



Synthesis, Characterization and Investigation of Antimicrobial Activity of a New Schiff Base, 2-(((2-((4-hydroxybenzylidene) amino)ethyl)imino)methyl) Phenol and Its Cu(II) and Ni(II) Complexes

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Authors' contributions

This work was carried out in collaboration among all authors. Authors MKEZ and FKC designed the study. Authors MFY, MB and MSH did the study, laboratory work and authors SN and NU managed the literature searches. Authors MA and MYR wrote the first draft of the manuscript. Authors MMH and LAB managed the analyses of the study. All authors read and approved the final manuscript.

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ABSTRACT

New complexes of Cu (II) and Ni (II) of the Schiff Base, 2-(((2-((4-hydroxybenzylidene) amino)ethyl)imino)methyl) phenol were synthesized and characterized by analytical and physico-chemical techniques including magnetic susceptibility, conductivity measurements, electronic and IR spectral studies. The infrared spectral studies revealed the tetra-dentate nature of the Schiff base in the complexes. On the basis of all characterizations, square- planar geometry has proposed for all the obtained complexes. The complexes showed moderate antimicrobial activity against *Escherichia coli* and *Staphylococcus aureus*.

Keywords: Schiff base ligands; transition metals; salicylaldehyde; antibacterial activity.

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1. INTRODUCTION

Schiff base named after Hugo Schiff (1864) are the compounds containing azomethine group (-HC=N-) formed by the condensation reaction of any primary amine with aldehyde or ketone [1]. During Schiff base formation, the active carbonyl group (-C=O) is replaced by an imine or azomethine group. Schiff base constitutes a very important group of N, O donor chelating ligands [2]. Schiff bases and its complexes are used as pigments and dyes, catalysts, intermediate in organic synthesis, and as a polymer stabilizer [3]. Schiff bases are versatile -C=N (imine) containing compounds possessing broad spectrum of biological activity and the incorporation of metals in the form of complexes showed some degree of antibacterial, antifungal, antitumor, anticancer and anti-inflammatory activity [4-8].

Metal complexes involving derivatives of salicylaldehyde and aromatic or aliphatic amines are of massive significance because of their potential use as catalyst for some reactions [9-13] and biological activities [14-15] etc. Salophen ligand offers a tetradentate chelating system to form stable metal complexes and thus they have very strong intermolecular interactions. Transition metal complexes derived from salophen-type ligands have widespread applications such as homogeneous and heterogeneous catalysts in various organic transformation reactions.

Metal complexes of Mn(II), Fe(II), Co(II) and Cd(II) ions with Schiff base ligand 4-((pyridin-2-ylimino)methyl)phenol derived from 2-amino pyridine with 4-hydroxybenzaldehyde have recently been reported by M.S. Hossain et al. [16]. The presented data indicated that all the synthesized complexes have octahedral geometry. The Schiff base and its metal complexes have been found to have moderate to strong antibacterial activity.

Two new symmetrical Schiff bases have been prepared by the condensation of ethylenediamine and two benzaldehyde derivatives, namely 2-hydroxybenzaldehyde and 2,4-dimethoxybenzaldehyde and Schiff base ligands and their Iron complexes were characterized by electronic absorption spectra, ¹H NMR and IR spectroscopies [17].

To the best of our knowledge, Cu(II) and Ni(II) metals complexes of unsymmetric Schiff base derived from 4-hydroxy benzaldehyde and

salicylaldehyde with ethane-1,2-diamine have not been reported yet. Keeping these facts in mind, we herein report the synthesis and characterization of Cu(II) and Ni(II) metals complexes with a new Schiff base ligand derived from salicylaldehyde, ethane-1,2-diamine and 4-hydroxybenzaldehyde with the ratio of 1:1:1 in ethanol solvent.

2. EXPERIMENTAL

2.1 Chemicals and Reagents

2-hydroxybenzaldehyde (99.99%), Parahydroxy benzaldehyde, Ethane-1,2-diamine (99.99%), CaCO₃(99.99%) and Ethanol, DMSO were used as a solvent. All chemicals with high purity used in this work were purchased from Merck and Loba Chemicals.

2.2 Materials

All metal(II) salts were used as nitrates. The solvents were purified by distillation procedure. The melting point or the decomposition temperature of all the prepared ligand and metal complexes were observed in an electro thermal melting point apparatus. Infrared spectra were recorded on a FTIR-8400, SHIMADZU, Japan, using a KBr disc, in Central Science Lab of Rajshahi University. The thermogravimetric analysis (TGA) was performed on Perkin Elmer Simultaneous Thermal Analyzer, STA-8000. UV-Visible spectra of the complexes in DMF were recorded in the region 200-800 nm on a THERMOELECTRON NICOLET evolution 300 UV-Visible spectrophotometer. The Gouy Method were used to measure the magnetic moment of the solid complexes. The electrical conductance measurements were made at room temperature in freshly prepared aqueous solution in DMSO. The purity of the ligand and metal complexes were tested by Thin Layer Chromatography (TLC).

2.3 Preparation of Schiff base 2-(((2-((4-hydroxybenzylidene) amino) ethyl) imino) methyl) phenol

Schiff base ligand was prepared according to the known method from the condensation of the respective diamine with the corresponding aldehydes in a molar ratio of 1:1:1, respectively, using ethanol as a solvent. To a stirring solution of ethane-1, 2-diamine (0.7 mL, 10.00 mmol) dissolved in about 10.00 mL ethanol, a solution

of salicylaldehyde (1.06 mL, 10.00 mmol) and 4-hydroxybenzaldehyde in 10.00 mL of ethanol was added drop wise through two different necks of a three-neck round bottom flask. This has resulted in a lemon yellow solution, which was refluxed and stirred for 5 hours. The reaction mixture was cooled and kept for evaporation at room temperature leading to isolation of a solid lemon yellow product. The precipitates were filtered off, washed several times with cyclohexane and finally dried in a desiccator over CaCl_2 [18-19]. The Schiff base was obtained in good yields (about 72%). The product (Ligand, L) was found to be soluble in EtOH, MeOH, DCM, DMF and DMSO.

2.4 General Procedure for Synthesis of Complexes

The Schiff base ligand (0.134 g, 0.5 mmol) was dissolved in 15.00 mL hot ethanol. The hot ethanolic solution of the ligand (metal: ligand = 1:1) was slowly added to a hot aqueous ethanolic solution of the metal salts in a reflux set. The resulting solution was refluxed for 6 h. The solution was reduced to one third by evaporating the solvent. After cooling the solution at room temperature, colored precipitates (for Cu^{2+} complex- parrot green, Ni^{2+} complex-brown) were separated by filtration. The solid was washed several times with ethanol. The complexes were all soluble in DCM, DMF and DMSO with the general formula $[\text{ML}]$, where M is a divalent metal ion.

2.5 Antibacterial Studies

Any chemical or biological agent that either destroys or inhibits the growth of microorganisms is called antimicrobial agent. The synthesized Schiff base ligand and the metal complexes were screened for their antibacterial activity against pathogenic bacterial strains, Gram negative (*Escherichia coli*) and Gram-positive (*Staphylococcus aureus*), the disc diffusion method [20-21] was adopted for the determination of antibacterial activity. All pathogenic bacteria under this study were collected from the Department of Pharmacy, University of Rajshahi, Rajshahi-6205, Bangladesh. The observed data of antimicrobial activity of all the compounds and the standard drug are given in Table 4.

3. RESULTS AND DISCUSSION

All of the synthesized ligand and metal complexes were air and moisture stable. The

complexes are intensely colored solids, which decomposes above 230°C . Their molar conductances in DMSO were low, indicating non-electrolytes property [22]. The analytical and physical data (color, melting point, molar conductivity and magnetic moment) of ligand and the complexes with $\text{Cu}(\text{II})$, $\text{Ni}(\text{II})$ metal ions are listed in Table 1. The effective magnetic moment for $\text{Cu}(\text{II})$ complex is 1.85 B.M indicating paramagnetic nature. This value corresponds to a square planar geometry [23-24]. For the $\text{Ni}(\text{II})$ complex, the value for the effective magnetic moment is 0.25 B.M indicates the diamagnetic complex of $\text{Ni}(\text{II})$ with square planar geometry [25].

3.1 Infrared Spectra

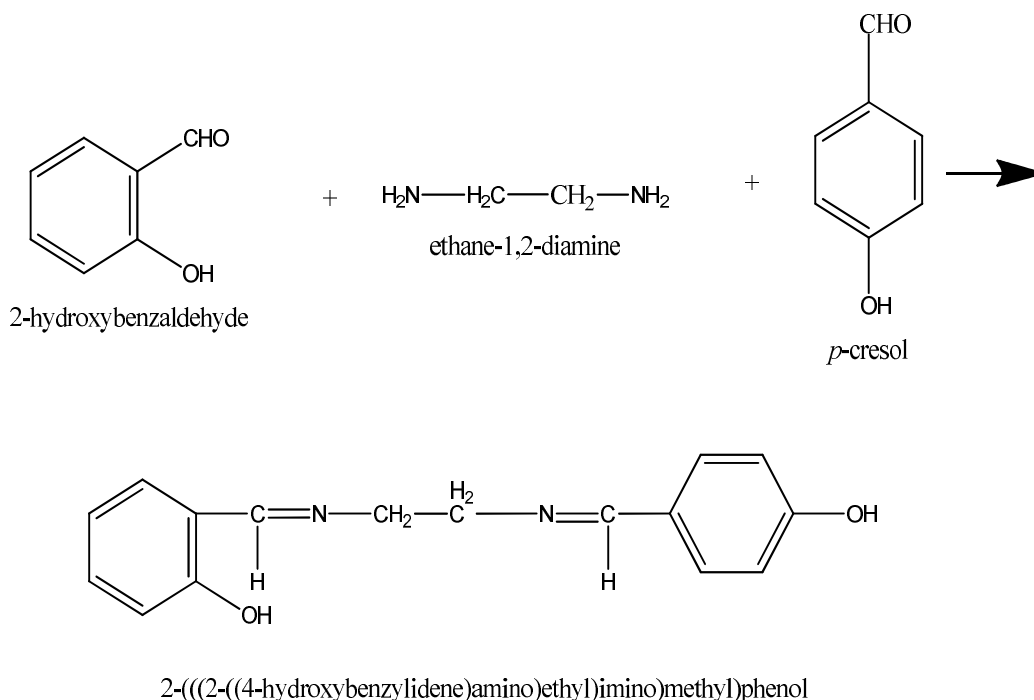
IR spectra of the Schiff base showed a strong bands at 1632 cm^{-1} assigned [20,26] to the azomethine, $\nu(-\text{HC}=\text{N})$ linkage. It was observed that amino and aldehyde moieties of the starting reagents were absent and had been converted into the azomethine moiety (Scheme 1). The band appearing at 1631 cm^{-1} and 1603 cm^{-1} due to azomethine ($-\text{CH}=\text{N}$) of Schiff base metal complexes was shifted to lower frequency represented [27]. In comparison of the spectra of Schiff base and its metal complexes (Table 2) suggested that Schiff base coordinated to metal ions through N atom of azomethine group. Two weak low frequency new absorption bands at 532 cm^{-1} and 467 cm^{-1} that assigned the $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ frequency of $\text{Cu}(\text{II})$ complexes. Another two frequency were observed at 517 cm^{-1} and 467 cm^{-1} assigning the $\nu(\text{M}-\text{O})$ and $\nu(\text{M}-\text{N})$ vibration of $\text{Ni}(\text{II})$ complex [20-21,28]. On the other hand, the $\nu(\text{C}-\text{O})$, which occur at 1291 cm^{-1} for the ligand, was moved to higher frequencies, $14-1302\text{ cm}^{-1}$ after complexation, this shift confirms the participation of phenolic oxygen of the ligand in $\text{C}-\text{O}-\text{M}$ bond formation [26].

3.2 Electronic Spectra

The UV-Visible spectral data recorded in DMSO have been presented in the Fig. 4 and all observations are recorded in Table 3. The electronic spectra of free ligand showed two absorption bands at 278 nm and 340 nm, which may be assigned as $\pi-\pi^*$ and $n-\pi^*$ transitions [29]. The electronic spectrum of $\text{Cu}(\text{II})$ complex showed an absorption band at 272 nm which may be assigned to $n-\pi^*$ transition and another band at 365 nm may be due to charge transfer transition(CT).The electronic spectra of the $\text{Ni}(\text{II})$

complex showed two bands at 275 nm and 375 nm, respectively. The absorption band observed at 275 nm corresponding to π - π^* transition whereas band at 375 nm may be assigned to CT. Both metal complexes may be supported square planar geometry [30]. For square planar Cu(II) complex, there should be one band at about 550

nm (due to ${}^2B_{1g} \rightarrow {}^2A_{1g}$ transition) and another one at about 900 nm for ${}^2B_{1g} \rightarrow {}^2B_{2g}$ transition. The concentration of metal complexes for UV-Vis characterization was not optimized, for this reason characteristic bands at visible region were not observed for Cu(II) and Ni(II) complexes in this study.



Scheme 1. Synthesis of Schiff base, 2-(((2-((4-hydroxybenzylidene) amino) ethyl)imino) methyl)phenol

Table 1. Analytical and physical properties of L and its complexes

Compounds	Molecular formula	Decomposed Temp/(° C)	Body color	Solubility in DMSO and DMF	Molecular conductance (Ohm ⁻¹ cm ² mol ⁻¹)	μ eff (B.M)
L	[C ₁₆ H ₁₆ O ₂ N ₂]	170	Lemon	(+)Ve	8	-
Cu-L	[C ₁₆ H ₁₄ N ₂ O ₂ Cu]	230	Parrot Green	(+)Ve	10	1.85
Ni-L	[C ₁₆ H ₁₄ N ₂ O ₂ Ni]	270	Brown	(+)Ve	12	Dia

Table 2. Characteristic IR absorption peaks in cm⁻¹ units

Symbol of compounds	Compounds	ν (OH)	ν (C=N)	ν (C-O) phenolic	ν (M-O)	ν (M-N)
L	[C ₁₆ H ₁₆ O ₂ N ₂]	3435	1632	1291	-	-
Cu-L	[C ₁₆ H ₁₄ N ₂ O ₂ Cu]	3436	1631	1301	532	467
Ni-L	[C ₁₆ H ₁₄ N ₂ O ₂ Zn]	3435	1623	1334	517	468

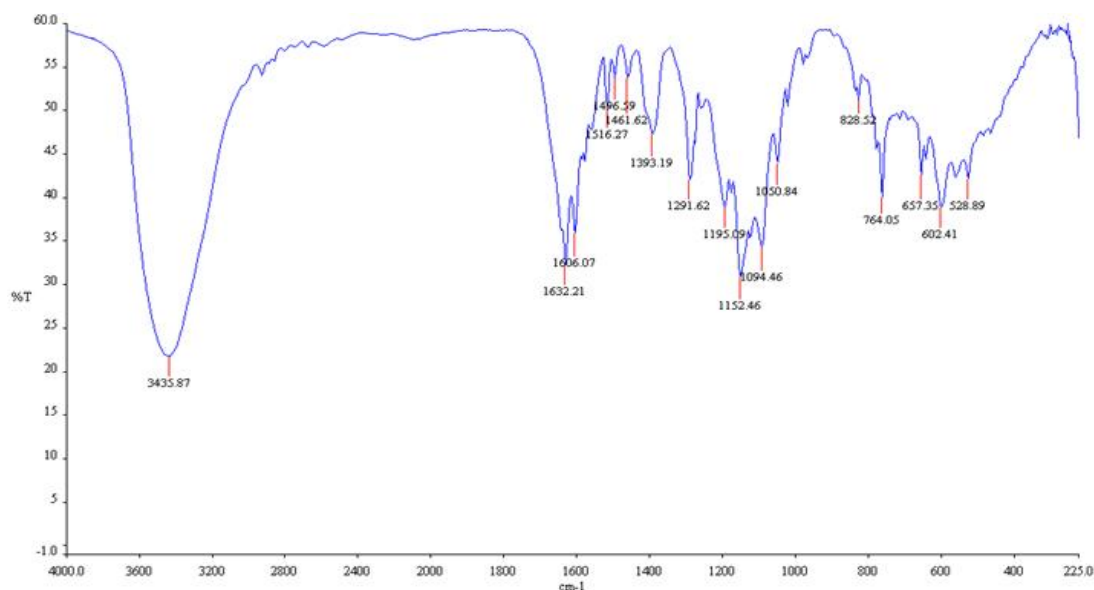


Fig. 1. IR Spectrum of L

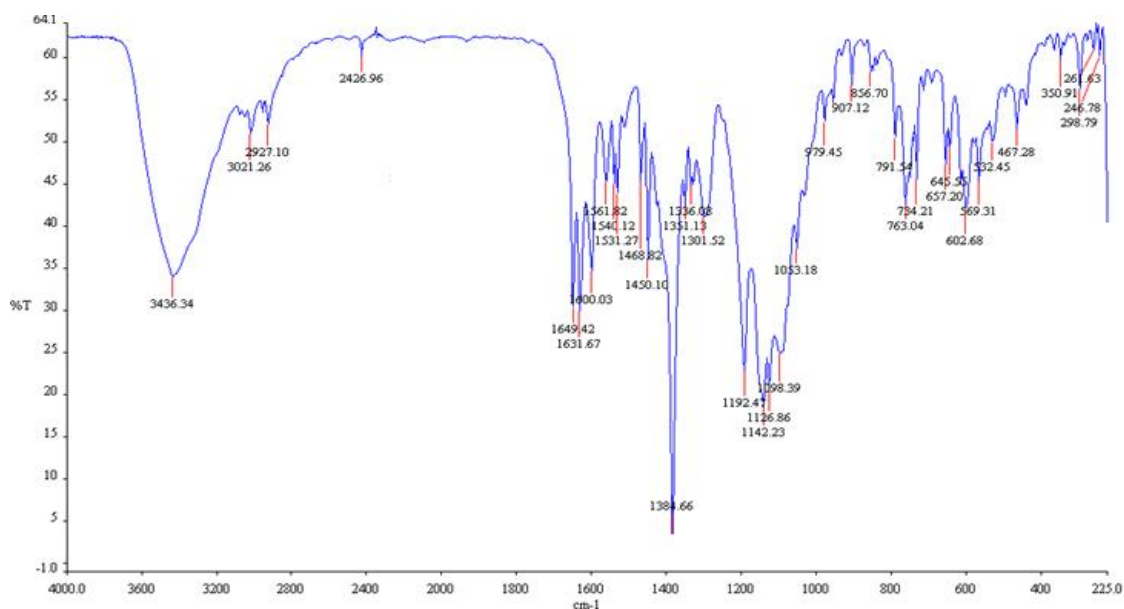


Fig. 2. IR Spectrum of Cu-L

Table 3. UV- visible spectrum of ligand, L and its complexes

Compounds	Molecular formula	Wavelength (nm)	Assignment
L	[C ₁₆ H ₁₆ O ₂ N ₂]	278	π-π*
		340	n-π*
Cu-L	[C ₁₆ H ₁₄ N ₂ O ₂ Cu]	272	π-π*
Ni-L	[C ₁₆ H ₁₄ N ₂ O ₂ Ni]	365	C.T transition
		375	C. T transition

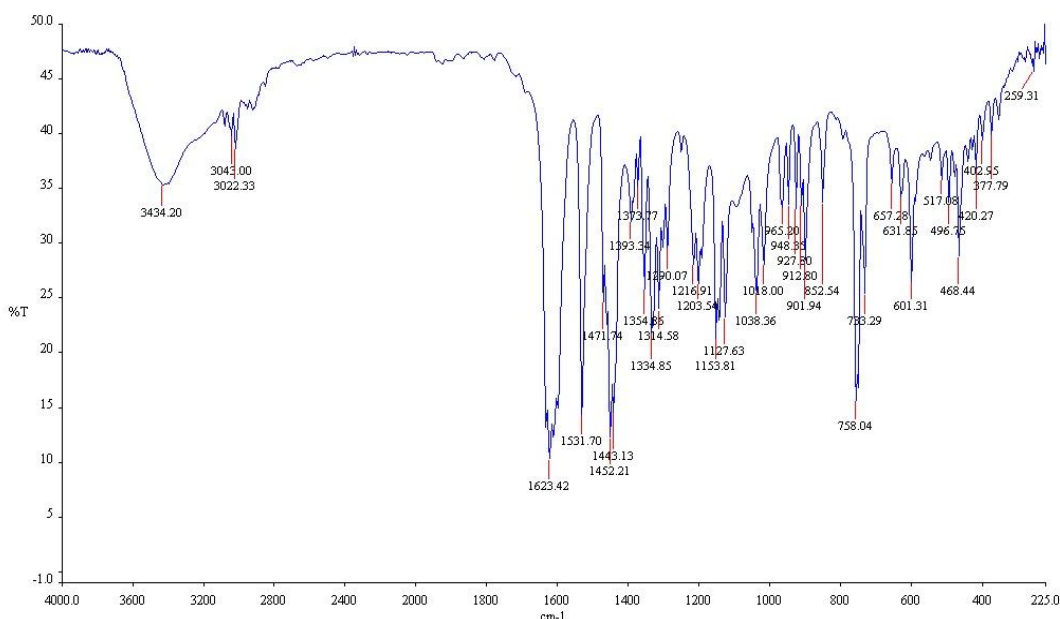


Fig. 3. IR Spectrum of Ni-L

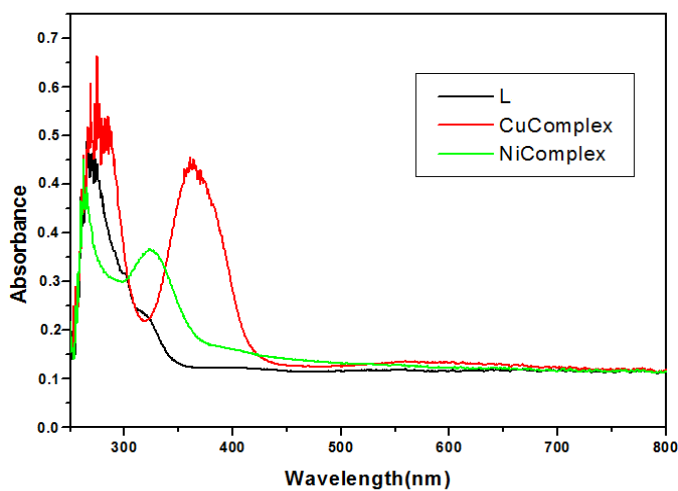


Fig. 4. UV- Visible spectra of the L and its complexes

On the basis of the above characterizations and published research article [31], the probable structure of the complex can be expressed as:

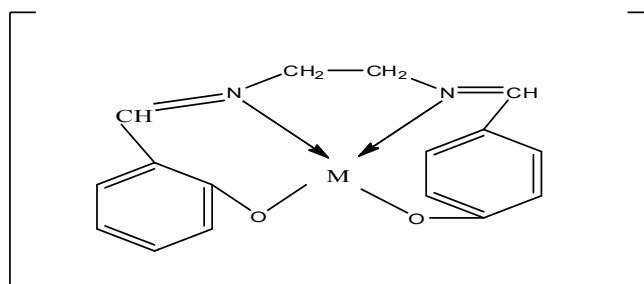


Fig. 5. Proposed structure of metal complex [Where M=Cu(II) and Ni(II)]

Table 4. Inhibition zone in mm of tested compound against two bacteria

Compounds	Zone of inhibition (mm)	
	<i>Escherichia coli</i> (Gram negative)	<i>Staphylococcus aureus</i> (Gram positive)
Kanamycin (30 µg /disc)	30	35
L	8	9
Cu-L	16	13
Ni-L	10	12

3.3 Antibacterial Result

The free Schiff base ligand and their metal complexes were screened for their antibacterial activity against the strains *Escherichia coli*, *Staphylococcus aureus*. The compounds were tested at a concentration of 60 µg in DMSO solution using the paper disc diffusion method [32-33]. The susceptibility zones were measured in diameter (mm) and the result are listed in Table 4. Standard Kanamycin evidently showed the best activity against two mentioned bacteria when compared with all our synthesized compounds. The susceptibility zones were the clear zones around the discs killing the bacteria. The Schiff base and metal complexes individually exhibited varying degrees of inhibitory effects on the growth of tested bacterial species. The metal complexes showed more antibacterial activity than Schiff base ligand. Such increased activity of the metal chelates can be explained on the basis of Overton's concept and Tweedy's chelation theory [34]. Activity against two pathogenic bacteria in this study follows the following trend: Kanamycin-30 > Cu-L > Ni-L > L.

4. CONCLUSIONS

In this paper, we have explored the synthesis and coordination chemistry of Cu(II) and Ni(II) complexes with new Schiff base ligand derived from the condensation reaction of Salicylaldehyde and 4-hydroxybenzaldehyde with ethane-1,2-diamine. The physicochemical analysis indicated the formation of four coordinated metal complexes. IR spectral analysis indicated that N and O atoms are coordinated to central metal atom. Magnetic moment, UV-Visible confirmed the proposed square planar structure of metal complexes. Biological activity revealed that the Cu complex showed strong antibacterial activities compared to the ligand and Ni complex.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

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