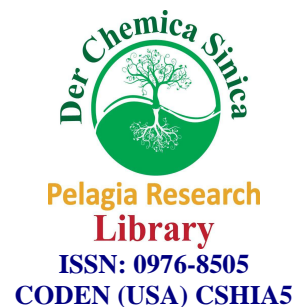




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Der Chemica Sinica, 2015, 6(11):12-20



# Synthesis and spectral characterization of new mononuclear Schiff base complexes derived from 4-aminoantipyrine, 2, 3-butadione and o-phenylenediamine

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### ABSTRACT

A novel series of transition metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) have been synthesized from their corresponding metal chlorides and macrocyclic Schiff base ligand derived from, 4-aminoantipyrine, 2,3-butadione and O-Phenylenediamine. Several tools like elemental analyses, magnetic susceptibility, molar conductance, Mass, FT-IR, Far IR, UV-Vis, VSM,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, SEM, EDX and ESR have been used to obtain the chemical structures of synthesized transition metal complexes. The UV-Vis, magnetic susceptibility and ESR the spectral data reveal that all complexes are found to have octahedral geometry. The antimicrobial screening test indicates that the metal complexes of Cu(II) have good antimicrobial activity than other metal complexes. DNA cleavage studies show the effectiveness cleavage of all the complexes.

**Keywords:** Macrocyclic complex; 2,3-butadione; 4-aminoantipyrine; O-Phenylenediamine and antimicrobial activity.

### INTRODUCTION

The cyclic and acyclic organic substrates which preferentially interact with particular metal ions is of fundamental importance in many areas of chemistry.<sup>1,2</sup> In model studies, the majority of the ligand systems is derived from Schiff bases.<sup>3</sup> Amino heterocyclic compounds containing two or more potential donor centers play an important role in the study of comparative reactivity of bidentate ligands systems.<sup>4</sup> In this paper, we are reporting a novel tetra dentate Schiff base [1+2+1] derived from 4-aminoantipyrine, O-Phenylenediamine and 2,3-butadione and its characterization using several spectroscopic and analytical methods.

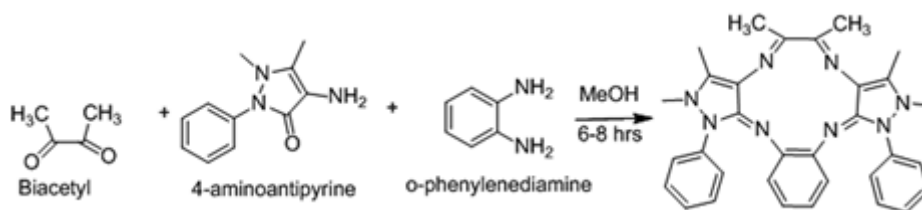
### MATERIALS AND METHODS

To the methanolic solution of 4-aminoantipyrine (0.40 g, 0.1 mmol), 2, 3-Butadione (0.04 g, 0.01 mmol) was added and the reaction mixture was kept over magnetic stirrer and stirred well for 3 h. The light brown colored solid separated out from the mixture was filtered and recrystallized from methanol and dried over vacuum. The solid thus obtained is refluxed with O-Phenylenediamine (0.040 g, 0.05 mmol) dissolved in 40 mL ethanol for 30 h. The brown colored solid separated out was filtered off and dried over  $\text{CaCl}_2$ .

#### Synthesis of Complexes

A solution of metal (II) chloride in methanol (0.2 mmol) was refluxed with methanolic solution of the Schiff base (0.2 mmol) for 6 h. The volume of the solution was then reduced to one third by keeping on a hot water bath. The solid complex precipitated was filtered, washed thoroughly with methanol and dried in a vacuum. (Scheme.1)

Scheme I



#### Analytical and physical measurements

All the reagents, such as benzil, 4-aminoantipyrine, *O*-Phenylenediamine and various metals(II)chlorides were of Aldrich and Merck products. The solvents like methanol, DMSO and DMF were purified and dried by standard procedures.<sup>5, 6</sup> The micro analytical data of the compounds were recorded in IISC Bangalore. The mass spectra of the ligands were recorded at IIT Madras. <sup>1</sup>H and, <sup>13</sup>C NMR spectra were recorded on a Bruker DPX - 300 MHz spectrometer using MeOD as solvent and TMS as an internal standard at IIT Madras. Far IR spectra of the complexes were recorded on a Perkin –Elmer 783 spectrometer in the range of 400-0 cm<sup>-1</sup> using KBr disks at IISC, Bangalore. The UV-Visible spectra were recorded on a Shimadzu UV spectrometer in the range 200-700 nm at CLRI, Madras. The magnetic susceptibility of the complex was recorded by vibrating sample magnetometer (VSM) at IIT Madras. The molar conductance was measured on ELICO CM-180 using DMSO as the solvent at room temperature. SEM-EDX for legends and its complexes were recorded in IISC Bangalore. The antibacterial activity of Schiff base ligands and their metal complexes were studied against bacteria like *E.coli*, *S.Aureus*, and fungus like *A.Niger* and *A.Flavas*. The DNA cleavage ability of the newly synthesized compound was examined by gel electrophoresis method.

#### Antimicrobial activity

The antimicrobial activity was determined for the investigated compounds against the bacteria: *E.coli*, *S.aureus*, and fungus: *A.niger* and *A.flavas* well diffusion method using agar nutrient as the medium<sup>7</sup>. The stock solution was prepared by dissolving (100 mg) of compounds in DMSO. In a typical procedure a well was made in the agar medium inoculated with the microorganism. The well was filled with the test solution using micropipette and the plate was incubated 24 h for bacteria and 72 h for fungi at 35 °C. During this period the test solution diffused and the growth of the inoculated microorganisms was affected.

#### DNA cleavage activity

The DNA cleavage ability of the newly synthesized compound was examined by gel electrophoresis method. The electrophoresis of the samples was done according to the following procedure (Sam brook et al., 1989)<sup>8</sup>. The compounds were added separately to the DNA sample. The sample mixtures were incubated at 37 °C for 2 h. 250 mg of agarose well dissolved in 25 mL of TAE buffer (4.84 g Tris base, pH 8.0, 0.5 M EDTA/1000 mL). When the gel attains ~55 °C, it was poured into the gel cassette fitted with a comb. When the gel gets solidified the comb was removed and the gel was placed in the electrophoresis chamber flooded with TAE buffer 20 µl of DNA sample (mixed with bromophenol blue dye @ 1:1 ratio), was carefully loaded into the wells, along with standard DNA marker and the constant 50 V of electricity was passed for around 45 min. The gel was removed carefully and stained with an ETBR solution (10 µg/mL) for 10-15 min and the bands were observed under UV transilluminator.

## RESULTS AND DISCUSSION

The complexes are soluble in methanol and DMSO. Conductivity measurement of these complexes in 10<sup>-3</sup> M solution DMSO indicated the non-electrolyte (below 2 S cm<sup>2</sup>mol<sup>-1</sup>). The analytical data of the reported complexes are as follows.

Co (C<sub>32</sub>H<sub>32</sub>N<sub>8</sub>) Cl<sub>2</sub> (1): yield: 60 %; F.W; 658; Anal. calcd :C,58.37; H,4.90; N,17.02; Co,8.95 %. Found: C, 58.31; H, 4.86; N, 17; Co, 8.91 %

Ni (C<sub>32</sub>H<sub>32</sub>N<sub>8</sub>) Cl<sub>2</sub> (2): yield: 65 %; F.W; 658.20; Anal. calcd: C,58.39; H,4.90; N,17.02; Ni,8.92 % Found: C,58.34; H,4.86; N,17.02, Ni, 8.90 %

Cu (C<sub>32</sub>H<sub>32</sub>N<sub>8</sub>) Cl<sub>2</sub> (3): yield: 70 %; F.W; 663.10; Anal. calcd: C,57.96; H,4.86; N,16.90; Cu,9.58 % Found: C,57.91; H,4.83; N,16.89; Cu, 9.56 %

Zn (C<sub>32</sub>H<sub>32</sub>N<sub>8</sub>) Cl<sub>2</sub> (4): yield: 68 %; F.W; 664.90; Anal. calcd: C,57.80; H,4.85; N,16.85; Zn, 9.83 % Found: C,57.75; H,4.81; N,16.84; Zn, 9.90 %



**Copper complexes:** Only one broad is observed at  $16500\text{ cm}^{-1}$  in the electronic spectrum of Cu(II) complex and is assigned to  $^2E_g \rightarrow ^2T_{2g}$  transition. This broad confirms the octahedral geometry of Cu(II) complex.<sup>23</sup>

#### Magnetic susceptibility measurement

The Vibrating scanning magnetization study was carried out for the entire complex at room temperature. The results of the study are shown in Table II & figure II.

Table II. Magnetic moment values of the Schiff base metal(II) complexes

Complex	Observed Magnetic moment (BM)
$[\text{Co}(\text{C}_{42}\text{H}_{36}\text{N}_8)\text{Cl}_2]$	2.16
$[\text{Ni}(\text{C}_{42}\text{H}_{36}\text{N}_8)\text{Cl}_2]$	3.55
$[\text{Cu}(\text{C}_{42}\text{H}_{36}\text{N}_8)\text{Cl}_2]$	1.81

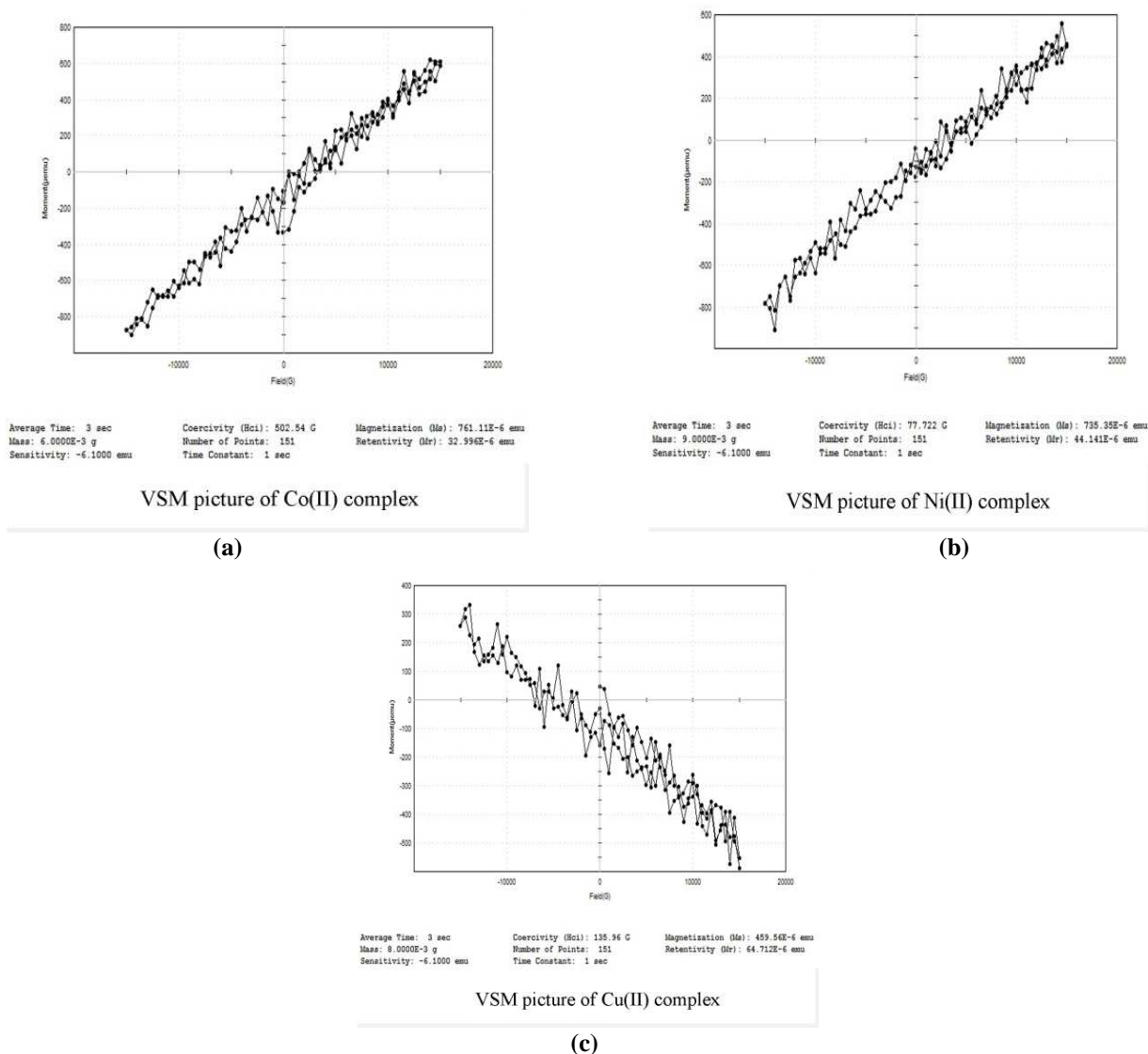


Figure II. (a, b and c) VSM spectra of the Co(II), Ni(II), Cu(II) complexes

**Cobalt complex.** The magnetic moment of the Co(II) complex was found in the range 2.16 BM. The lower magnetic moments of monomeric Co(II) complex suggested that the complex was not pure octahedral and is flattening towards planar arrangement.<sup>24-27</sup>

**Nickel complex:** The magnetic moment of Ni(II) complex was found in the range 3.55 BM. The magnetic moment value ranges 3.14-3.68 BM reported earlier for Ni(II) octahedral complex.<sup>28</sup> This increase in magnetic moments from spin only value (2.83 BM) is due to slight distortion from pure octahedral to  $D_{4h}$  symmetry.

**Copper complex:** The magnetic moment of the Cu(II) complex was found in the range 1.81 BM indicates the paramagnetism complex due to one unpaired electron. The magnetic moment of the complex, which is slightly higher than the spin only value (1.77 BM) which explains that the complex is monomeric in nature and there is no metal-metal interaction along axial position in the complex and have distorted octahedral environment.<sup>29-31</sup>

#### Mass spectra

The stoichiometry composition of ligand [L] and its copper complex were compared using the mass spectra. The molecular ion peak of Schiff base mass 528 obeys the nitrogen rule since the compound contains 8 nitrogen atoms. The copper complex exhibit molecular ion peak at  $m/z$  658 confirms the stoichiometry of metal of chelates as ML type.<sup>32</sup> The results of the study are shown in Figure. 3

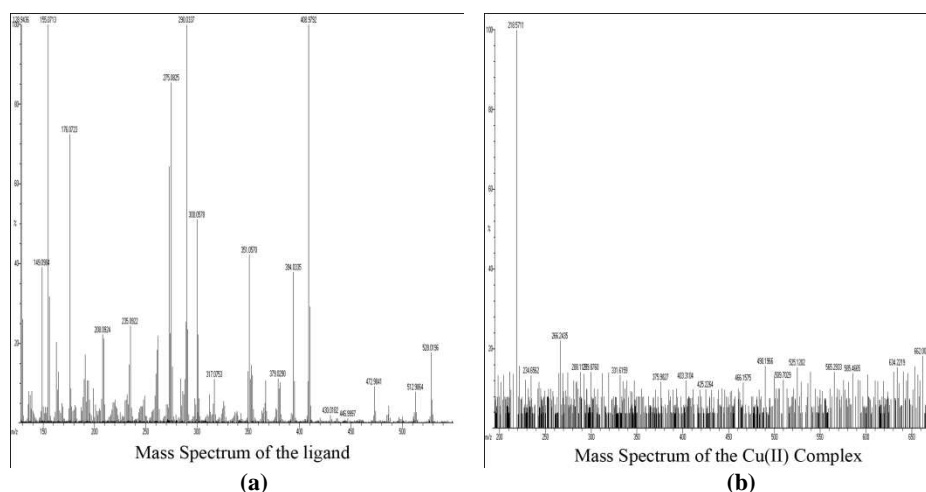


Figure. III. (a,b) Mass spectra of the ligand and its Cu(II) complex

#### SEM- EDX analysis

The surface morphology of ligand and Cu(II) complexes have been examined using scanning electron microscope at a magnification of 2000 X. The distinct morphology of the free ligand and Cu(II) complex can be observed. From the SEM analysis, it is observed that, the Cu(II) complexes are highly porous when compared to the free ligand. The results of the study are shown in Figure. IV

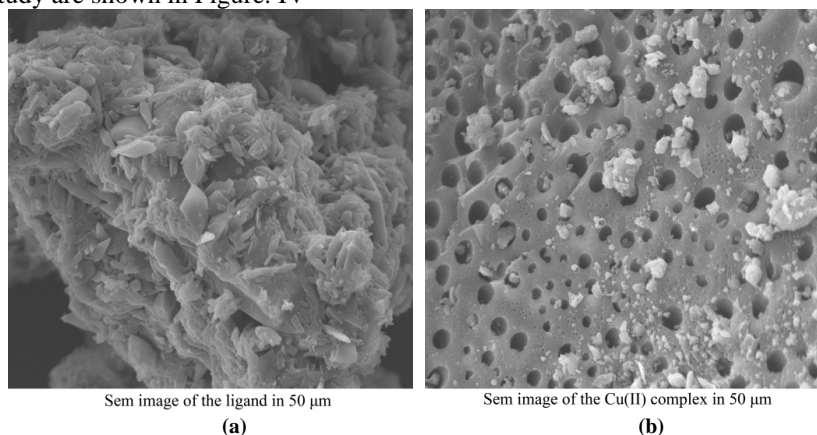


Figure. IV (a, b). SEM images of the ligand and its Cu(II) complex

EDX analysis is used to calculate the percentage level of various elements present in the metal complex. The results by energy dispersive x-ray analysis (EDX) indicated that there was no contamination. The percentages of elements present in the complex are in agreement with the proposed structure. The results of the study are shown in Figure. V

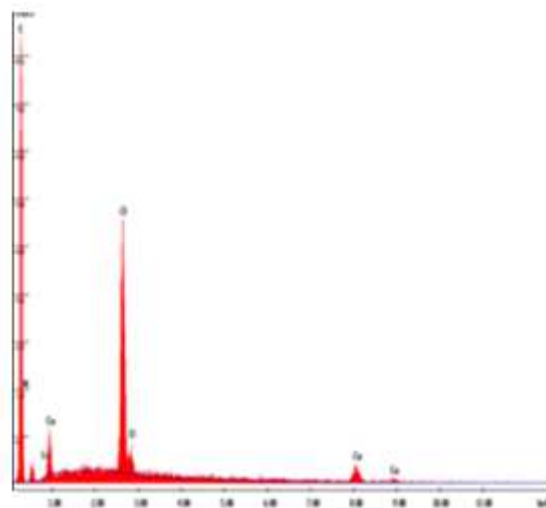


Figure. V EDX of the Cu(II) complex

*ESR spectra*

The ESR spectra of Cu(II) complexes were recorded at room temperature (300 K). The four well resolved peaks in the low field region corresponding to  $g_{\parallel}$  (2.274) and  $g_{\perp}$  (2.095). The trend  $g_{\parallel}$  (2.274) >  $g_{\perp}$  (2.095) >  $g_e$  (2.0023) observed in copper complex suggests that the unpaired electron is localized in  $dx^2-y^2$  orbital for copper ion.<sup>33,34</sup> According to Hathaway if the value of  $G$  is greater than four ( $G > 4$ ), the exchange interaction is negligible whereas when the value of  $G$  is less than four ( $G < 4$ ), a considerable exchange interaction is indicated in the complex. It is observed that the  $G$  value for these complexes are less than four ( $G < 4$ ), indicating considerable exchange interaction the complexes.<sup>35,36</sup> The spin orbit coupling constant,  $A$  value ( $-750 \text{ cm}^{-1}$ ) calculated using relations

$g_{av} = 1/3(g_{\parallel} + 2 g_{\perp})$  and  $g_{av} = 2(1 - 2\lambda/10Dq)$  is less than the free Cu(II) ion ( $-832 \text{ cm}^{-1}$ ) which also supports

covalent character of the M-L bond in complex.<sup>37</sup> The covalency parameter  $\alpha^2$  is calculated using the following equation.  $\alpha^2 (\text{Cu}) = -(A_{\parallel}/0.036) + (g_{\parallel} - 2.0023) + 3/7(g_{\perp} - 2.0023) + 0.04$ . If the value of  $\alpha^2 = 0.5$ , it indicates a complete covalent bonding, while the value of  $\alpha^2 = 1.0$  suggest complete ionic bonding. The observed value of  $\alpha^2$  (0.87) of the complex is less than unity which indicates that the complex has some covalent character in the ligand environment.<sup>38</sup> The results of the study are shown in Figure.VI

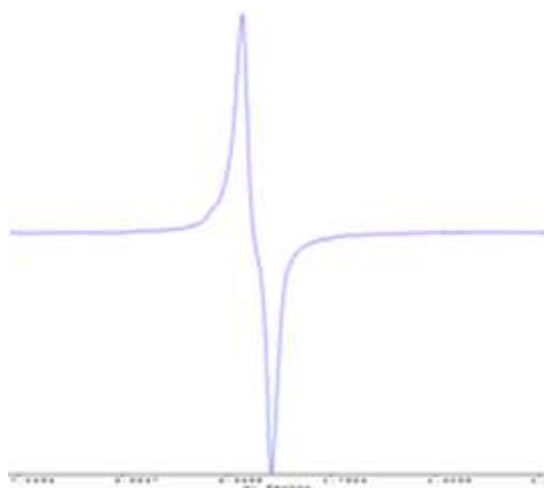
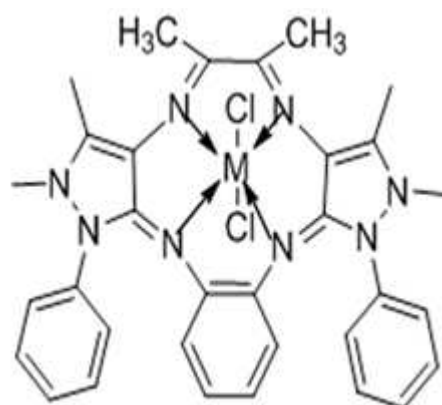


Figure.VI ESR spectra of Cu(II) complex

Based on the above physical methods and spectral analysis the structure of the complex is proposed.



Scheme II



Proposed structure of synthesized complexes, where M = Co(II), Ni(II), Cu(II) or Zn(II) and X = Cl<sup>-</sup>

#### Antibacterial activity

In vitro antimicrobial activity was studied metal [Co(II), Ni(II), Cu(II) and Zn(II)]chloride solutions, DMSO solvent, free ligand and DMSO solution of metal complex. The test was studied against the bacteria: *E.coli*, *S.Aureus*, and fungi: *A.Niger* and *A.Flavas*. From the result of the antimicrobial, it has been revealed that the metal complexes are found as higher activity than the free ligand. This is explained by chelation theory,<sup>39</sup> the polarity of the metal ion will be reduced to a greater extent due to the overlap of the legend orbital and partial sharing of the positive charge of the metal ion with donor groups. This causes increase in delocalization of the  $\pi$ -electrons over the whole chelate ring and enhances the penetration of the complexes into lipid membranes and blocks the metal binding sites in the enzymes of micro organisms. These complexes also disturb the respiration process of the cell and thus block the synthesis of proteins, which restricts further growth of the organisms.<sup>40</sup> The results of the study are shown in Plate 1: Anti bacterial activity, Plate 2: Anti Fungal activity

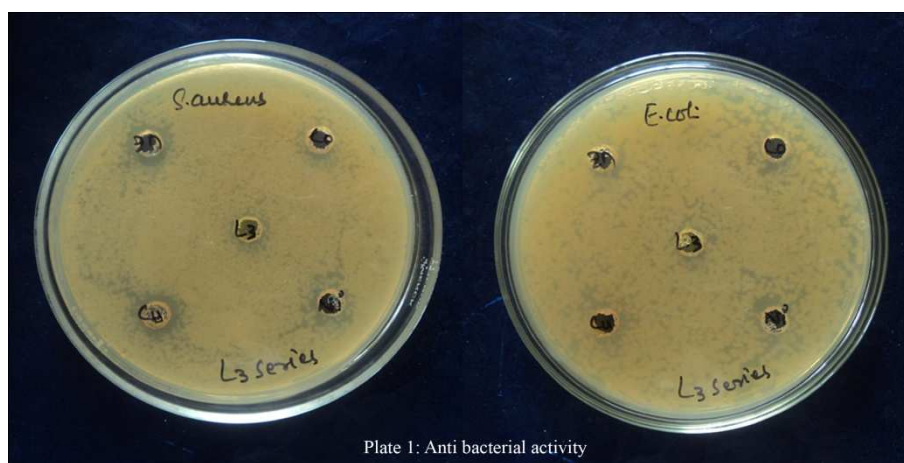


Plate 1: Anti bacterial activity

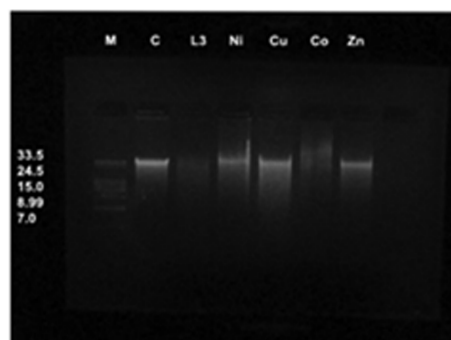
Plate 1: Anti bacterial activity



Plate 2: Anti Fungal activity

### DNA cleavage activity

It is evident from gel electrophoresis analysis that because of the difference in molecular weight between the control and the treated DNA samples, the ligand and its metal complexes have acted on DNA. Compared to control DNA, the difference in the migration of the lanes of Schiff base ligand (L) and its metal(II) complexes is shown clearly in the present gel electrophoresis. It has been shown that ligand and its  $[\text{Co}(\text{L})\text{Cl}_2]$  complex completely cleaves the super coil. On the other hand, there is only partial cleavage of super coil by  $[\text{Ni}(\text{L})\text{Cl}_2]$ ,  $[\text{Cu}(\text{L})\text{Cl}_2]$  and  $[\text{Zn}(\text{L})\text{Cl}_2]$  complexes. From the studies, it is evident that only the control DNA does not show any apparent cleavage, but the ligand and its metal complexes show the apparent cleavage. From the finding of this study, we can come to the conclusion that all the newly synthesized compound are good inhibitors of pathogenic microorganisms, which is evident from the observation on the DNA cleavage. The results of the study are shown in Figure.7



Agarose gel electrophoretic pattern of CT DNA induced by  $\text{H}_2\text{O}_2$  and metal complexes M:DNA alone(lane 1),C: Control DNA (lane 2), Ligand (lane 3),  $[\text{Ni}(\text{L})\text{Cl}_2]$  (lane 4),  $[\text{Cu}(\text{L})\text{Cl}_2]$  (lane 5),  $[\text{Co}(\text{L})\text{Cl}_2]$  (lane 6),  $[\text{Zn}(\text{L})\text{Cl}_2]$  (lane 7)

Figure. VII DNA cleavage activity

### CONCLUSION

The elemental analyses magnetic susceptibility, molar conductance, mass, FT-IR, FAR-IR, UV-Vis,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR, ESR and SEM EDS suggests that Zinc(II) complex have octahedral geometry, where as Cobalt(II) copper(II) and nickel(II) complexes have distorted octahedral geometry from the data it is established that the synthesized Schiff base is a tetra dentate ligand which coordinates through its four azomethine nitrogen. Cu(II) complexes posses greater antimicrobial activity than other complexes. The interaction of these complexes with CT-DNA was investigated by gel electrophoresis. From the observation, interestingly the DNA band was found to shift up in molecular weight by treating with sample Co(II) complex though significant DNA cleavage was found.

### Acknowledgment

The Head of the Department is acknowledged for providing all the necessary facilities for doing the research work



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