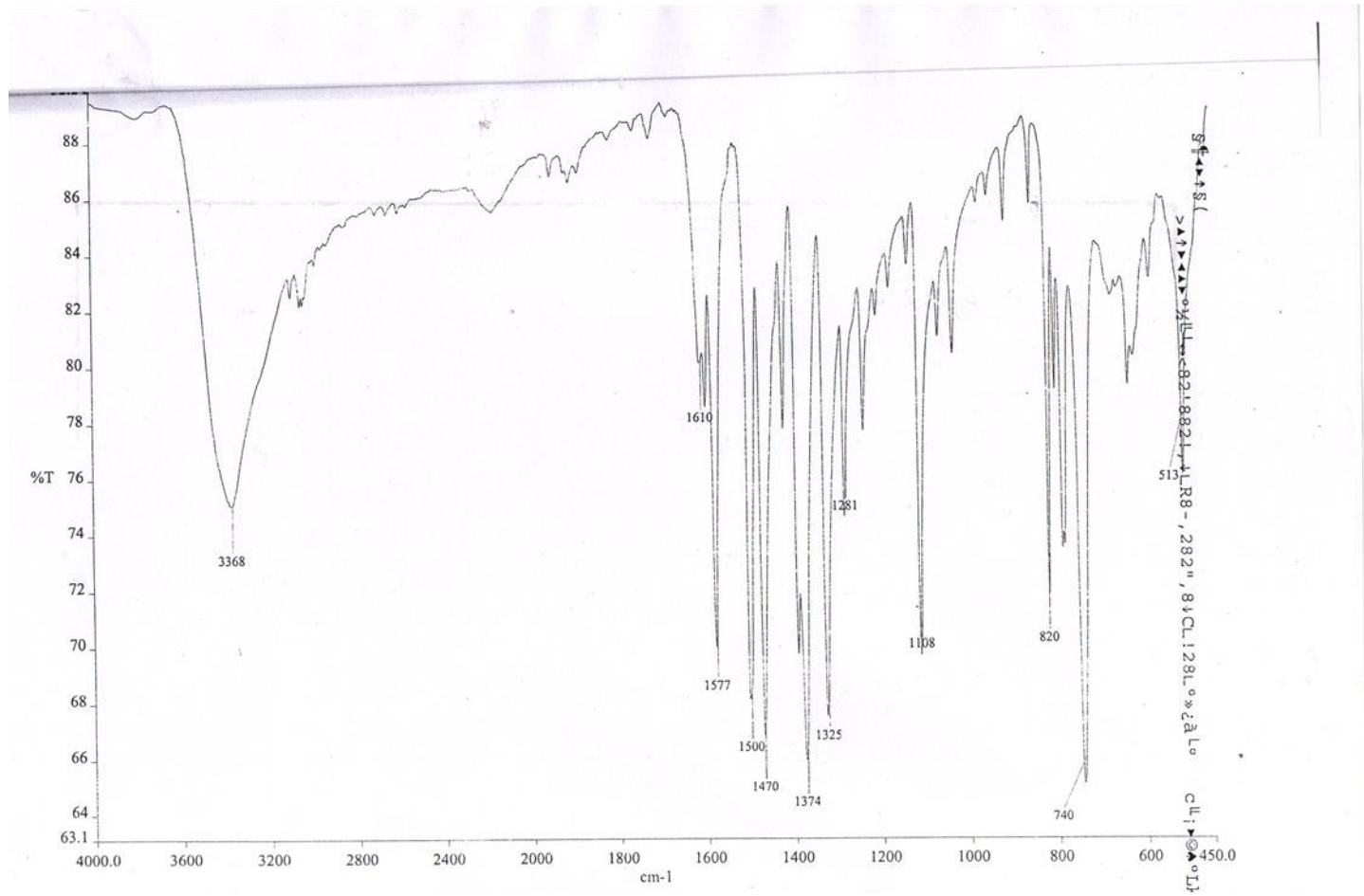
Fig.3.3 FT-IR spectrum of [CuCl$_2$ (Oxin)$_2$](2)

Fig.3.4 FT-IR spectrum of of [CuBr$_2$(Oxin)$_2$](3)
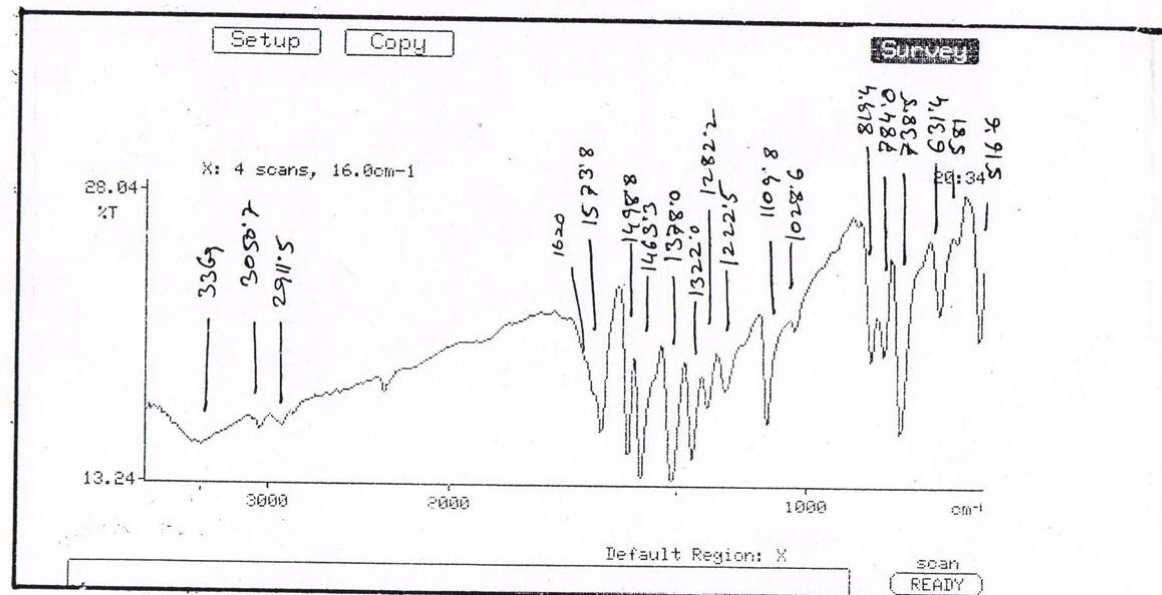
Fig.3.5 FT-IR spectrum of [CuF$_2$(Hleu)(H$_2$O)](4)
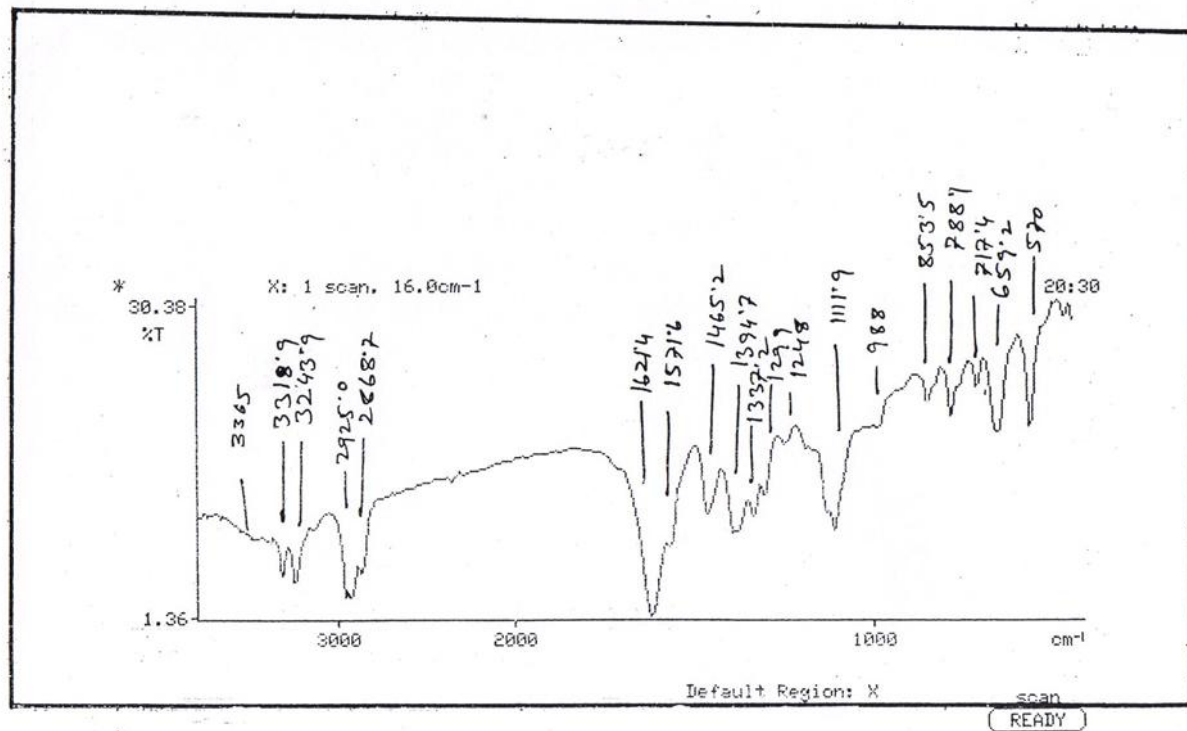
Fig.3.6 FT IR Spectrum of [CuBr$_2$(Hleu)(H$_2$O)] (5)
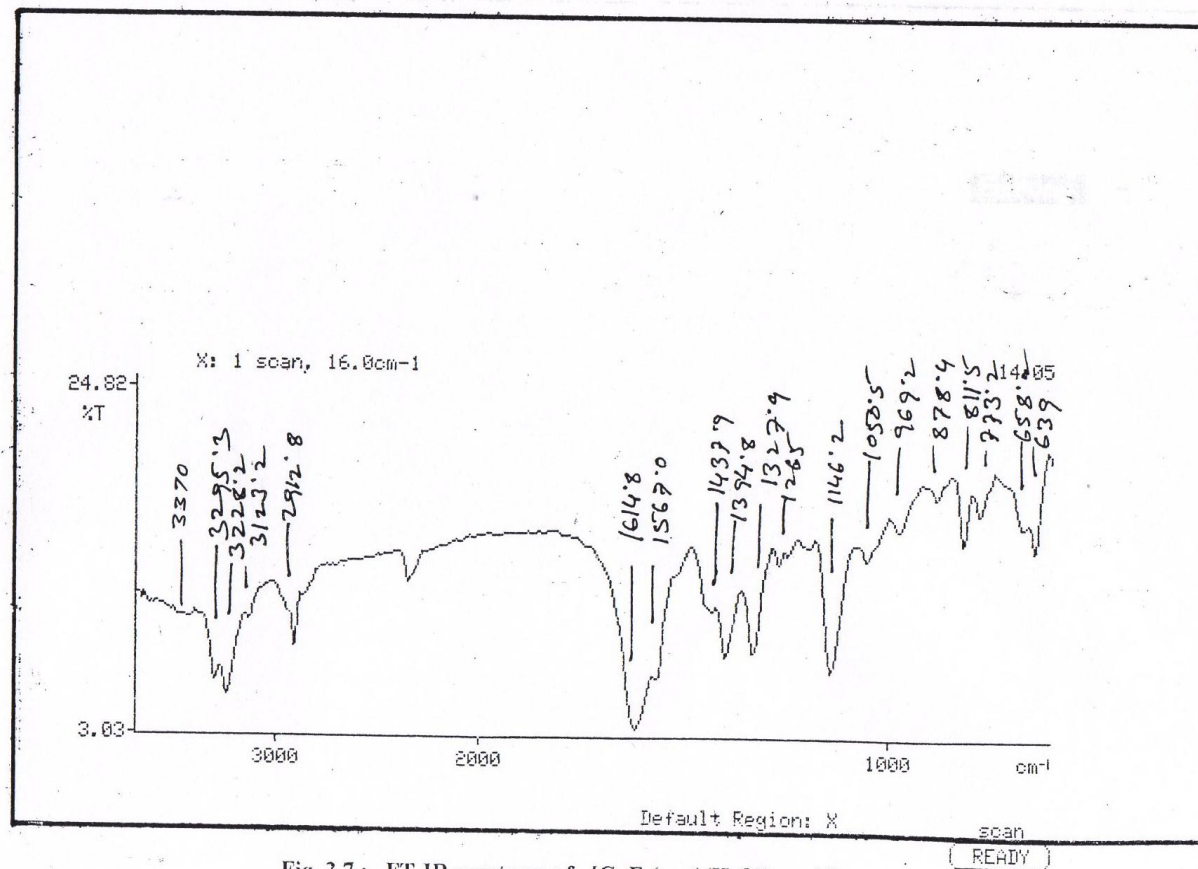
Fig. 3.7 : FT-IR spectrum of [CuF₂(met)(H₂O)]   (6)
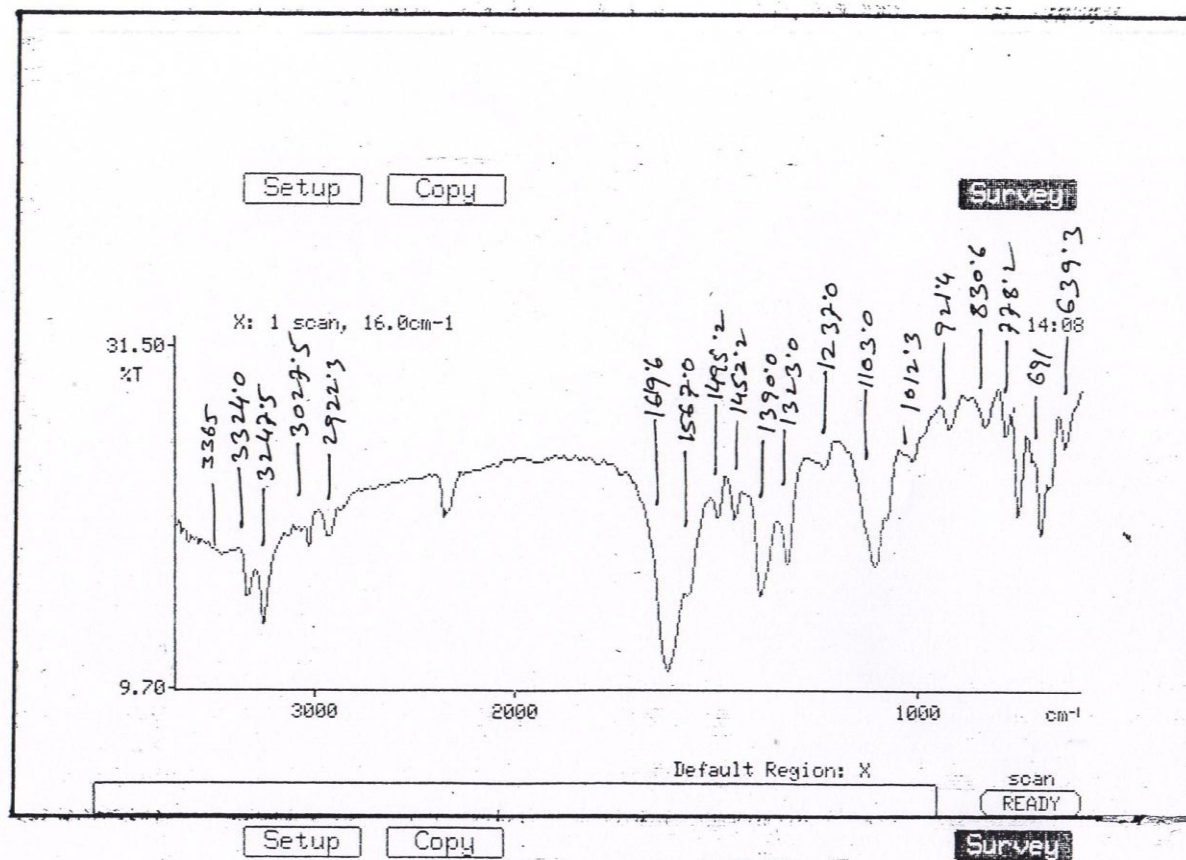
Fig. 3.8 : FT-IR spectrum of [CuF$_2$(phe.ala)(H$_2$O)] (7)
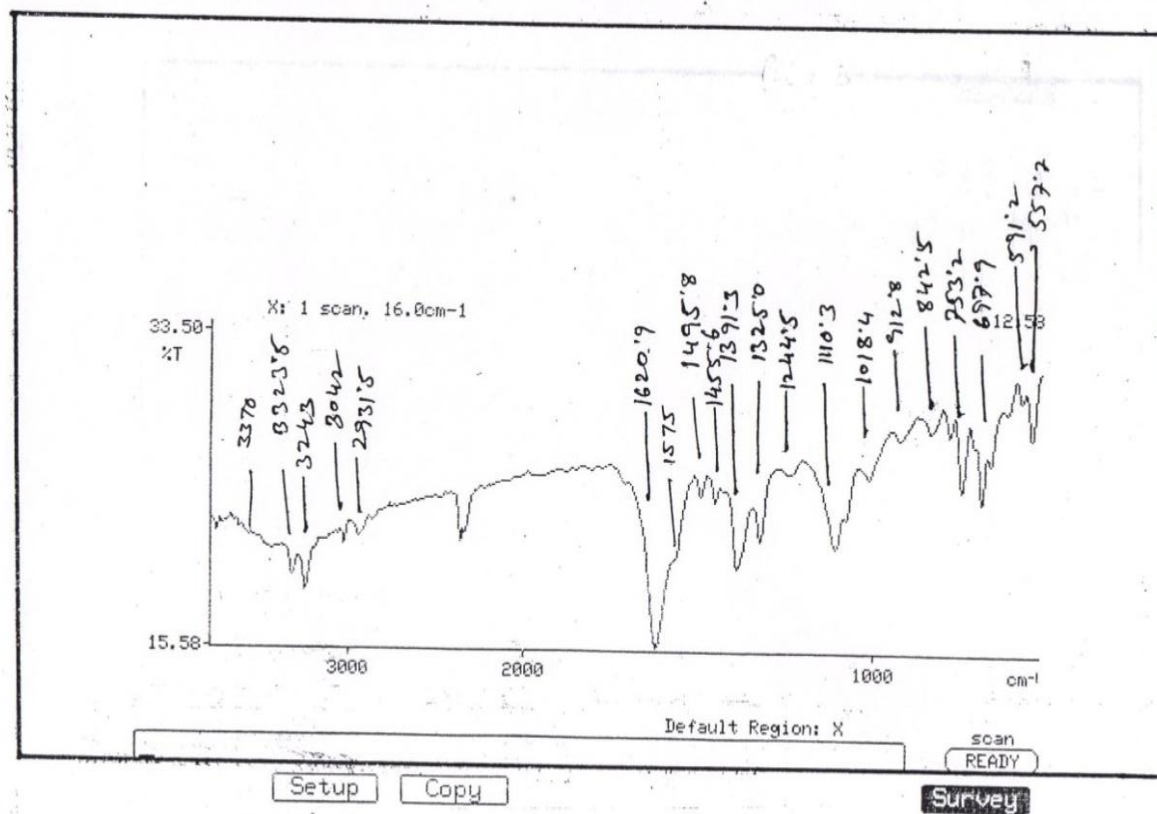
Fig. 3.9 : FT-IR spectrum of   [CuBr$_2$(phe.ala)(H$_2$O)]   (8)
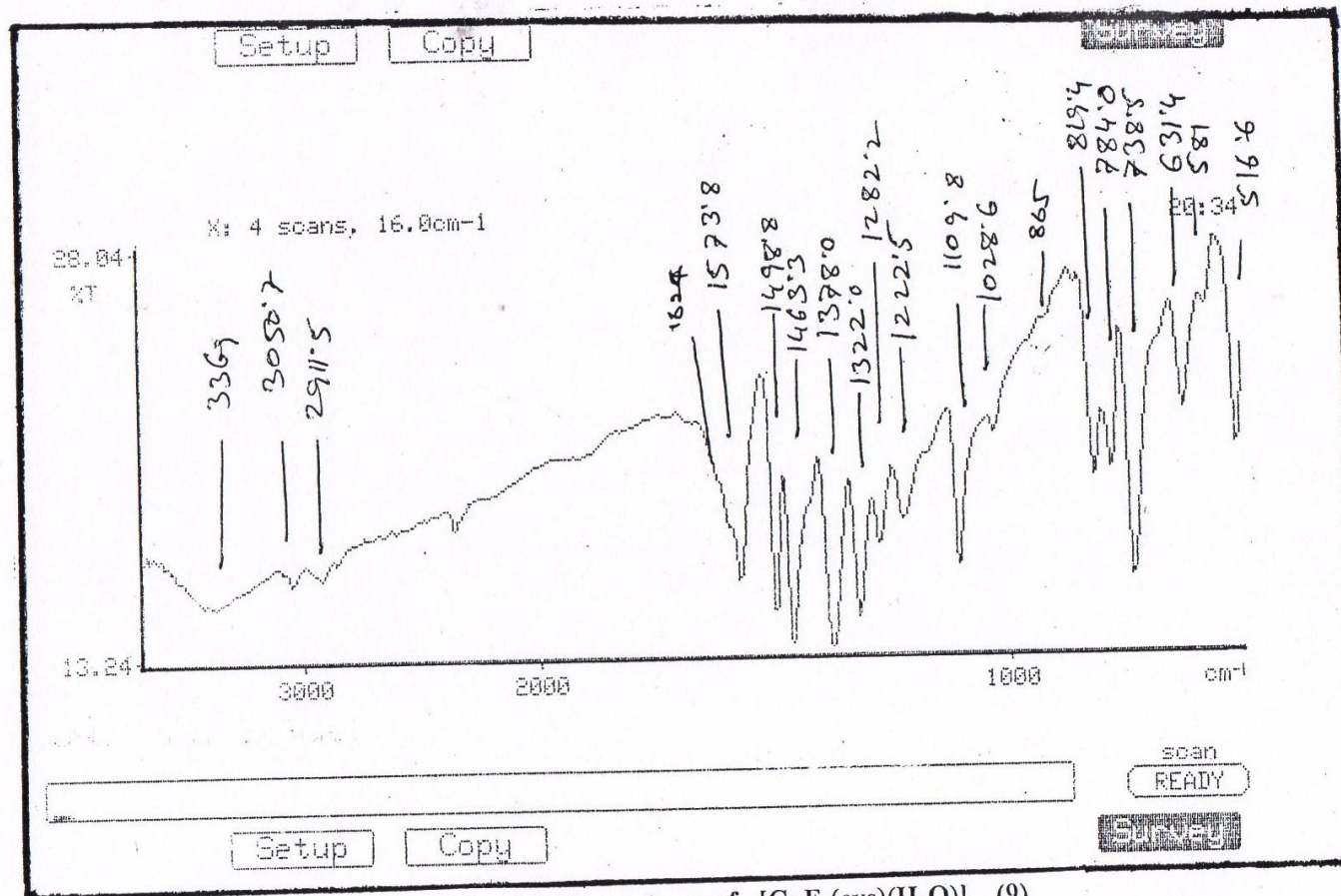
Fig. 3.10 : FT-IR spectrum of [CuF$_2$(cys)(H$_2$O)] (9)
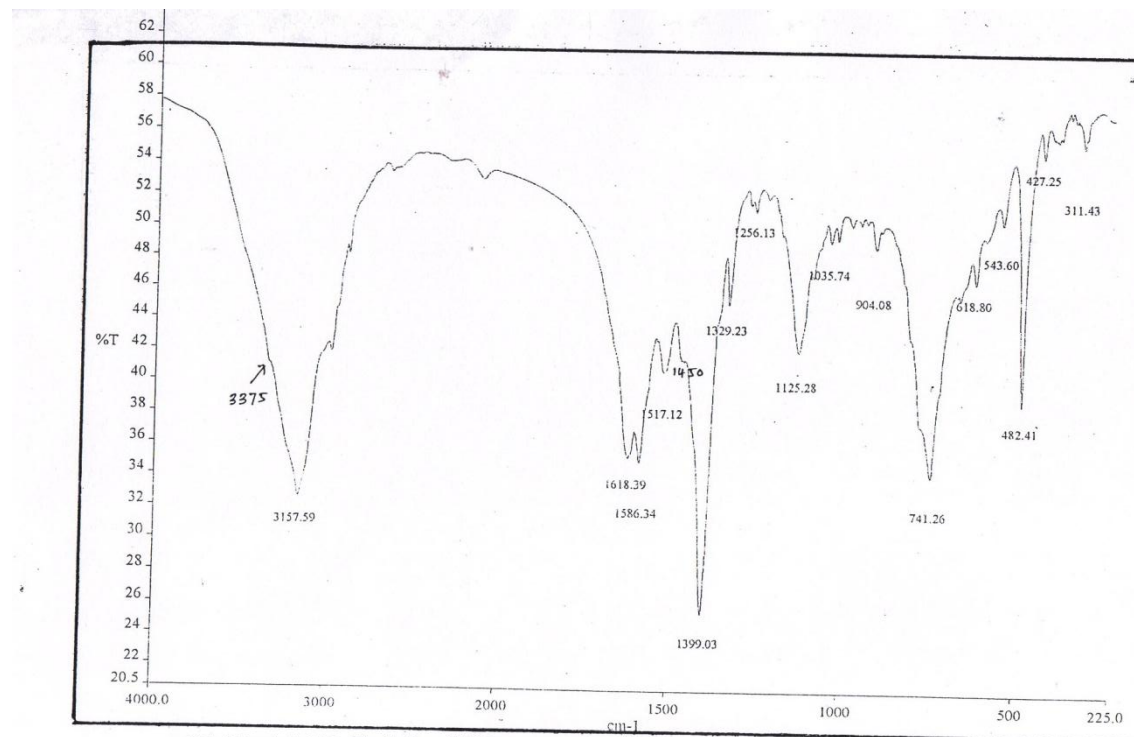
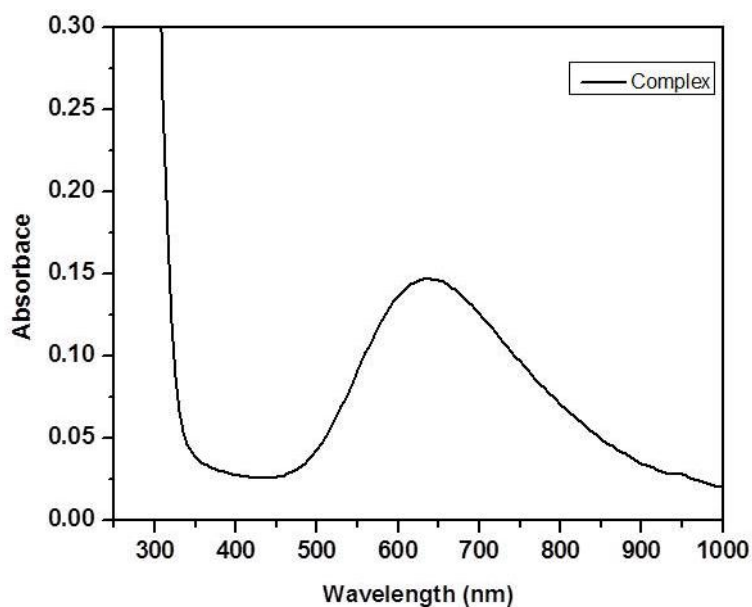**Fig 3.11:** FT-IR spectrum of [Cu(val)$_2$(H$_2$O)] **(10)**

Fig 3.12: UV-Visible spectrum of [Cu(val)$_2$(H$_2$O)] **(10)**

As for the FT-IR spectrum of complexes **(4)** – **(9)** with aminoacids as coligand exhibited rather general features. Absorption bands were observed at ~1575 cm^{-1} ($\nu_{a\ C=O}$),   1440 cm^{-1} ($\nu_{S\ C-O}$) and 1380 cm^{-1} (ν_{NH2}). A comparison with free ligand spectrum indicated hardly any alteration for δ_{NH2} mode and the ($\nu_{a\ C=O}$)   was found to have shifted by ~ 20cm^{-1} to higher wave number suggesting monodenate carboxylato (via – O) coordination of a zwitterionic aminoacid ligand **[23].** A rather strong band at ~745 cm^{-1} in the lower wave number region in the complexes assigned to $\delta_{c=o}$, was also observed in the free ligand spectrum. Thus on careful scrutiny, it appeared that the aminoacid ligand occurring in its neutral form is O – coordinated to the metal center. Band at ~1625 cm^{-1} in compound **(4)** – **(9)**, a medium intensity peak was found   merged with the strong ~ 1575 cm^{-1} (resolved in complex **10**) peak and was assigned to δ_{H2O} mode. An unresolved broad band at ~3370 cm^{-1} occurring as a hump on the 3155 s cm^{-1} (ν_{N-H}) band was assigned to ν_{OH} stretching mode of H$_2$O. A somewhat weak band at ~ 865 cm^{-1} assignable to ρ_r (H$_2$O)

60

Table 3.1 : Analytical data and magnetic moment values of complexes **(1-10)**

Complexes	Colour	μ_{eff} (BM)	Analysis* (%)				
			Cu	**^{a}X**	**C**	**N**	**H**
[CuF$_2$(oxin)$_2$] **(1)** (M = 391.5)	Sky blue	1.89	16.8 (16.2)	^{b} 11.1 (9.7)	54.7 (55.2)	7.1 (7.2)	3.1 (3.6)
[CuCl$_2$(oxin)$_2$] **(2)** (M = 424.5)	Light green	1.92	15.3 (14.9)	^{c} 16.2 (16.7)	51.3 (50.9)	6.2 (6.6)	2.8 (3.3)
[CuBr$_2$(oxin)$_2$] **(3)** (M = 513.3)	Green	1.90	12.5 (12.4)	^{d} 31.3 (31.1)	41.4 (42.1)	4.8 (5.5)	1.2 (2.7)
[CuF$_2$(Hleu)(H$_2$O)] **(4)** (M = 250.69)	Sky blue	1.88	25.1 (25.3)	^{b} 15.2 (15.1)	27.9 (28.7)	6.0 (5.6)	5.7 (5.9)
[CuBr$_2$(Hleu)(H$_2$O)] **(5)** (M = 372.48)	Sky blue	1.88	17.3 (17.0)	^{d} 43.5 (42.9)	19.7 (19.3)	3.8 (3.8)	3.6 (4.0)
[CuF$_2$(Hmet)(H$_2$O)] **(6)** (M = 268.71)	Blue	1.90	23.5 (23.6)	^{b} 14.5 (14.1)	23.3 (22.3)	6.2 (5.2)	4.7 (4.8)
[CuF$_2$(Hphe)(H$_2$O)] **(7)** (M = 284.69)	Sky blue	1.94	22.4 (22.3)	^{b} 13.7 (13.3)	40.8 (37.9)	5.2 (4.9)	4.6 (4.6)
[CuBr$_2$(Hphe)(H$_2$O)] **(8)** (M = 406.49)	Sky blue	1.90	15.7 (15.6)	^{d} 39.0 (39.3)	27.1 (26.6)	3.2 (3.4)	2.4 (3.2)
[CuF$_2$(Hcys)(H$_2$O)] **(9)** (M = 240.57)	Sky blue	1.94	26.6 (26.4)	^{b} 16.0 (15.8)	14.5 (15.0)	6.0 (5.8)	3.4 (3.7)
[Cu(val)$_2$(H$_2$O)] **(10)** (M = 315.56)	Blue	1.90	19.7 (20.1)	---	37.7 (38.0)	8.6 (8.9)	7.2 (7.6)

* Calculated values are in parentheses.
^{a}X : F, Cl, Br ; ^{b}F , ^{c}Cl , ^{d}Br ; M = mol. wt.

Table 3.2 :   Structurally significant FT-IR data of complexes (**1 –- 10**)

Complex	IR bands (cm^{-1})						
	ν_{COO} (as)	ν_{COO} (s)	ν_{NH}	$\delta_{(NH_4^+)}$ / oxin #	ν_{OH}	δ_{OH_2}	ρ_r (H$_2$O)
[CuF$_2$(oxin)$_2$] **(1)**	–	–	–	1499 #	3370 *	–	–
[CuCl$_2$(oxin)$_2$] **(2)**	–	–	–	1499 #	3370 *	–	–
[CuBr$_2$(oxin)$_2$] **(3)**	–	–	–	1499 #	3370 *	–	–
[CuF$_2$(Hleu)(H$_2$O)] **(4)**	1575	1465	3050	–	3370	1620	820
[CuBr$_2$(Hleu)(H$_2$O)] **(5)**	1570	1465	2925	–	3365	1620	855
[CuF$_2$(Hmet)(H$_2$O)] **(6)**	1570	1440	2910	–	3370	1615	811
[CuF$_2$(Hphe)(H$_2$O)] **(7)**	1570	1455	3025	–	3365	1620	830
[CuBr$_2$(Hphe)(H$_2$O)] **(8)**	1575	1455	3040	–	3370	1620	845
[CuF$_2$(Hcys)(H$_2$O)] **(9)**	1575	1465	3050	–	3370	1625	820
[Cu(val)$_2$(H$_2$O)] **(10)**	1585	1450	3155	1400	3375	1620	–

* originated from -OH group of serine.

$\nu_{C\text{-}OH}$ mode of oxine.

mode in complex **(4) - (9)** suggested the occurrence of coordinated water molecule in the complexes, [Cu X_2 L (H_2O)]   (L = amino acid). Simple pyrolytic experiment conducted on **(4)** and **(6)** revealed loss of water molecule alongwith one fluoride beyond 270^0 C implying existence of coordinated water.
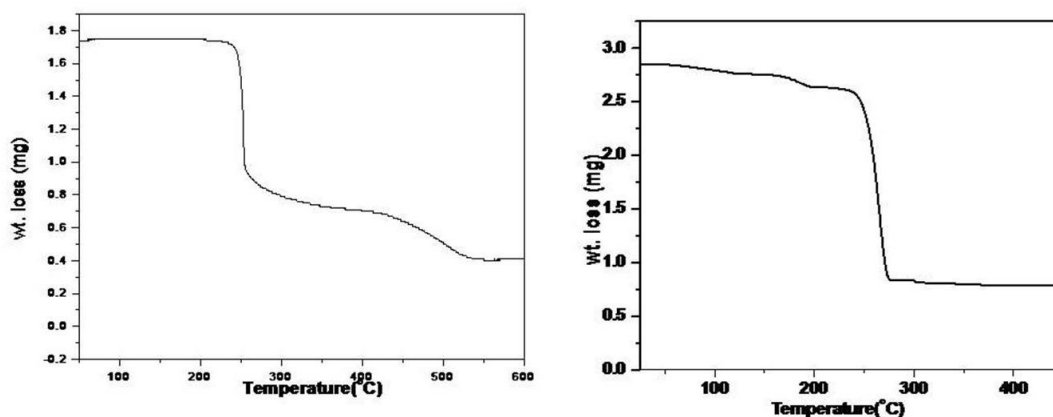

Fig. 3.13:   TGA spectra of the Cu (II) compounds **(7)** and **(10)**

Table 3.3: TGA data of the selected compounds,**(7)** and **(10)**

Compound	TGA plateau (^{0}C)	% of mass loss		process
		observed	calculated	
[CuF$_2$(Hphe)(H$_2$O)] **(7)** **(M = 284.69)**	230 -- 352 352 -- 558	58.2 19.0	58.2 19.56	Loss of organic ligand Loss of two F atom and one water molecule
[Cu(val)$_2$(H$_2$O)] **(10)** **(M = 315.56)**	57 -- 202 210 --282	7.3 63.0	5.7 ----	Loss of water molecule Partial loss of the organic ligand Decomposition

For the complex **(10),** such weight–loss experiment indicated simultaneous loss of uncharacterisable multiple fragmaents beginning at $\sim170^0$ C. Bands at 1620s cm^{-1}

(ν_{as} : COO$^-$) and 1395 cm^{-1} (ν_s : COO$^-$) associated with carboxylate moiety are typical of chelated aminoacid(s) as was also validated by single crystal X-ray crystallography.

The structure of two representative copper complexes [CuF$_2$(Hphe)(H$_2$O)] **(7)** and [CuF$_2$(Hcys)(H$_2$O)] **(9)** were fully optimized using BLYP functional and DNP basis sets as implemented in the program DMol3 [**44,45**]. In order to confirm the stability of the complexes we performed vibrational frequencies calculations at the optimized structure with the same level of theory.

The DFT optimized geometries of copper complexes [CuF$_2$(Hphe)(H$_2$O)] **(7)** and [CuF$_2$(Hcys)(H$_2$O)] **(9)** are shown in Fig.3.14 In the vibrational frequency calculations, no imaginary frequency is observed for both the compound which suggests that the optimized compounds signify stable structures ie., shows local minima in the potential energy surfaces. Structural parameters are given in table(3.4). From Fig.3.14, it is observed that in complex[CuF$_2$(Hphe)(H$_2$O)] **(7)** and complex [CuF$_2$(Hcys)(H$_2$O)] **(9),** copper metal forms four co-ordinated distorted tetrahedral complex. Values of HOMO-LUMO gap and hardness are given in **Table 3.5.**

Table.3.4: DFT, Selected bond lengths (Å) and bond angles (°) for copper complexes

Structural parameters	Complex[CuF$_2$(Hphe)(H$_2$O)] **(7)**	Complex[CuF$_2$(Hcys)(H$_2$O)] **(9)**
Cu—F1	1.810	1.795
Cu—F2	1.988	1.846
Cu—O1	2.152	1.818
Cu—O2	1.989	1.912
F1—Cu—F2	105.23	93.79
O1—Cu—F1	93.46	105.77
O1—Cu—O2	87.31	94.88
O2—Cu—F2	88.66	101.32

Table.3.5: Selected reactivity parameters of DFT computed energy

Compounds	DFT computed energy values and dipole moment data				
	LUMO (eV)	HOMO (eV)	$\Delta E_{(LUMO\text{-}HOMO)}$eV	Hardness(eV) $\eta = \dfrac{E_{LUMO} - E_{HOMO}}{2}$	Dipole Moment (D)
[CuF$_2$(Hphe)(H$_2$O)]**(7)**	-4.463	-5.801	1.338	0.669	8.968
[CuF$_2$(Hcys)(H$_2$O)]**(9)**	-6.387	-6.665	0.278	0.139	9.181
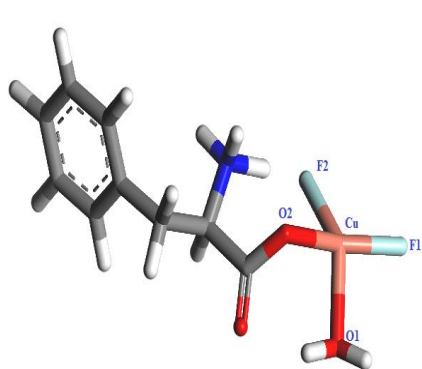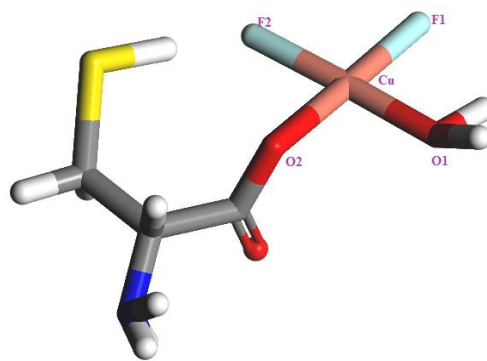
[CuF$_2$(Hphe)(H$_2$O)] **(7)**   [CuF$_2$(Hcys)(H$_2$O)] **(9)**

Fig 3.14: Optimized structure of **(7)** and **(9)**
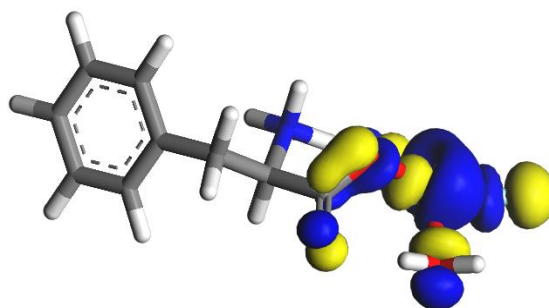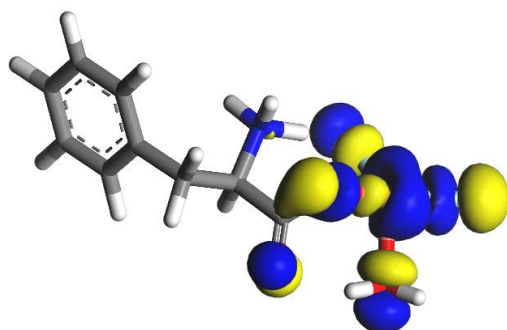
Fig. 3.15: HOMO, LUMO of [CuF$_2$(Hphe)(H$_2$O)] **(7)**
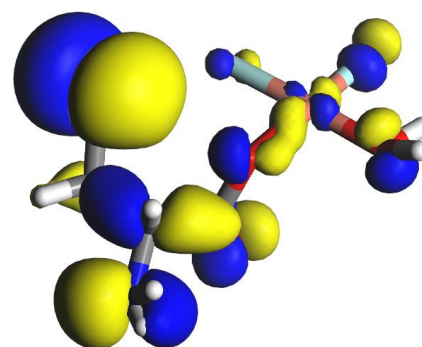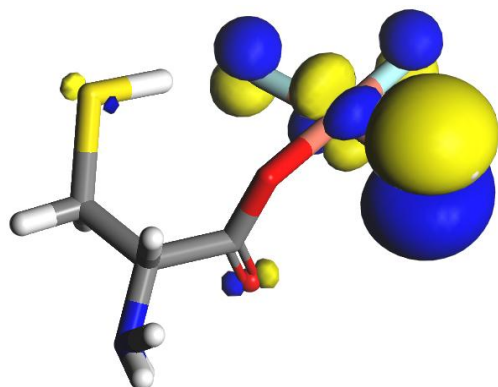
Fig. 3.16: HOMO, LUMO of [CuF$_2$(Hcys)(H$_2$O)] **(9)**

Table 3.6: Crystallographic data for [Cu(val)$_2$(H$_2$O)] **(10)**.

Emperical formula	C$_{10}$H$_{22}$N$_2$O$_5$Cu
Formula weight	
Temperature/K	296K
Volume(Å^3)	1446.6 (3)
Space group	C2
Hall group	C2y
a/ Å	21.396 (3)
b/Å	9.6059 (11)
c/Å	7.4458 (9)
α /°	90
β /°	109.04
γ /°	90
Z	4
D, gcm^{-3}	1.432
$h, k, l_{max.}$	22, 10, 7
$\theta_{max.}$	22.05
R (reflections)	0.0781
WR2 (reflections)	0.1984

Based on analytical and spectroscopic data, a four coordinate distorted tetrahedral structure has been tentatively proposed for the complexes **(1 – 9) {Fig. 3.17 a,b}.** For complexes **(1) – (3),** the two terminal halide and two neutral N – coordianted oxine ligand completes the coordination around Cu(II) centre **(Fig. 3.17a),** while for those containing aminoacid as coligand, **(4) – (9),** the tetrahedral co-ordination is completed by two halides, one neutral O – coordinated amino acid and one aquo group **(Fig. 3.17b).).** Single crystal XRD evidence for such zwitterionic α-aminoacid ligand viz. glycine, alanine, proline, valine, leucine, serine, asparagine, glutamine, and glutamic acid binding metal ion through the carboxylato-oxygen in a monodentate fashion has been furnished by Djordjevic et al [46]. Metal coordination by

carboxylato-oxygen for zwitterionic amino acid ligand has also been shown to be favored by DFT calculations **[47].**
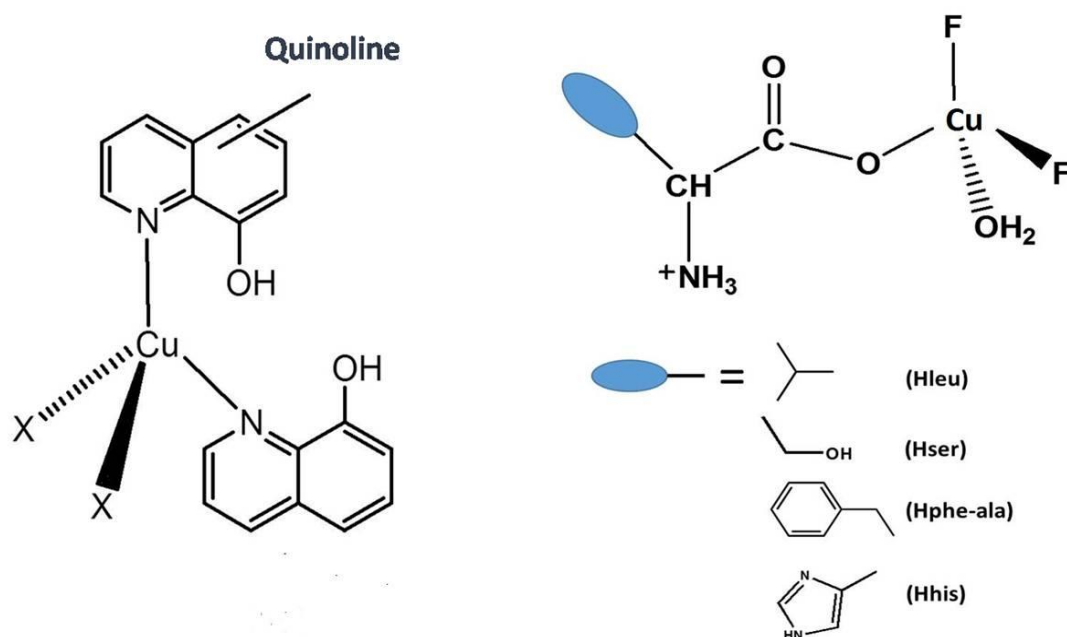

Fig. 3.17 : Proposed structures of complexes **of** quinoline **(1)** to **(3)** and aminoacid
(4) to (9) ;   geometry : distorted tetrahedral

Single crystal X- ray structure of the compound cis-[Cu(val)$_2$(H$_2$O)] **(10)** is shown in **Fig. 3.18**
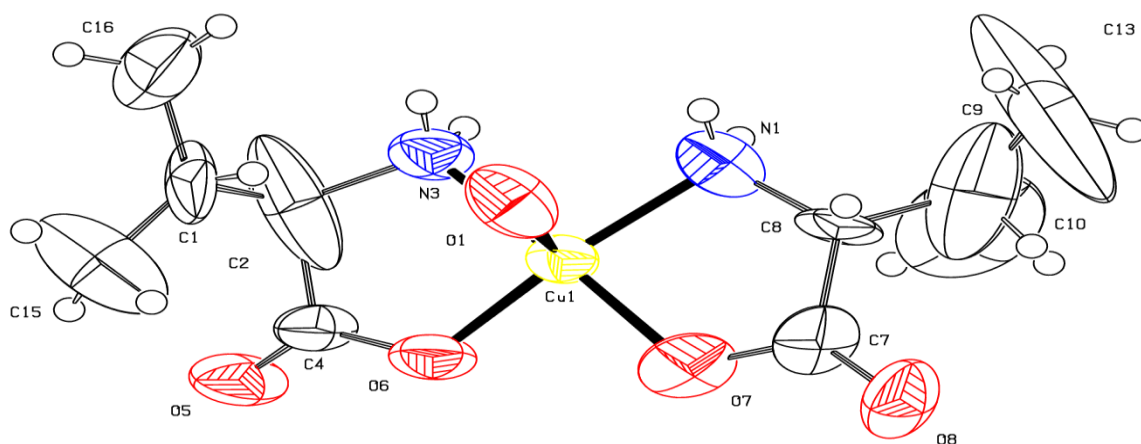
Fig. 3.18 :   X-Ray Structure of cis-[Cu(val)$_2$(H$_2$O)]   **(10)**

Simple synthetic strategies for mixedligand copper(II) complexes were developed. A comparative assessment with compounds with similar ligands prepared earlier in our laboratory has been made. Attempts to prepare iodo complexes under similar reaction

Fig.**3.19:** XRD pattern of cis-[Cu(val)$_2$(H$_2$O)]   **(10)**

condition did not afford any such mixed ligand complexes. No chloro complexes with aminoacid as coligand could be obtained.

Fig.3.20 Fluorescent microscopic image of crystals of cis-[Cu(val)$_2$(H$_2$O)]   **(10)**

CuO.nH$_2$O

(i) NH$_4$HF$_2$ pH ~ 6
→ **[CuF$_2$(oxin)$_2$] (1)**
(ii (Oxin)   Δ   (1:2)

(i) NH$_4$Cl,   (ii) HCl   pH ~ 6
→ **[CuCl$_2$(oxin)$_2$](2)**
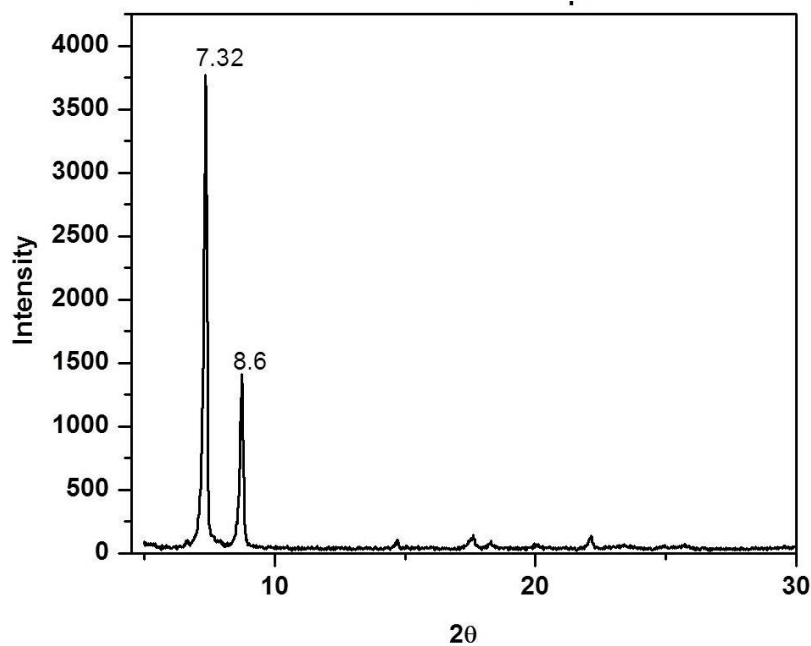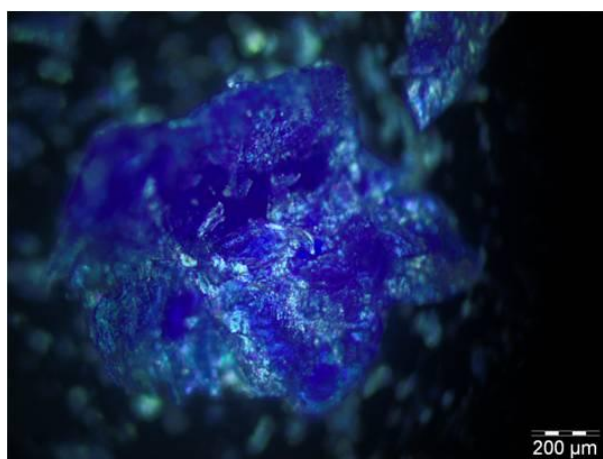(iii) (Oxin)   Δ   (1:2)

(i) NH$_4$Br,   (ii) HBr   pH ~ 6
→ **[CuBr$_2$(oxin)$_2$](3)**
(iii) (Oxin)   Δ   (1:2)

(i) NH$_4$HF$_2$,   pH ~ 3-4
→ **[CuF$_2$(Hleu)(H$_2$O)] (4)**
(ii) (leu)   Δ   (1:1)

(i) NH$_4$Br,   (ii) HBr   pH ~ 3-4
→ **[CuBr$_2$(Hleu)(H$_2$O)](5)**
(iii) (leu)   Δ   (1:1)

(i) (met),   pH ~ 3
→ **[CuF$_2$(Hmet)(H$_2$O)](6)**
(ii) NH$_4$HF$_2$ Δ   (1:1)

(i) NH$_4$HF$_2$,   pH ~ 4-5
→ **[CuF$_2$(Hphe)(H$_2$O)] (7)**
(ii) (phe.ala)   Δ   (1:1)

(i) NH$_4$Br,   (ii) HBr   pH ~ 3-4
→ **[CuBr$_2$(Hphe)(H$_2$O)] (8)**
(iii) (phe.ala)   Δ   (1:1)

(i) NH$_4$HF$_2$,   pH ~ 3-4
→ **[CuF$_2$(Hcys)(H$_2$O)] (9)**
(ii) (cys)   Δ   (1:1)

(i) (val),   pH ~ 5-6
→ **[Cu(val)$_2$(H$_2$O)] (10)**
(ii) NH$_4$HF$_2$ Δ   (1:2)

Scheme.3.1: Formation of copper complexes **(1 – 10)**

70

References

1. B. Barszcz, **Coord. Chem. Rev**. 2005, **249**, 2133.

2. K. D. Karlin, Z. Tyeklar **Bioinorganic Chemistry of Copper**, 1993, Chapman and Hall, New York and references therein.

3. H.O. Davies, R.D. Gillard, M.B. Hursthouse, A. Karaulou, **J. Chem. Soc. Dalton Trans.** 1995, 2333.

4. M.A.S. Goher, L.A. Al-Satti, F.A. Mantner, **Inorg. Chem**. 1997, **16**, 889.

5. C.R. Bhattacharjee, P.K. Choudhury, **Transition. Met. Chem**. 1998, **23**, 561.

6. H. Sigel (ed.), **Metal Ions in Biological Systems**, 1973-79, Vol. 1-9, Marcell-Dekker.

7. O. Yamauchi, T. Sakurai, A. Nakahara, **J. Am. Chem. Soc**. 1979, **101**, 4164.

8. T. Sugimori, H. Masuda, N. Ohata, K. Koiwai, A. Odani, O. Yamauchi, **Inorg. Chem.** 1997, **36**, 576.

9. E. Farkas, E.A. Enyedy, G. Micera, E. Garribba, **Polyhedron**, 2000, **19**, 1727.

10. B. Sarkar, T.P.A. Kruck, in : J. Peisach, P. Aisen, W. Blumberg (Eds), **Biochemistry of copper**, Academic Press, New York, 1966, p. 183.

11. B. Sarkar, **J. Inorg. Biochem**. 200, **79**, 187.

12. C. Marzano, M. Pellei, F. Tisato, C. Santini, **Med. Chem.** 2009, **9**, 185.

13. S. Tardito, L. Marchiò,. **Curr. Med. Chem.** 2009, **16**, 1325.

14. S. Dhar, M. Nethaji, A. R. Chakravarty, **Inorg. Chem**. 2006, **45**, 11043.

15. S. Dhar, D. Senapati, P. K. Das, P. Chattopadhyay, M. Nethaji, A. R. Chakravarty, **J. Am. Chem. Soc**. 2003, **125**, 12118.

16. M. Scarpellini, A. Neves, R. Horner, A. J. Bortoluzzi, B. Szpoganics, C. Zucco, R. A. N. Silva, V. Drago, A. S. Mangrich, W. A. Ortiz, W. A. C. Passos, M. C. B de Oliveira, H. Terenzi, **Inorg. Chem**. 2003, **42**, 8353.

17. C. H. Chen, D. S. Sigman, **Proc. Natl. Acad. Sci. U.S.A.** 1986, **83**, 7147.

18. N. Berthet, V. Martel-Frachet, F. Michel, C. Philouze, S. Hamman, X. Ronot, F. Thomas, **Dalton Trans**. 2013, **42**, 8468.

19. R. Buchtik, Z. Travnicek, J. Vanco, R. Herchel, Z. Dvorak, **Dalton Trans**. 2011, **40**, 9404.

20. S. Roy, P. U. Maheswari, M. Lutz, A. L. Spek, H. den Dulk, S. Barends, G. P. van Wezel, F. Hartl, J. Reedijk, **Dalton Trans**. 2009, 10846.

21. S. Y. Tsang, S. C. Tam, I. Bremner, M. J. Burkitt, **Biochem. J**. 1996, **317**, 13.

22. M. E. Bravo-Gomez, J. C. Garcia-Ramos, I. Gracia-Mora, L. Ruiz- Azuara, **J. Inorg. Biochem**. 2009, **103**, 299.

23. W.H. Mahmoud, N.F. Mahmoud, G.G. Mohamed, A.A. El-Bindary, A.Z. El-Sonbati, **J. Mol. Struct**. 2015, **1086,** 266.

24. R.N. Patel, N. Singh, K.K. Shukla, U.K. Chauhan, J. Niclós-Gutiérrez, A. Castinˇeiras, **Inorg. Chim. Acta** 2004, **357,** 2469.

25. A.Z. El-Sonbati, M.A. Hefni, **Polym. Deg. Stab**. 1994, **43,** 33.

26. A.Z. El-Sonbati, A.A.M. Belal, M.S. El-Gharib, Sh.M. Morgan, **Spectrochim. Acta A**, 2012, **95,** 627.

27. A.Z. El-Sonbati, A.A. El-Bindary, M.A. Diab, S.G. Nozha, **Spectrochim. Acta A** , 2011, **83**, 490.

28. A.Z. El-Sonbati, M.A. Diab, A.A. El-Bindary, M.K. Abd El-Kader, **Spectrochim. Acta A,** 2012, **99,** 211.

29. A.Z. El-Sonbati, M.A. Diab, A.A. El-Bindary, M.I. Abou-Dobara, H.A. Seyam, **Spectrochim. Acta A**, 2013, **104**, 213.

30. S.A. Lahsasni, R.A. Ammar, M.F. Amin, E.M. Shoukry, **Int. J. Electrochem. Sci**. 2012, **7**, 7699.

31. C. Li , **Adv. Drug Delivery Rev**. 2002,**54**,695.

32. H. Tapiero, K.D. Tew, **Biomed. Pharmaco**. 2003, **57**,399.

33. P.Doz, H. Sigel, **Angew. Chem**. 1975, **14**, 394.

34.   G. Wu, Y. Fang, S. Yang, J. Lupton, N. Turner, **J. Nutr**. 2004, **134**, 489.

35.   K. Pisarewicz, D. Mora, F. Pflueger, G. Fields, F. Mari, **J. Am. Chem. Soc.** 2005, **127**, 6207.

36.   P.Z. Neumann, A. Sass-Kortsak, **J. Clin. Invest**. 1967, **46**, 646.

37.   V. Brumas, N. Alliey, G. Berthon, **J. Inorg. Biochem**.. 1993, **52**, 287.

38.   P.M. May, in : G. Berthon (Ed.), **Handbook of Metal-Ligand Interactions in Biological Fluids – Bioinorganic Chemistry**, Marcel Dekker, New York, 1995, p. 1184.

39.   I. Sanyal, R.W. Strange, N.J. Blackburn, K.D. Karlin, **J. Am. Chem. Soc**. 1991, **113**, 4692.

40.   D.M. Dooley, M.A. MeGuirl, C.E. Cote, P.F. Knowles, I. Singh, M. Spiller, R.D. Brown III, S.H. Koenig, **J. Am. Chem. Soc**. 1919, **113**, 754.

41.   H. Nakata, T. Yamauchi, H. Fujisawa, **J. Biol. Chem**. 1979, **254**, 1829.

42.   C.R. Bhattacharjee, P.K. Choudhury, **Transition Met. Chem**. 2001, **26**, 730.

43.   P. Choudhury, **Ph.D. Thesis on Synthetic and Physico Chemical Investigation of some halo and mixedhalo complexes of copper(II),** 1999, Gauhati University, P. 86.

44.   K. Nakamoto, **Infrared and Raman spectra of coordination compounds**, 4th edn. Wiley Interscience, London, 1986, p. 234.

45.   Delly B. **J Chem Phys** 1990, 92, 508.

46.   C. Lee, W. Yang, R.G. Parr, Phys. Rev. B 1988, **37**, 785

46   C. Djordjevic, N. Vuletic, B.A. Jacobs, E. Sinn, **Inorg Chem**. 1997, **36**, 1798.

47.   P. Umadevi, R. Senthilkumar, **RSC Adv**. 2014, **4**, 49040.

✼ ✼ ✼ ✼ ✼