

# SYNTHESIS AND SPECTRAL CHARACTERIZATION OF ANTIMICROBIAL ACTIVITY OF THE BINUCLEAR Co(II), Ni(II), Cu(II) AND Zn(II) COMPLEXES OF A NOVEL MACROCYCLIC BIPHENYL BRIDGED SCHIFF BASE LIGAND

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## ABSTRACT

A novel macrocyclic Schiff base ligand was synthesized by reacting 4-(4-aminophenoxy)benzenamine with 2,6-diformyl-4-methyl phenol and a series of metal complexes with this new Schiff base was synthesized by reaction with Co(II), Ni(II), Cu(II) and Zinc(II) metal salts. The Schiff base and its complexes have been characterized by elemental analysis, IR, <sup>1</sup>H NMR, UV-vis, ES<sup>+</sup> mass, ESR spectra, fluorescence, thermal, magnetic and molar conductance data. The analytical data reveal that the Co(II), Ni(II), Cu(II) and Zn(II) complexes possess 1:1 metal-ligand ratios. All the complexes are non-electrolytes in DMF and DMSO due to their low molar conductance values. Infrared spectral data suggest that the azomethanine Schiff base behaves as a hexadentate ligand with NON donor sequence towards the metal ions. The ESR spectral data of copper complexes show that the metal-ligand bond has considerable covalent character. The electrochemical behavior of the copper (II) complex was investigated by cyclic voltammetry. The Schiff base and its complexes have also been screened for their antibacterial (*Escherichia coli*, *Staphylococcus aureus*, *Shigella dysentery*, *Micrococcus*, *Bacillus subtilis*, *Bacillus cereus* and *Pseudomonas aeruginosa*) and antifungal activities (*Aspergillus niger*, *Penicillium* and *Candida albicans*) by MIC method.

**Key words:** Metal(II) Schiff base complexes, Magnetic Susceptibility, ESR, Cyclic Voltametry, Antimicrobial activity.

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## INTRODUCTION

Biphenyl bridged ligands are a special group of compounds in the Schiff base family. More recently, they have been extensively used in detection and determination of several metals. They also find applications as indicators and spot test reagents.<sup>1</sup> Recently, a number of attempts have been made to obtain Cu(II), Ni(II), Co(II) and Zn(II) complexes with bis biphenyl bridged azomethanine formed by condensation of with 2,6-diformyl-4-methyl phenol, which have been well characterized, Co(II), Ni(II), Cu(II), and Zn(II) complexes have been synthesized by the condensation of diphenyaldiamine ether complexes have been synthesized from the bis-Schiff bases of 2,6-diformyl-4-methyl phenol.<sup>3</sup> All these compounds have been characterized by elemental analyses, magnetic, thermal, IR, <sup>1</sup>H NMR, UV-vis, ESR and spectral data.<sup>2</sup> This Schiff base has donor sites with the NON sequence and varied coordination abilities as Scheme-1. These are also evaluated for their antibacterial and antifungal properties against various pathogenic bacterial strains using the minimum inhibitory concentration method.

## EXPERIMENTAL

### Materials and Methods

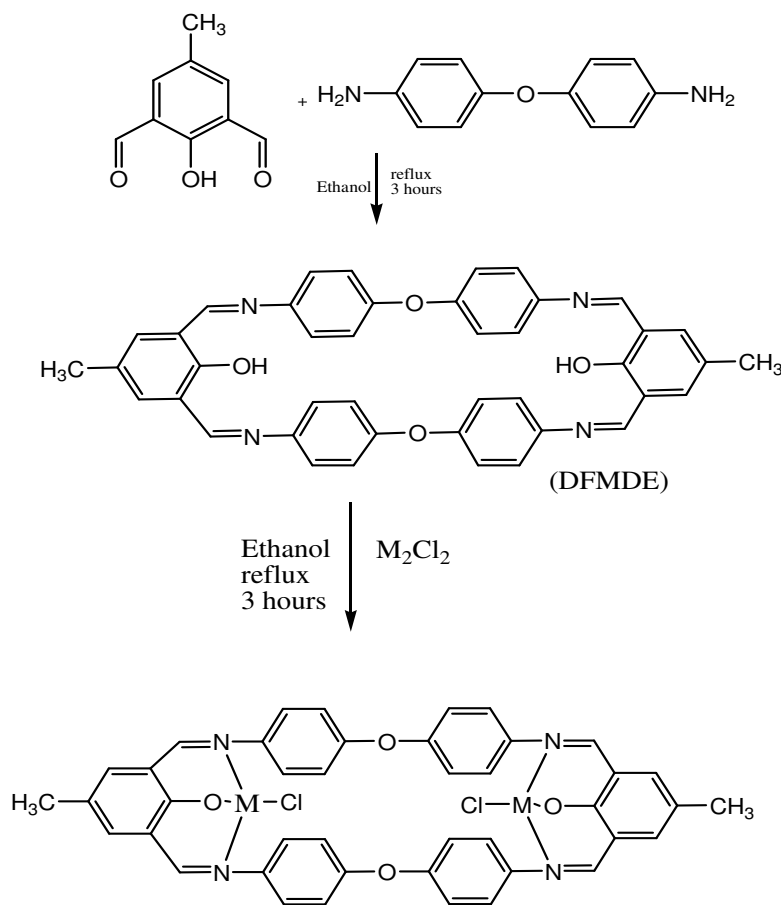
All reagents and solvents were of analytical grade and used without further purification. 2, 6-diformyl-4-methyl phenol was prepared in the same manner as reported in the literature.<sup>4-6</sup>

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### Physical Measurement

$^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker DPX FT-NMR spectrometer; using TMS as an internal reference at room temperature operating at 400 MHz. Infrared absorption spectra ( $4000\text{--}400\text{cm}^{-1}$ ) were obtained from a JASCO FT/IR-5300 spectrometer. Mass spectra ( $\text{ES}^+\text{-MS}$ ) were determined on Perkin Elmer (SCIEX API- 2000, ESI) at 12.5 eV. Carbon, nitrogen and hydrogen elemental analyses were performed on an LECO CHNS-932 analyzer. Melting points were determined on DSC Model: Q 10 TA Instruments. Thermal analyses of these samples were performed on a Thermal Advantage DSC Q2000 V 9.8 Build 296 (TA Instrument, USA) module which was calibrated for temperature and cell constants using indium and sapphire. Electrochemical instrumental model: CHI660C. The magnetization studies were carried out at temperatures ranging from 5 to 300K, in applied fields of up to 10 kOe with a Quantum Design Physical Properties Measurement System. A JEOL JES PE 3X model spectrometer was used for running the ESR spectra.



**Scheme 1 :**  $\text{M}_2(\text{DFMDE})\text{X}_2$

$\text{M} = \text{Co(II)}, \text{Ni(II)}, \text{Cu(II)}$  and  $\text{Zn(II)}$

$\text{X} = \text{Cl}$

### Synthesis of Macrocyclic Schiff base ligand

2,6-Diformyl-4-methylphenol (2 mmol) in methanol (20 mL) was added to a methanolic solution of 4-(4-aminophenoxy)benzenamine (2 mmol, 30 mL). The reaction mixture was refluxed for 3 hours. The mixture was cooled to room temperature and the solvent removed under reduced pressure until a solid product was formed that was washed with cold ethanol and dried under vacuum. Yield 70–75%. M.P:  $336.83^\circ\text{C}$ :  $^1\text{H}$  NMR ( $\text{CDCl}_3$ , 400 MHz):  $\delta$  7.77 (2H, s, benzene),  $\delta$  2.39 (3H, s, methyl),  $\delta$  11.45 (1H, s, aldehyde),  $\delta$  10.21 (2H, s, aldehyde).  $^{13}\text{C}$  NMR ( $\text{CDCl}_3$ , 100 MHz):  $\delta$  163.30, 159.55, 155.35, 133.58, 131.58, 128.39, 119.58, 20.3 MS- $\text{ES}^+$ :  $m/z$  657  $[\text{M}+\text{H}]^+$ , IR (KBr) in  $\text{cm}^{-1}$ : 3036, 1624, 1354, UV-visible ( $\text{CHCl}_3$ ): 380.5 nm 503.5.

### Synthesis of Co(II), Ni(II), Cu(II) and Zn(II) complexes

A mixture of ligand (0.01 mol) and metal chloride (0.02 mol) was refluxed for an hour in alcohol. To the reaction mixture sodium acetate (0.02 mol) in water was added and the reflection was continued for another 2h. The complex was precipitated by adding distilled water. The complex separated was filtered, washed with water, then with hot alcohol and finally dried in vacuum desiccators over P<sub>2</sub>O<sub>5</sub> (Yield 60-70%).

### Biological activities

The In-vitro Antibacterial and Antifungal Assays of the newly synthesized Schiff base and its metal complexes have been studied for their antibacterial and antifungal activities by disc diffusion method.<sup>7,8</sup> The antibacterial activities were done by using the following organisms (Escherichia coli, Staphylococcus aureus, Shigella dysentery, Micrococcus species, Bacillus subtilis, Bacillus cereus and Pseudomonas aeruginosa).

## RESULTS AND DISCUSSION

Physical characteristics, micro analytical and magnetic susceptibility data of the complexes are given in Table-1. The analytical data of all the complexes correspond to the general formula M<sub>2</sub>L<sub>2</sub>X<sub>2</sub>. Magnetic susceptibility values of the complexes at room temperature are consistent with square-planar geometry around the central metal ions. The chelates show no appreciable conductance, and this supports the hypothesis of their neutral nature.

### <sup>1</sup>H NMR spectra

The <sup>1</sup>H NMR and <sup>13</sup>C-NMR spectrum of the ligand assigned to the enolic OH, phenyl, groups protons respectively. In the <sup>1</sup>H-NMR and <sup>13</sup>C-NMR spectrum of Zn(II) Complex in CDCl<sub>3</sub> as shown Fig. 1&2, the zinc complex, the enolic, OH proton signal is found to be absent, confirming deprotonation and its subsequent involvement in coordination.<sup>10-11</sup>

### IR spectra

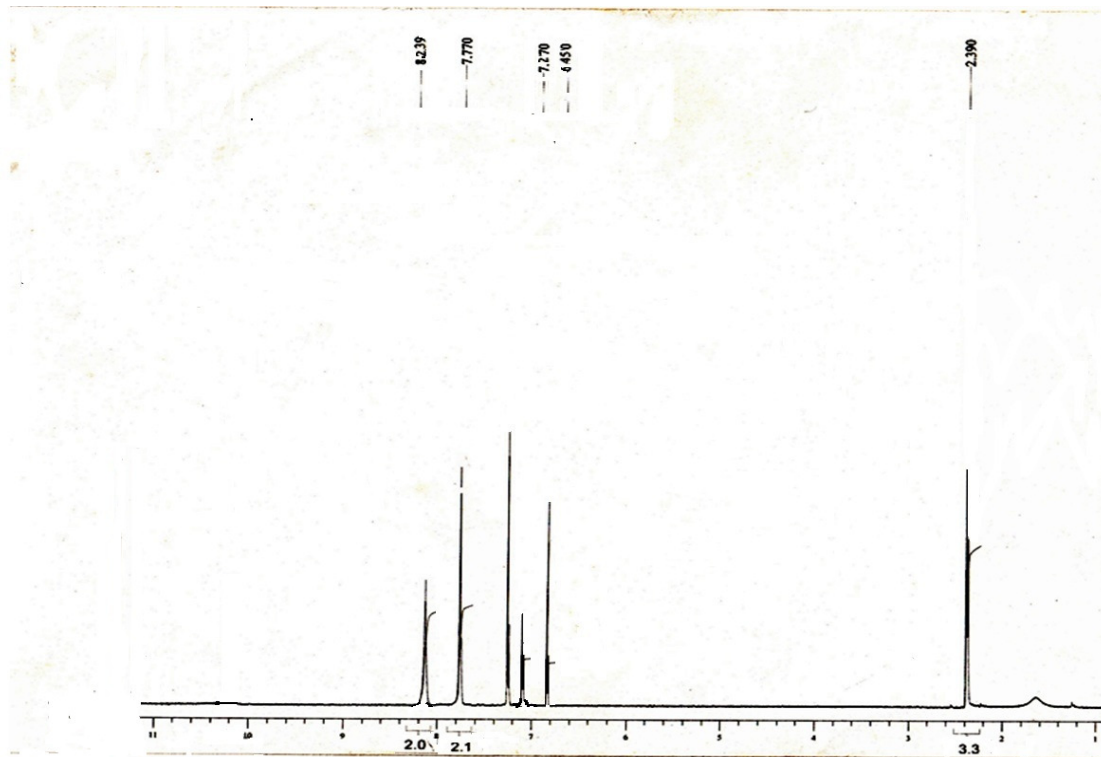


Fig.-1: <sup>1</sup>H-NMR Spectrum of Zn<sub>2</sub>(DFMDE)Cl<sub>2</sub>

Table-1: Physical, Analytical and Magnetic data of the Biphenyl Bridged Schiff base M(II) Complexes

Compound	Mol. Formula (mol.weight)	Color	M. P Decomposition demp( <sup>0</sup> C)	Elemental analysis Calculated(found)				% Yield	Magnetic Susceptibili ty $\mu_{\text{eff}}$ B. M
				% C	% H	% N	% M		
DFMDE	C <sub>42</sub> H <sub>32</sub> N <sub>4</sub> O <sub>4</sub> (656.73)	Brick red	336.01	76.81 (76.78)	4.91 (4.93)	8.53 (8.52)	-	90	-
[Zn <sub>2</sub> (DFMDE)Cl <sub>2</sub> ]	Zn <sub>2</sub> C <sub>42</sub> H <sub>30</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>4</sub> (856.4)	Yellow	384.38	58.90 (58.35)	3.53 (3.54)	6.54 (5.64)	15.27 (15.10)	87	-
[Cu <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	Cu <sub>2</sub> C <sub>42</sub> H <sub>30</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>4</sub> (852.71)	Black	363.81	59.16 (58.98)	3.55 (3.60)	6.57 (6.28)	14.90 (14.01)	89	1.70
[Ni <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	Ni <sub>2</sub> C <sub>42</sub> H <sub>30</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>4</sub> (843)	Pale Green	484.48	59.84 (59.50)	3.59 (3.79)	6.65 (5.53)	13.92 (13.15)	70	2.72
[Co <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	Co <sub>2</sub> C <sub>42</sub> H <sub>30</sub> Cl <sub>2</sub> N <sub>4</sub> O <sub>4</sub> (843.43)	Orange	481.61	59.84 (58.35)	3.59 (3.92)	6.65 (6.64)	13.92 (13.01)	82	5.21

Table-2: Important IR freq. with assignment of M(II) metal complexes

Compound	IR spectra (cm <sup>-1</sup> )					
	$\nu(\text{O-H})$	$\nu(\text{C-H})$	$\nu(\text{C=N})$	$\nu(\text{C-O})$	$\nu(\text{M-N})$	$\nu(\text{M-O})$
DFMDE	3450	3042	1616	1240	484	422
[Zn <sub>2</sub> (DFMDE)Cl <sub>2</sub> ]	-	3024	1616	1188	589	418
[Cu <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	-	3034	1616	1211	555	447
[Ni <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	-	3030	1618	1205	518	434
[Co <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	-	3034	1616	1211	565	424

The FTIR spectra of some representative complexes relevant spectral data are given in Table-2. The spectra of the ligands display sharp peaks characteristics of the C=N bond at 1624-1618  $\text{cm}^{-1}$ . The complexes exhibit a shift to a lower frequency (1602-1616  $\text{cm}^{-1}$ ) this is with the coordination of the imino nitrogen to the metal ion. The band observed for the complexes in the region 505–553  $\text{cm}^{-1}$  is attributed to (M-phenolic O) and that in the region 434– 489  $\text{cm}^{-1}$  to (M–N). All the IR data suggest that the metal is bonded to the Schiff bases through the phenolic oxygen and imino nitrogen.<sup>12-16</sup>

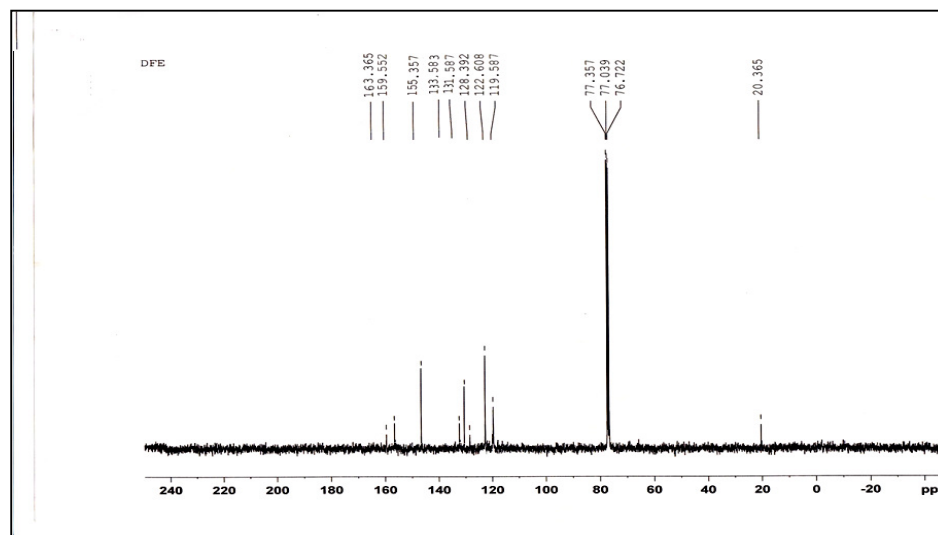


Fig.-2:  $^{13}\text{C}$ -NMR Spectrum of  $\text{Zn}_2(\text{DFMDE})\text{Cl}_2$

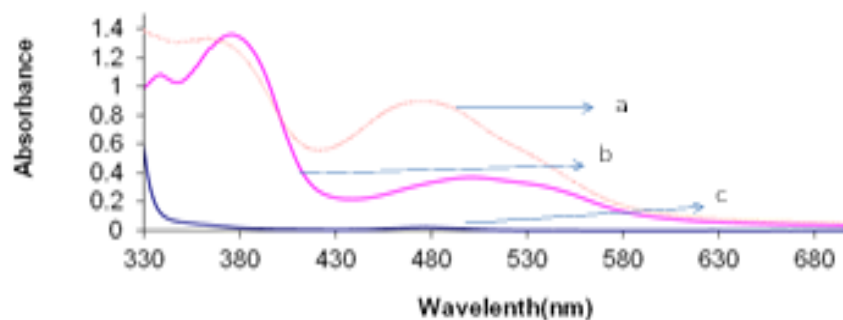


Fig.-3: Electronic spectrum of (a) complex of  $\text{Cu}_2(\text{DFMDE})\text{Cl}_2$ , (b) ligand of DFDMDE, (c)  $\text{CuCl}_2$  of ( $C_0 = 4 \times 10^{-5} \text{ M}$ ) in DMF solution

### Electronic spectral studies

The Cu(II) complex exhibited a high-intensity band at 480  $\text{cm}^{-1}$  in the UV region as in Fig.-3. The appearance of this band is due to  $\pi\text{-}\pi^*$  transition associated with the azomethine linkage and L→M charge transfer transition. The Cu(II) and Ni(II) complex may be suggested to the geometry is trigonal bipyramidal. The Co(II) and Zn(II) complexes may be suggested to the geometry is tetrahedral geometry as shown in the relevant spectral data in Table-3.<sup>17-18</sup>

### Magnetic susceptibility studies

The magnetic moments of the Co(II), Ni(II) and Cu(II) complexes obtained at room temperature are listed in Table-1. The Co(II) and Ni(II) complexes showed magnetic moment values around 5.21 and 2.72 BM, respectively, which are lower than the respective spin values only and indicates weak antiferromagnetic coupling interaction between the metal ions which further confirm the dinuclear

nature of the complexes. The Cu(II) complex showed a magnetic moment around 1.70 BM which is considerably lower than the spin only value for Cu(II) complexes.

Table-3: Electronic spectral data of M(II) metal complexes

Compound	Electronic data in DMF	
	$\lambda_{\max}$ (nm)	$(\nu)$ ( $\epsilon_{\max}, M^{-1}cm^{-1}$ )
DFMDE	440.5(22,727)	(28,250)
	323(30,959)	(59,975)
[Zn <sub>2</sub> (DFMDE)Cl <sub>2</sub> ]	443(22,573)	(16,235)
	322(21,250)	(31,055)
[Cu <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	481.5(79,002)	(14,750)
[Ni <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	404(47,524)	(54,250)
	322(31,061)	(59,320)
[Co <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	399.5(25,626)	(35,250)
	326(25,250)	(30,674)

The low value of the magnetic moment is attributed to the antiferromagnetic coupling interaction between two metal ions. This fact suggests the dinuclear nature of the Cu(II) complexes magnetic susceptibility data were obtained for Cu<sub>2</sub>(DFMDE)Cl<sub>2</sub> from 4.5 to 300k, and fitted to the modified Langevin in dimer equation. The fit was excellent, yielding the following values for the magnetic parameters: J = 20 cm<sup>-1</sup>, g = 2.15 and  $\theta = -2.06$  k. The compound possesses a triplet ground state with a singlet state 20 cm<sup>-1</sup> as shown in Fig -5. The experimental data are shown as open circles and the lines represent the theoretical values obtained using the modified Langevin equation.<sup>19</sup>

$$\chi = \frac{N g^2 \beta^2}{3k(T - \theta)} \left(1 + \left(\frac{1}{3}\right) \exp[-2J/kT]\right)^{-1}$$

and the values of  $2J = +20$  cm<sup>-1</sup>, g = 2.15 and  $\theta = -2.06$  k. The calculations were carried out with matlab programs written by us for a windows 7 computer.

### ESR studies

The 77k temperature liquid state ESR spectra of the Cu(II) complex in Fig.-4 show  $d_{x^2-y^2}$  as a ground state, suggesting distorted octahedral or tetrahedral geometries around M(II) centers. The molar conductance measurements proved that the complexes are non-electrolytes. The solution ESR spectra do not resolve the electron-nuclear spin coupling of the Cu(II) complexes. Computer simulation has been used to obtain the tensorial values of  $g_{\parallel}$ ,  $g_{\perp}$  and  $g_0$  those of  $A_{\parallel}$ ,  $A_{\perp}$  and  $A_0$  as shown in Table-4.

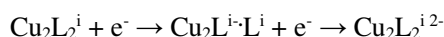
Table-4: ESR Spectral data of Cu(II) complex

Compound	$g_{\parallel}$	$g_{\perp}$	$g_0^a$	$g_{iso}^b$	$A_{\parallel}$	$A_{\perp}$	$A_0$	$A_{iso}^c$
[Cu <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	2.04	2.04	2.04	2.32	11	53	39	24

a:  $g_0 = 1/3(g_{\parallel} + 2g_{\perp})$ ; b: room temperature (DMF solution); c:  $A_0 = 1/3(A_{\parallel} + 2A_{\perp})$

### Cyclic Voltammetry

The Cu(II) analogous of Cu<sub>2</sub>(DFMDE)Cl<sub>2</sub> also exhibit both cathodic as well as anodic electron transfer characteristics. In Fig.-6, is shown a typical cyclic voltammogram. Though the nonaqueous (DMF) electrochemical response of Cu<sub>2</sub>(DFMDE)Cl<sub>2</sub> on the cathodic region on solid electrodes is either reversible (GCE) For want of hydrogen ion the reduction of the azomethine moiety must be involving free radical mechanism as:



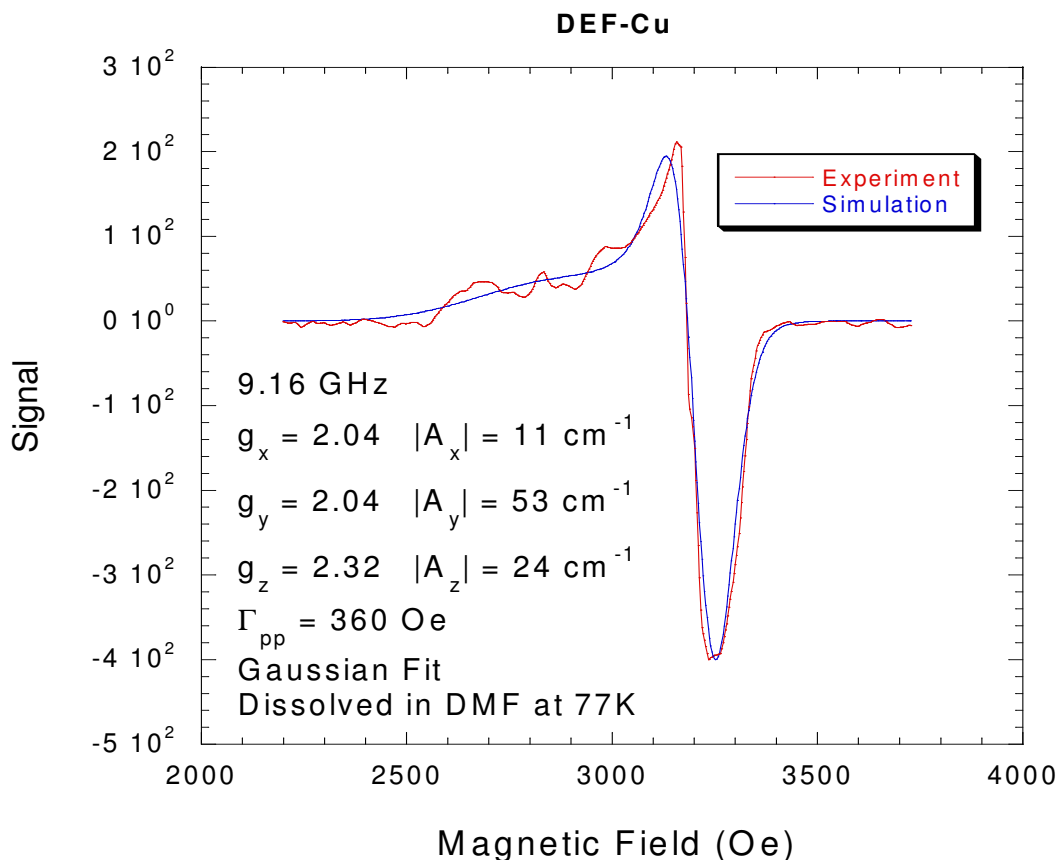


Fig.-4: Experimental and simulated EPR spectra of  $[\text{Cu}_2(\text{DFMDE})\text{Cl}_2]$  complexes in DMF solution at 77K temperature

Usually, reduction of organic unsaturated sites on mercury electrode with free radical mechanism occurs by adsorptive manner. The linearity of  $i_p$  vs  $v$  supports an adsorption complicated reduction of the azomethine sites.<sup>20-22</sup>

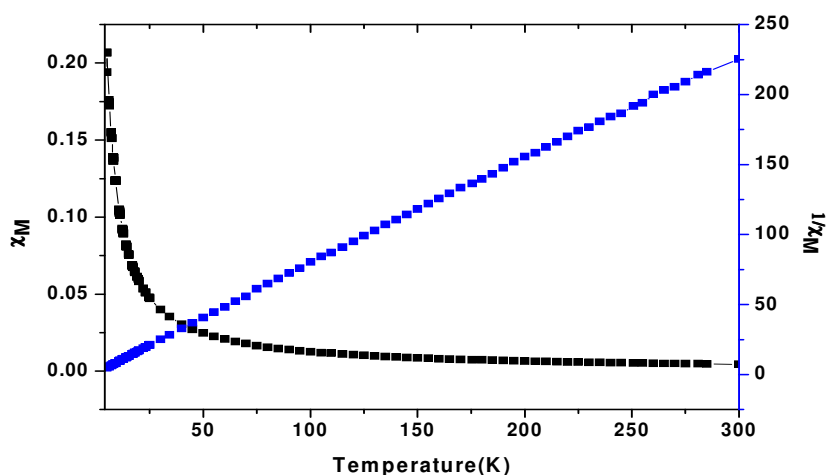


Fig.-5: Variable temperature of magnetic susceptibility curves of  $\text{Cu}_2(\text{DFMDE})\text{Cl}_2$  complex

### Biological studies

The microbial results of Schiff base and its Co(II), Ni(II), Cu(II) and Zn(II) complexes are systematized in Table-5. The biological activity of the Schiff base exhibited a considerable enhancement on coordination with the metal ions against all fungal strains. However, the metal

complexes showed good antifungal activity against *A. niger*, *Penicillium* and *C. albicans* as shown in Figures-7 and 8.<sup>9</sup>

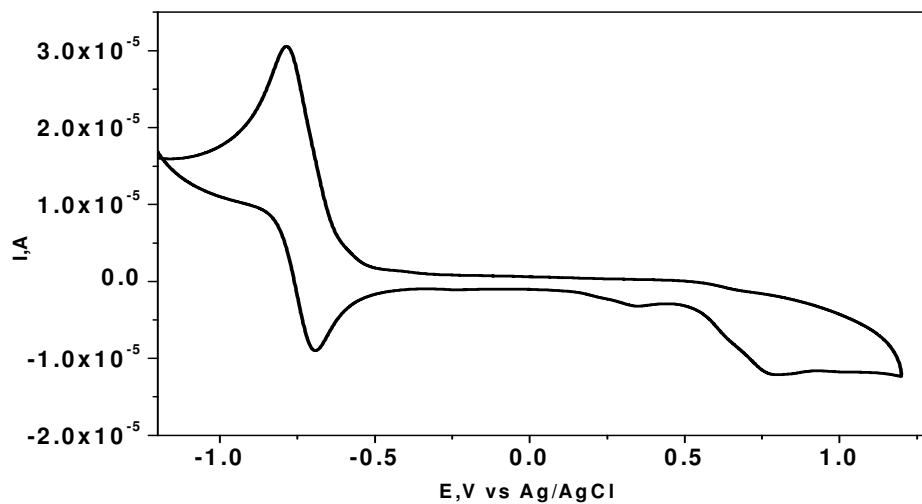


Fig.-6: Cyclic Voltammogram spectrum of  $\text{Cu}_2(\text{DFMDE})\text{Cl}_2$  complex scan rate 0.1 V

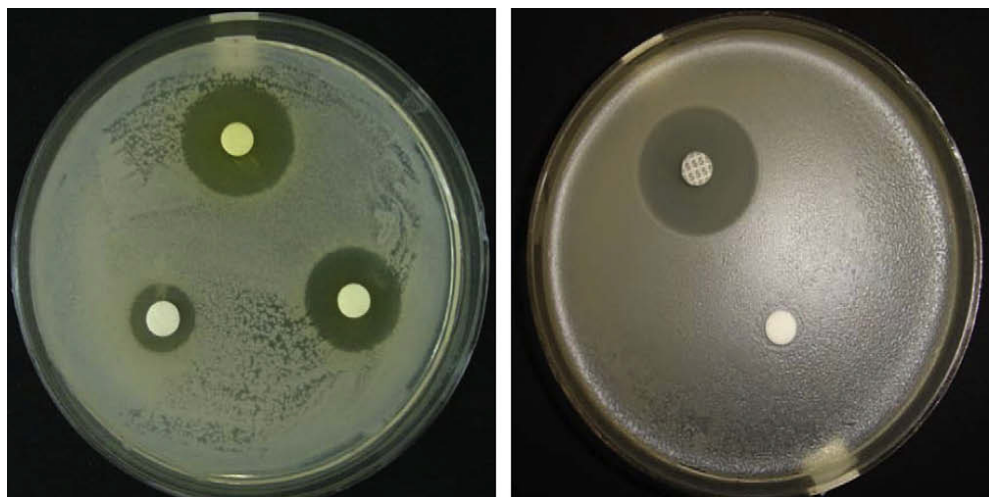


Fig.-7: Photograph (*Bacillus subtilis*) showing antibacterial screening of Schiff base and Gentamycin



Fig.-8: Photograph (*A. niger*) showing antifungal screening of Schiff base and Fluconazole



Table-5: Bacteriological results of Schiff base and its Co(II), Ni(II), Cu(II) and Zn(II) complexes at 10 mg mL<sup>-1</sup> concentration

Compound	Activity against bacteria (mm)							Activity against bacteria (mm)		
	E.coli	P. aeruginasa	b. cereus	s. aureus	s. dysentery	Micrococcus	b. subtilis	A. nigar	Pencillium	c. albicans
DFMDE	18	16	18	12	16	15	20	22	20	18
[Zn <sub>2</sub> (DFMDE)Cl <sub>2</sub> ]	12	14	10	16	12	10	14	18	20	20
[Cu <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	14	16	12	18	14	12	16	20	22	22
[Ni <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	16	14	16	12	18	18	18	22	20	20
[Co <sub>2</sub> (DFMDE)(Cl) <sub>2</sub> ]	12	18	18	14	16	14	14	22	20	20
Gentamycin	22	22	22	22	22	22	22	-	-	
Fluconazole	-	-	-	-	-	-	-	26	26	26
DMF	14	14	14	14	14	14	14	14	14	14

### CONCLUSION

The newly synthesized compound acts as hexadentate Schiff base ligand. The metals are coordinated to azomethine nitrogen and phenolic oxygen atoms. The analytical, spectral, and magnetic, studies confirm the bonding of Schiff base to metal ions. Electrochemical study of Cu(II) complex can provide the degree of the reversibility of one-electron transfer reaction and they have a quasi-reversible character. Schiff base was found potentially active towards microbial strains. All these observations put together to lead us to propose the following structure (Scheme I) in which the Ni(II) and Cu(II) complexes as shown may be suggested to the geometry is trigonal bipyramidal. Geometry and Co(II) and Zn(II) complexes exhibit may be suggested to the geometry is tetrahedral.

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