



Research Article

The work is licensed under



## Synthesis, Characterization Antimicrobial and Antioxidant Studies of Complexes of Fe(III), Ni(II) and Cu(II) with Novel Schiff Base Ligand (E)-Ethyl 3-((2-Aminoethyl)Imino)Butanoate

K. Subin Kumar\*, K. K Aravindakshan

Department of Chemistry, University of Calicut, 673 635, Malappuram, Kerala, India

\*Corresponding Author: K. Subin Kumar, Department of Chemistry, University of Calicut, 673 635, Malappuram, Kerala, India

Received: 31 July 2017

Revised: 26 August 2017

Accepted: 29 August 2017

### ABSTRACT

Schiff base coordination complexes of Fe(III), Ni(II) and Cu(II) have been prepared with a multi-dentate ligand synthesized from ethylenediamine and ethylacetoacetate. The identification and characterizations were done based on their analytical and IR, UV-Visible and  $^1\text{H}$  NMR spectral measurements. The Schiff base acted as a tetradentate ligand, coordination through the N of imine, N of amine and O of enolic groups atoms. Based on the magnetic measurements and various spectral studies, geometries have been assigned to these complexes. One of the Cu(II) complex was found to be square planar and dimeric. All the other Cu(II), Ni(II) and Fe(III) compounds were observed to be distorted octahedral. Ligand and their metal compounds were tested in vitro for their antifungal activity against two pathogenic fungi, *Fusarium semitectum* and *Aspergillus flavus*, and antibacterial study against gram positive (*Pseudomonas aeruginosa*) and gram negative (*Streptococcus mutans*) bacteria was evaluated. The potential of the copper and nickel compounds to scavenge hydrogen peroxide was ascertained by the technique developed by Ruch et al. in 1989. The metal complexes have appreciably improved antibacterial and antifungal activity against microbial strains in compared with the free ligand. Thus, they may find application as a new antimicrobial agent after further study of their biological properties. The antioxidant study revealed that the Ni(II) Schiff base complexes are better antioxidants than Cu(II) complexes.

**Keyword:** (E)-ethyl 3-((3-aminopropyl)imino)butanoate; square planar; distorted octahedron; antibacterial; antifungal and antioxidant.

### INTRODUCTION

A large number of multidentate and macrocyclic Schiff base ligands have been synthesized from the active methylene compounds and daimines. These Schiff base ligand molecules have recalled significant interest by virtue of their applicability as model compounds in both bioinorganic and analytical studies [1,2]. The formation of Schiff base or imine metal compounds can be effected very readily through

reactions of imines with the carbonyl compounds in the presence of an ion of metal salts. Nucleophilic amine attack on the carbonyl group is increased by the carbonyl group polarization by coordination of the oxygen atom to a metal ion. The coordination of the product, imine is a significant aspect in promoting the reaction by suitable metal ion. The initial reactions of these types were used to produce  $\text{Cu}^{2+}$  complexes of salicylaldehyde, where additional coordination

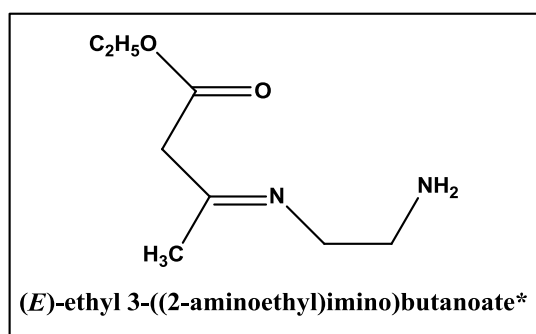
support is provided by the phenolate oxygen atom. Several bi- and tridentate ligand systems have been prepared by this method[3-5]. Tetradentate Schiff bases with  $N_2O_2$  donor sites have been extensively investigated for their potential capability to coordinate with various transition metal ions. The properties of these metal compounds were identified by the electronic character of the ligands as well as by their conformational behavior [6-9]. Synthesis of such quadridentate imine chelate usually requires the addition of two equivalent dicarbonyl compounds and a diamine[10,11]

Schiff base ligands such as thiosemicarbazones and semicarbazone are used in pharmacology as antibacterial, anticancer, and antifungal agents. Also, they are of significant interest for biochemistry, biomedicine and environmental protection owing to their ability for chemical recognition of anions and metals. Thiosemicarbazones and semicarbazone belong to important class of mixed nitrogen-sulphur/oxygen donor ligands. Commonly, they coordinate with a metal atom via the sulphur/oxygen and nitrogen atoms to form chelates. Thiosemicarbazones are known as analytical reagents. Metal chelates of the

complexes slow down the tumor growth and enhance biological action of some drugs.

Rafat M. El-Shazly *et al*[12] reported a synthesis of a Schiff base from ethylacetoacetate and ethylenediamine by combining 2:1 ratio. This ligand treated with Cu(II) ion to give,  $[Cu_2LCl_6]$ ,  $[Cu_4LCl_5]$ ,  $[Cu_5LCl_{10}]$ , etc types of polynuclear complexes. Elemental analysis, molar conductivities, magnetic susceptibility, and IR spectral techniques have been used to identify these complexes. The tetradentate binding manner of the Schiff base find out from IR spectra and also spectral and magnetic evaluation suggest the presence of chlorine-bridge between the copper atoms. In the present study, the coordination compounds of the Schiff base, ethyleneamino-imine(ethylacetoacetate) (LH) with Fe(III), Ni(II), and Cu(II) where synthesized and characterized and its antimicrobial activities were studied. The structure of the ligand was determined based on their analytical and spectral data. The structure of ligand molecule is given in Fig.1.

The complexes were characterized by elemental analysis, magnetic measurement, IR and electronic spectral techniques.



**Fig.1: Structure of the ligand, ethyleneamino-imine(ethylacetoacetate) (LH)**

\*IUPAC name: (E)-ethyl 3-((2-aminoethyl)imino)butanoate\*

## EXPERIMENTAL

Elements C, H and N were estimated by microanalysis techniques using Hitachi CHN-O rapid analyzer. The ligand  $^1H$ - NMR spectral data was recorded in DMSO- $d_6$  on Varian 300 NMR spectrometer. CHNS and  $^1H$ - NMR spectrum were obtained from STIC Cusat kochin. The infrared spectra of the ligand and the metal compounds were recorded using FTIR DR-8031 Shimadzu spectrophotometer. UV-Vis

spectra of the samples were determined using UV-1601, Shimadzu spectrophotometer, were obtained from Chemistry department, University of Calicut. Insoluble or partially soluble metal complexes, the UV spectra were recorded using mull technique[13]. The magnetic moment data of the complexes were obtained from the instrument Gouy-type magnetic balance. All measurement was done at room

temperature, using  $\text{Hg}[\text{Co}(\text{NCS})_4]$  as calibrant[14].

### Synthesis of Schiff base ligand (E)-ethyl 3-((3-aminopropyl)imino)butanoate

Ethylacetoacetate (0.025 mol) in minimum amount of methanol was added to ethylenediamine (0.025 mol) in methanol in 250 ml round bottom flask. Add a single drop of mineral acid as a catalyst. The solution of the mixture was allowed to reflux for 3 h, and then the volume was concentrated to half. The Schiff base precipitates after standing overnight at room temperature. The filtered product was washed with ethanol and water and dried.

### Synthesis of metal complexes

A solution of the metal salt (0.005 mol in 25 ml methanol) was added to a solution of the ligand (0.005 mol in 25 ml methanol) and it was refluxed for 4 h. It was then allowed to cool and evaporated. The filtered solid complexes were washed several times with petroleum benzene and finally with methanol. It was then allowed to dry over anhydrous  $\text{CaCl}_2$ .

### Biological evaluation

#### Antifungal activity

The ligand, (E)-ethyl 3-((3-aminopropyl)imino)butanoate (LH) and their metal compounds were analysed *in vitro* for their antifungal assay against two pathogenic fungi, *Fusarium semitectum* and *Aspergillus flavus*, by the agar plate method using Sabouraud Dextrose Agar as selective medium. The medium has the following composition: dextrose 40 g, mycological peptone 10 g, agar 15 gm, and distilled water 1000 mL; pH was maintained to 5.6– 5.9 at  $28 \pm 2^\circ\text{C}$ . Then, a required amount of the test solution (ethanol solution) was introduced into it to obtain a concentration of 50, 100, and 200 ppm. The medium was then transferred into Petri plates and the spores of the fungi were inserted into the medium through an inoculum needle. The Petri plates were wrapped in polythene bags enclosing little drops of alcohol and placed in an incubator at  $25 \pm 4^\circ\text{C}$ . The activity, i.e., the fungal growth, was examined after 96 hour of incubation by calculating the diameter of the fungal colony. The inhibition percentage was calculated as:  $\text{Inhibition} = \frac{C-T}{C} \times 100\%$  where  $C$  is the control and  $T$  is the test plates diameter

of fungal colony respectively, after 96 hour. The antifungal activity of the compounds was compared with that of the standard compound.

#### Antibacterial activity

The antibacterial assay of the Schiff base ligand and their Cu(II), Fe(III) and Ni(II) complexes against gram positive (*Pseudomonas aeruginosa*) and gram negative (*Streptococcus mutans*) bacteria was evaluated. Test organisms were grown on a Mueller- Hinton agar. The agar medium contained starch (0.15 g), beef infusion (30 g), casein hydrolysate (1.75 g), agar (1.7 g), and distilled water (1000 mL); its  $\text{pH}$  was maintained to neutral at  $37 \pm 2^\circ\text{C}$ . The desired compounds in methanol in concentrations 500 and 1000 ppm and soaked in Whatman no. 1 filter paper discs of 5 mm diameter. The discs were dried and placed on the formerly seeded Petri plates and allowed to incubate at  $35^\circ\text{C}$  for 24 h. The inhibition zone diameter approximately on each disc was calculated in mm and compared with that of the standard antibiotic (Streptomycin), whose antibacterial activity was also determined by the same procedure.

#### Antioxidant activity

##### Hydrogen peroxide scavenging ability

The capability of the copper and nickel complexes to scavenge  $\text{H}_2\text{O}_2$  was analysed by the method [15] developed by Ruch et al. in 1989. A 40 mM  $\text{H}_2\text{O}_2$  solution was prepared in phosphate buffer ( $\text{pH} = 7.4$ ). The concentration of  $\text{H}_2\text{O}_2$  was found out spectro-photometrically (8500 II Biochrom spectrophotometer, Switzerland). The cobalt and nickel complexes (50  $\mu\text{g}/\text{mL}$  solutions in distilled water) were added to a 0.6 mL of  $\text{H}_2\text{O}_2$  solution. Absorbance of  $\text{H}_2\text{O}_2$  at 230 nm was found out after 10 min against a phosphate buffer blank solution without  $\text{H}_2\text{O}_2$  (Table 5). The percentage scavenging activity of hydrogen peroxide by control and compounds was estimated from the following equation:

The percentage scavenging activity of  $\text{H}_2\text{O}_2 = \frac{[A_0 - A_1]}{A_0} \times 100\%$ , where  $A_0$  is the control absorbance and  $A_1$ , is the sample the absorbance.

### RESULTS AND DISCUSSION

#### Characterization of the ligand

The ligand was subjected to elemental analysis on a CHN-O instrument. The experimentally

found out-and calculated percentages of C, H and N were in good agreement, confirming a molecular formula,  $C_8H_{16}N_2O_2$  for the ligand. (Table 1) The ligand electronic spectrum indicated that an intense band at 286 nm (34965

$cm^{-1}$ ) which can be attributed to  $\pi-\pi^*$  transition. Similarly, a band at 436 nm (22935  $cm^{-1}$ ) in the ligand spectrum may be attributed to  $n-\pi^*$  transition. The data are given in the Table 2.

**Table 1: Analytical Data**

Compound (Empirical formula)	% of Yield	Melting point ( $^{\circ}C$ )	Color of the Compound	Anal. Found (Calcu) %					$\mu_{eff}$ (B.M)
				M	C	H	N	S	
$C_8H_{16}O_2N_2$ (LH)	85	110	Off white						
[CuLCl(H <sub>2</sub> O) <sub>3</sub> ]	56	<300	Green	16.9 (18.9)	26.1 (28.6)	4.9 (5.9)	7.9 (8.3)	--	2.12
[CuL(SO <sub>4</sub> ) <sub>1/2</sub> H <sub>2</sub> O]	60	<300	Sky blue	17.9 (18.3)	26.1 (27.5)	4.9 (5.2)	6.9 (8.1)	5.1 (4.6)	1.82
[CuLBr(H <sub>2</sub> O) <sub>3</sub> ]	65	298	Dark red	15.9 (17.8)	25.5 (26.9)	5.2 (5.6)	4.9 (7.8)	--	2.01
[Ni(LH) <sub>2</sub> (SO <sub>4</sub> )H <sub>2</sub> O]	55	275	Light blue	7.5 (8.1)	25.0 (26.8)	4.0 (4.4)	8.1 (7.8)	3.9 (4.4)	2.87
[FeL <sub>2</sub> ClH <sub>2</sub> O]	60	265	Brown	14.0 (12.4)	6.9 (7.5)	40.0 (42)	11.9 (12.4)	--	2.50

**Table 2: UV-Visible spectral data**

Species	Spectral Bands		Assignment
	$\lambda_{max}$ (nm)	( $cm^{-1}$ )	
$C_8H_{16}O_2N_2$ (LH)	286	34965	$\pi \rightarrow \pi^*$ transition
	436	22935	$n \rightarrow \pi^*$ transition
[CuLCl(H <sub>2</sub> O) <sub>3</sub> ]	479	20876	$E_g \rightarrow T_{2g}$
	906	11037	
[CuL(SO <sub>4</sub> ) <sub>1/2</sub> H <sub>2</sub> O]	417	23980	${}^2B_{1g} \rightarrow {}^2E_{2g}$
	572	17482	${}^2B_{1g} \rightarrow {}^2A_{1g}$
[CuLBr(H <sub>2</sub> O) <sub>3</sub> ]	479	20876	$E_g \rightarrow T_{2g}$
	905	11049	
[Ni(LH) <sub>2</sub> (SO <sub>4</sub> )H <sub>2</sub> O]	400	25000	${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(P)$ ( $\gamma_1$ )
	639	15649	${}^3A_{2g}(F) \rightarrow {}^3T_{1g}(F)$ ( $\gamma_2$ )
	1040	9615	${}^3A_{2g}(F) \rightarrow {}^3T_{2g}(F)$ ( $\gamma_3$ )

The ligand IR spectrum showed broad bands of medium intensities at 3295 and 3228  $cm^{-1}$ . They may be due to  $NH_2$  stretching. A band at 3445  $cm^{-1}$  may be due to  $\nu_{OH}$  of water present as an impurity in the sample. The bands at 2967 and 2939  $cm^{-1}$  were due to the symmetric-and asymmetric stretching vibrations of  $CH_2$  group. Sharp bands at 1647 and 1603  $cm^{-1}$  may be due to  $\nu_{C=O}$  and  $\nu_{C=N}$ , respectively. Sharp band at 1258  $cm^{-1}$  was due to the  $\nu_{C-O}$  of ethoxy group. (Table 3)

The ligand  ${}^1H$  NMR spectrum showed a sharp deshielding singlet at 8.6 ppm, which is due to

free  $NH_2$  a proton. There is a singlet at 4.4 ppm which was attributed to the protons of active methylene. The quartet appeared at 4.1 ppm was due to  $CH_2$  protons of the acetyl group and a signal appeared at 3.3 ppm was due to  $CH_3$  protons of the acetyl group. The signals appeared at 2.1 and 1.2 ppm were due to the  $CH_2$  protons adjacent to the amine and imine, respectively. (Table 4)

From the above data, we confirmed that the synthesized product was a Schiff base of the following structure.

**Table 3: IR spectral data (in cm<sup>-1</sup>)**

C <sub>8</sub> H <sub>16</sub> O <sub>2</sub> N <sub>2</sub> (LH)	[CuLCl(H <sub>2</sub> O) <sub>3</sub> ]	[CuL(SO <sub>4</sub> ) <sub>1/2</sub> H <sub>2</sub> O]	[CuLBr(H <sub>2</sub> O) <sub>3</sub> ]	[Ni(LH) <sub>2</sub> (SO <sub>4</sub> )H <sub>2</sub> O]	[FeL <sub>2</sub> ClH <sub>2</sub> O]
3445	3445	3444	3307	3440	3441
3295	3295	3294	--	3295	3188
3228	3228	3227	--	--	3009
2967	--	2968	3005	2966	--
2939	2939	2941	2956	2940	--
2884	2884	2885	2834	2886	2495
1647	1634	1636	1635	1647	1590
1603	1568	1568	1582	1602	1562
1258	1268	1267	1279	1258	--
1116	1124	1116	1172	1116	1134
1001	1015	1036	1007	1029	1006
931	974	972	929	980	970
619	676	619	704	618	811
538	527	525	564	519	--
445	475	471	477	--	--

**Table 4: <sup>1</sup>H NMR data of Schiff base ligand**

Sl.No.	Chemical shift (ppm)	Assignment
1.	4.1	Ethoxy CH <sub>2</sub>
2.	3.3	CH <sub>3</sub> adjacent to the ethoxy group
3.	8.6	NH <sub>2</sub> proton
4.	4.4	Active methylene proton
5.	2.1	CH <sub>2</sub> adjacent to the amine
6.	1.2	CH <sub>2</sub> adjacent to the imine
7.	1.1	CH <sub>3</sub> Proton

**Characterization of the complexes****Cu(II) complexes**

The Cu(II) complexes, [CuLCl(H<sub>2</sub>O)<sub>3</sub>], [CuL(SO<sub>4</sub>)<sub>1/2</sub>H<sub>2</sub>O] and [CuLBr(H<sub>2</sub>O)<sub>3</sub>] were soluble in methanol, ethanol, DMSO, CHCl<sub>3</sub>, diethyl ether, etc. The non-electrolytic nature of the complexes gave the information that the metals were coordinated with the anions in the complexes. The analytical data are given in the Table.1. They are in close confirmation with the proposed compositions of the complexes. The observed magnetic moment for [CuLCl(H<sub>2</sub>O)<sub>3</sub>] and [CuLBr(H<sub>2</sub>O)<sub>3</sub>] were 2.12 and 2.01 B.M. respectively, indicating their distorted octahedral or trigonal bipyramidal structures. The magnetic moment value of [CuL(SO<sub>4</sub>)<sub>1/2</sub>H<sub>2</sub>O] was 1.82 B.M., indicating its square planar structure.

Virtually all the complexes of Cu(II) are blue or green in color. Exceptions are typically due to strong UV bands (charge-transfer bands) tailing

into the blue end of the visible spectrum and thus causing the substance to appear red or brown [16,17]. In the present case, [CuLCl(H<sub>2</sub>O)<sub>3</sub>] and [CuL(SO<sub>4</sub>)<sub>1/2</sub>H<sub>2</sub>O] are green and blue, respectively, which may be due to the presence of an absorption, 600-900 nm range. These Cu(II) complexes registered bands at ~420 and ~600 nm which may be assigned, respectively, to <sup>2</sup>B<sub>1g</sub>→<sup>2</sup>E<sub>g</sub> and <sup>2</sup>B<sub>1g</sub>→<sup>2</sup>B<sub>2g</sub> transitions typical of a distorted octahedral/square planar Cu(II) complex. The energy level diagram for a Cu(II) complex having D<sub>4h</sub> symmetry predicts three vibronically induced transitions viz., <sup>2</sup>B<sub>1g</sub>→<sup>2</sup>A<sub>1g</sub>, <sup>2</sup>B<sub>1g</sub>→<sup>2</sup>B<sub>2g</sub> and <sup>2</sup>B<sub>1g</sub>→<sup>2</sup>E<sub>g</sub>. Mostly, all these transitions occur as a single broad asymmetric envelop in the spectrum. The electronic spectra are, therefore, of not much help in distinguishing planar-and tetragonal configurations of Cu(II) complexes. (Table 2)

The bands around 3295, 3228 and 2967  $\text{cm}^{-1}$  in the IR spectra of the ligand and the complexes account for the NH stretching vibrations. These may be assigned to the asymmetric and the symmetric  $\nu_{\text{N-H}}$  of the  $\text{NH}_2$  group, respectively. In the spectra of the metal complexes new bands were observed around 1124  $\text{cm}^{-1}$ , indicating the enolization of  $-\text{CH}_2-\text{C}=\text{O}$  to  $-\text{CH}=\text{C}-\text{OH}$  and subsequent coordination through the deprotonated oxygen. A band of medium intensity at 1603  $\text{cm}^{-1}$  in the spectrum of ligand may be attributed to  $\nu_{\text{C}=\text{N}}$ . However, in the spectra of all the complexes, this band was found

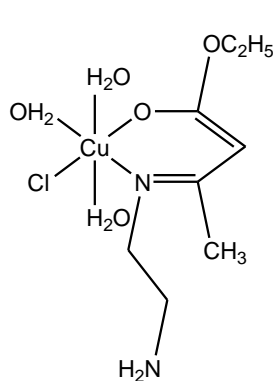


Fig.2:  $[\text{CuLCl}(\text{H}_2\text{O})_3]$

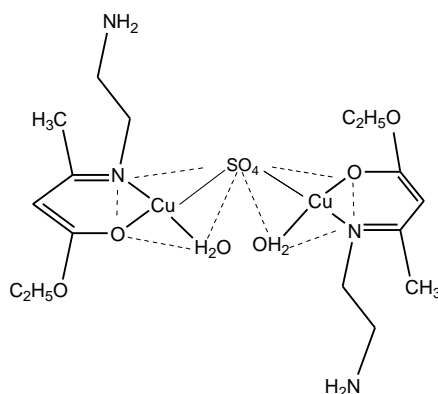


Fig.3:  $[\text{CuL}(\text{SO}_4)_{1/2}(\text{H}_2\text{O})]$

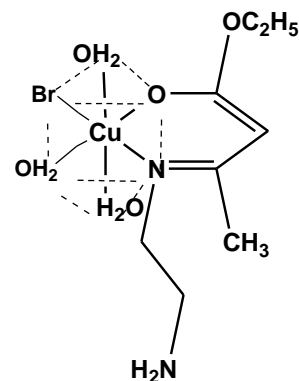


Fig.4:  $[\text{CuLBr}(\text{H}_2\text{O})_3]$

### Ni(II) complex

Data obtained from analytical studies were given in the Table 1, confirm the correct composition of the complex. For octahedral Ni(II) complexes, the magnetic susceptibility values fall in the range 2.60 to 3.30 B.M., due to spin-orbit coupling or higher state mixing with ground state. The Ni(II) complex investigated here registered a magnetic moment value 2.87 B.M., indicating its octahedral geometry. It registered an strong band at  $\sim 400$  nm and two broad spectral bands observed at 630 and 900 nm. These may be, respectively, due to  ${}^2\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{1g}(\text{P})$ ,  ${}^3\text{A}_{2g} \rightarrow {}^3\text{T}_{1g}(\text{F})$  and  ${}^3\text{A}_{2g}(\text{F}) \rightarrow {}^3\text{T}_{2g} \rightarrow {}^3\text{T}_{2g}(\text{F})$  transitions of a typical octahedral complex. (Table 2)

The bands around 3295, 3228 and 2967  $\text{cm}^{-1}$  in the ligand spectrum account for the asymmetric  $\nu_{\text{NH}}$  and the symmetric  $\nu_{\text{NH}}$  of the  $\text{NH}_2$  group. They were observed to be retained almost at the same region in the metal complexes IR spectrum. The band at 1655  $\text{cm}^{-1}$  in the spectrum of ligand was assigned to  $\nu_{\text{C}=\text{O}}$ . A shift of this band to lower frequency by a few  $\text{cm}^{-1}$  was noticed in the spectrum of Ni(II) complex,

to be shifted to a lower frequency region by a few  $\text{cm}^{-1}$ , indicating the participation of azomethine nitrogen in coordination. Broad bands at  $\sim 3500$   $\text{cm}^{-1}$  in the spectra of the complexes were attributed to the hydroxyl stretching modes of water molecules. In addition, strong bands at  $\sim 864-973$  and  $\sim 660$   $\text{cm}^{-1}$  suggested that the water molecules were coordinated[18]. Medium bands around 530 and 450  $\text{cm}^{-1}$  in the spectra all the complexes may be assigned<sup>17</sup> to  $\nu_{\text{(M-N)}}$  and  $\nu_{\text{(M-O)}}$ , respectively. (Table. 3) The data are consist with the following structure of the complexes (Fig. 2 to 4)

showing the coordination of  $\nu_{\text{C}=\text{O}}$  without enolisation. A peak of medium intensity at 1603  $\text{cm}^{-1}$  in the ligand spectrum may be attributed to  $\nu_{\text{(C=N)}}$ . However, in the complex this band was found to be moved to a lower frequency region by a few  $\text{cm}^{-1}$ , representing the participation of azomethine nitrogen in coordination. A broad band at  $\sim 3440$   $\text{cm}^{-1}$  in the spectrum of the complex was assigned to the -OH stretching modes of water molecule. In addition, strong bands at  $\sim 870-980$   $\text{cm}^{-1}$  suggest that the water molecule is coordinated.<sup>17</sup> Medium bands at around 530 and 450  $\text{cm}^{-1}$  in the metal complex IR spectrum may be assigned[20] to  $\nu_{\text{(M-N)}}$  and  $\nu_{\text{(M-O)}}$ , respectively (Table. 3). Based on the above data, we have assigned an octahedral geometry for the Ni(II) complex. (Fig. 5)

### Fe(III) complex

The analytical data are given in the Table 1. It corresponded to the proposed composition of the complex,  $[\text{FeL}_2\text{ClH}_2\text{O}]$ . It registered a magnetic moment of 2.53 B.M. This may be due to either binuclear or low-spin configuration of the complex, facilitating antiferromagnetic exchange

interactions [21].  $[\text{FeL}_2\text{ClH}_2\text{O}]$  registered two bands, one at 340 nm and a broad band at 510 nm. The bands around 3295, 3228 and 2967 $\text{cm}^{-1}$  in the spectra of the ligand and complex account for the asymmetric  $\nu_{(\text{NH})}$  and the symmetric  $\nu_{(\text{NH})}$  of the  $\text{NH}_2$  group. In the spectrum of the complex a new band was observed around 1034  $\text{cm}^{-1}$ , indicating the enolization of  $-\text{CH}_2-\text{C}=\text{O}$  to  $-\text{CH}=\text{C}-\text{OH}$  and subsequent coordination through the deprotonated oxygen. A band of medium intensity at 1603  $\text{cm}^{-1}$  in the spectrum of ligand may be assigned to  $\nu_{(\text{C}=\text{N})}$ . However, in the Fe(III) complex IR spectrum, this band was observed to

be moved to a lower frequency area by a few  $\text{cm}^{-1}$ , indicating the contribution of azomethine nitrogen in coordination. A broad peak at  $\sim 3411 \text{ cm}^{-1}$  of the complex was due to the  $-\text{OH}$  stretching mode of water molecule. In addition, strong bands at  $\sim 811-970 \text{ cm}^{-1}$  suggested that the water molecule was coordinated [19]. Medium bands around 530 and 450  $\text{cm}^{-1}$  in the complex may be assigned [19,20] to  $\nu_{(\text{M}-\text{N})}$  and  $\nu_{(\text{M}-\text{O})}$ , respectively. (Table. 3) All the above data are consistent with the proposed structure of the complex (Fig 6).

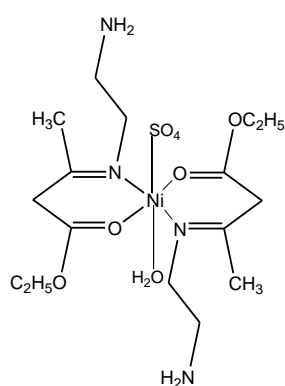


Fig.5  $[\text{Ni}(\text{LH})_2(\text{SO}_4)\text{H}_2\text{O}]$

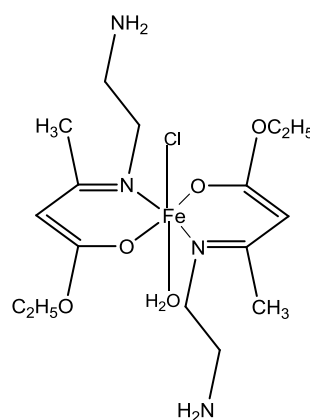


Fig.6  $[\text{FeL}_2\text{ClH}_2\text{O}]$

## Bioactivity

### Antimicrobial activity

The antimicrobial activity of the ligands and their Fe(II), Ni(II) and Cu(II) complexes against pathogenic fungi and bacteria. As seen, the Schiff bases possess biological activity and the antifungal and antimicrobial activity of their metal complexes against microbial strains is significantly higher compared to the ligands. The fungicidal and bacterial activities increase with increasing concentration. Thus, it is evident that the concentration plays a vital role in enhancing the degree of inhibition. The enhanced activity of the synthesized complexes, as compared to the activity of the ligands, may be explained in terms of the Overtone's concept and Tweedy's chelation theory [22, 23]. According to the Overtone's concept, a lipid membrane surrounding the cell facilitates the passage of substances that dissolve in lipids. Therefore, the liposolubility is an important factor to control antimicrobial activity. On the chelation, the polarity of the metal ion is

reduced to a larger extent owing to overlapping of the ligand orbitals and a partial sharing of the positive charge of the metal ion with the charge of the donor groups. (Table 5, 6 & 7).

Moreover, delocalization of  $\pi$ -electrons over the entire chelate ring is higher and lipophilicity of the complexes is enhanced. Owing to increased lipophilicity, the complexes can easily penetrate into a lipid membrane and block the metal binding sites in enzymes of microorganisms.

### Antioxidant activity

$\text{H}_2\text{O}_2$  is highly important because of its capability to penetrate into biological membranes systems.  $\text{H}_2\text{O}_2$  itself is not potent reactive to biological cell membrane, but it can sometimes be toxic to cell due to it may give rise to hydroxyl radicals ( $\text{OH}^*$ ) in the cells. Scavenging of  $\text{H}_2\text{O}_2$  by samples may be attributed to their donation capacity of electrons to  $\text{H}_2\text{O}_2$ , thus neutralizing it to water. The results show (Table 8) the all the complexes had potent  $\text{H}_2\text{O}_2$  scavenging activity which may be

due to the antioxidant compounds. As the antioxidant components present in the Schiff base metal complexes are good electron donors, they may speed up the conversion of H<sub>2</sub>O<sub>2</sub> to H<sub>2</sub>O.

**Table 5: Inhibition zones (mm) of complexes and ligand against bacterial strains**

Compounds	Bacteria (D* mm)	
	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>
C <sub>8</sub> H <sub>16</sub> O <sub>2</sub> N <sub>2</sub> (LH)	8	6
[FeL <sub>2</sub> ClH <sub>2</sub> O]	14	11
[Ni(LH) <sub>2</sub> (SO <sub>4</sub> )H <sub>2</sub> O]	--	11
[CuLBr(H <sub>2</sub> O) <sub>3</sub> ]	15	10
Ampicilin	14	--
Choloramphenicol	13	8
Imipeneme	20	--
DMSO	--	--

\* (D) Diameter inhibition zone (in mm).

**Table 6: Minimum Inhibition Concentration, mg/ml**

Compounds	Bacteria (D* mm)	
	<i>Staphylococcus aureus</i>	<i>Pseudomonas aeruginosa</i>
C <sub>8</sub> H <sub>16</sub> O <sub>2</sub> N <sub>2</sub> (LH)	2.50	5.00
[FeL <sub>2</sub> ClH <sub>2</sub> O]	0.15	2.50
[Ni(LH) <sub>2</sub> (SO <sub>4</sub> )H <sub>2</sub> O]	0.61	1.25
[CuLBr(H <sub>2</sub> O) <sub>3</sub> ]	0.65	1.25

**Table 7: Antifungal Studies of ligand and metal complexes**

Compounds	Fungi , % Inhibition (growth diameter in mm)	
	<i>Fusarium semitectum</i>	<i>A. Flavus</i>
Emcarb*	(00)100	(00)100
Bavistin*	(00)100	(00)100
DMSO (control)	(21)29	(32)40
C <sub>8</sub> H <sub>16</sub> O <sub>2</sub> N <sub>2</sub> (LH)	(12)15	(15)19
[FeL <sub>2</sub> ClH <sub>2</sub> O]	(23)24	(15)25
[Ni(LH) <sub>2</sub> (SO <sub>4</sub> )H <sub>2</sub> O]	(19)28	(17)23
[CuLBr(H <sub>2</sub> O) <sub>3</sub> ]	(20)32	(24)39

\*standard fungisides

**Table 8: Percentage of H<sub>2</sub>O<sub>2</sub> Scavenging activity**

Samples	% of H <sub>2</sub> O <sub>2</sub> Scavenging activity (100 µg/L)
[CuLCl(H <sub>2</sub> O) <sub>3</sub> ]	32.11
[CuLBr(H <sub>2</sub> O) <sub>3</sub> ]	30.40
[Ni(LH) <sub>2</sub> (SO <sub>4</sub> )H <sub>2</sub> O]	37.98
BHA	45.26
α-tocopherol	67.15

BHA= Butylatedhydroxyanisole



## CONCLUSION

Coordination complexes of Fe(III), Ni(II) and Cu(II) with a multi-dentate ligand, ethyleneamino-imine(ethylacetoacetate) (LH) have been prepared and their physico-chemical properties have been studied. The complexes have the formulae,  $[\text{CuLCl}(\text{H}_2\text{O})_3]$ ,  $[\text{CuL}(\text{SO}_4)_{1/2}\text{H}_2\text{O}]$ ,  $[\text{CuLBr}(\text{H}_2\text{O})_3]$ ,  $[\text{Ni}(\text{LH})_2(\text{SO}_4)\text{H}_2\text{O}]$  and  $[\text{FeL}_2\text{ClH}_2\text{O}]$ . Based on the magnetic measurements and various spectral studies, geometries have been assigned to these complexes.  $[\text{CuL}(\text{SO}_4)_{1/2}\text{H}_2\text{O}]$  complex was found to be square planar-and dimeric. All the other metal complexes were found to be distorted octahedral. The metal complexes have significantly enhanced antibacterial and antifungal activity against microbial strains in comparison with free ligands. Thus, they may find application as a new antimicrobial agent after further study of their biological properties. The study of the antioxidant activity showed that the Ni(II) Schiff base complexes are better antioxidants than Cu(II) complexes.

## CONFLICTS OF INTEREST

The authors declare that there is no conflict of interests regarding the publication of this paper.

## ACKNOWLEDGEMENT

The authors are thankful to SAIF Cusat, Kochin for providing the CHN analysis and spectral data.

## REFERENCES

1. Busch DH. Distinctive coordination chemistry and biological significance of complexes with macrocyclic ligands. *Acc Chem Res* 1978; 4(11): 392-396
2. Lindoy LF. Transition metal complexes of synthetic macrocyclic ligands. *Chem Soc Rev* 1975; 6(4) 421-427
3. Holm H, Evertte GW, Chakrovorty. Metal complexes of Schiff bases and  $\beta$ -ketoamines. *Prog Inorg Chem* 1966; 3(7): 183-214.
4. Lindoy LF, Livngstone SE. Reactions of nickel chelates derived from 2-aminobenzenethiol. *Inorg Chem* 1968; 6(7): 1149-1150.
5. Lions F, Mastin KV. Tridentate chelate compounds I. *J Amer Chem Soc* 1957; 79(11): 2733-2738.
6. Dwyer FP, Gill NS, Gyrfas EC, Lions F. The Resolution of a Bis-Tridentate Iron(II) complex. *J Amer Chem Soc* 1957; 75(15): 3834-3835.
7. Nelson SM. Development in the synthesis and coordination chemistry of macrocyclic Schiff base ligands. *Pure & Appl Chem* 1980; 52(2): 2461-2476.
8. Curtis NF. Macrocyclic coordination compounds formed by condensation of metal-amine complexes with aliphatic carbonyl compounds. *Coord Chem Rev* 1968; 233(3): 3-47.
9. Lindoy LF. Metal ion control in the synthesis of Schiff base complexes. *Quart Rev* 1971; 25(11): 379-382.
10. Thompson MC, Busc DH. Reaction of coordinated ligands. II Nickel(II) complexes of some Novel Tetradentate Ligands. *J Amer Chem Soc* 1962; 5(84): 1762-1763.
11. Shannon RD. Revised effective ionic radii and systematic studies of interatomic distances in halides and chalcogenides. *Acta Cryst* 1976; 56(A32): 751-756.
12. Rafel M. El-Shazly, Magdy MB, Fatma LT. Spectral and magnetic studies of polynuclear copper(II) complexes of Schiff base derived from ethylenediamine and ethyl-acetoacetate. *Transition. Met Chem* 1990; 15(2): 337.
13. Dyer G, Venanzi LM. The visible and Ultraviolet spectra of triogonal bipyramidal complexes of nickel(II), palladium(II) and platinum(II). *J Chem Soc* 1965; 11(14): 2771-2778
14. Eanshaw. *Indroduction to Magneto-chemistry*. London and Newyork: Academic Press; 1968, p 355.
15. Ruch RJ, Cheng SJ, Klaunig JE. Prevention of cytotoxicity and inhibition of intracellular communication by antioxidant catechins isolated from Chinese green tea. *Carcinogenesis* 1989; 5(10): 1003-1008.
16. Waters TN, Hall D. The colour isomerism and structure of some copper co-ordination compounds. Part.II Absorption spectra of solid. *J Chem Soc* 1959; 23(11): 1203-1205.
17. Waters JM, Waters TN. The colour isomerism and structure of some copper co-ordination compounds. Part.IV. The visible absorption spectra of copper complexes. *J Chem Soc* 1964; 9(11): 2489-2492.

- 
18. Nakamoto K. Infrared spectra and Raman spectra of Inorganic and Coordination Compounds. New York: John Wiley; 1978, p 357.
  19. Bellamy LJ. The Infrared spectra of Complex Molecules. London: Chapman and Hall; 1980, p 255.
  20. Bellamy LJ. Advances in Infrared group frequencies. London: Methuen; 1968, p 137.
  21. Dutta RL, Syamal A. Elements of Magnetochemistry. New Delhi: Affiliated East-West Press; 1993, p 245.
  22. Tweedy BG. Plant extracts with metal ions as potential antimicrobial agents. *Phytopathol* 1964; 2(55): 910-914.
  23. Droge W. Free radical in the physiological control of cell function. *Physiol. Rev* 2002; 6(82): 47-95.

**Cite this article as:**

K. Subin Kumar, K. K Aravindakshan. Synthesis, Characterization Antimicrobial and Antioxidant Studies of Complexes of Fe(III), Ni(II) and Cu(II) with Novel Schiff Base Ligand (E)-Ethyl 3-((2-Aminoethyl)Imino)Butanoate. *J Pharm Chem Biol Sci* 2017; 5(3):177-186