



Synthesis, Characterization, Antibacterial and Antioxidant Studies of Isoniazid-based Schiff Base Ligands and Their Metal Complexes

Farzana Khanm Camellia^{a*}, Md. Ashrafuzzaman^a, Md. Nazrul Islam^a,
Laila Arjuman Banu^a and Md. Kudrat-E-Zahan^{a*}

^a Department of Chemistry, University of Rajshahi, Rajshahi-6205, Bangladesh.

Authors' contributions

This work was carried out in collaboration among all authors. All authors read and approved the final manuscript.

Article Information

DOI: 10.9734/AJACR/2022/V11i330257

Open Peer Review History:

This journal follows the Advanced Open Peer Review policy. Identity of the Reviewers, Editor(s) and additional Reviewers, peer review comments, different versions of the manuscript, comments of the editors, etc are available here: <https://www.sdiarticle5.com/review-history/88447>

Original Research Article

Received 07 April 2022
Accepted 14 June 2022
Published 16 June 2022

ABSTRACT

The condensation of aromatic aldehyde with amine results in the formation of Schiff's bases, which are considered to be one of the most significant groups of ligands. Schiff's base metal complexes have received a lot of attention because of their high biological activity. Such include antimicrobial, anticancer, antibacterial, and antifungal activities. The current research is focused on the synthesis and characterization of two Schiff's base ligands obtained from the reaction of isoniazid with 4-(N,N-dimethylamino)benzaldehyde (L1) and 5-nitro-2-furfuraldehyde (L2), respectively and their metal complexes with Cu²⁺, Zn²⁺, and Ni²⁺ ions. FT-IR, UV-Vis, conductivity, and magnetic susceptibility (μ_{eff}) measurements were used to describe the ligands (L1 and L2) and their complexes. The square planar geometry of Cu²⁺ and Ni²⁺ complexes, as well as the tetrahedral geometry of Zn²⁺ complexes, are supported by the Uv-Vis spectra and magnetic moments data. Their antibacterial effectiveness against various pathogenic microorganisms was evaluated in the presence of standard Kanamycin-30. The CuL2 complex, among all the metal complexes derived from the L2 ligand, exhibited better antibacterial activity against *S. aureus* than that of Kanamycin-30. When compared to the BHT antioxidant, all Cu²⁺ complexes showed excellent efficacy.

Keywords: Schiff base; transition metals; isoniazid, kanamycin-30; antioxidant.

*Corresponding author: Email: farzanakhanm2012@gmail.com, kudrat.chem@ru.ac.bd;

1. INTRODUCTION

Schiff bases are regarded as an exceptionally significant family of organic compounds with multiple uses in several biological fields [1-4]. Furthermore, Schiff base is an appealing family of ligands that has played an important role in the advancement of coordination chemistry. Schiff bases and their complexes have excellent applications in several disciplines, such as antibacterial, antifungal, anti-oxidative, anti-inflammatory, antitumor, anticancer, anti-HIV, chemical sensor, therapeutic, optical materials, analytical, and electrochemistry [5-8].

Schiff bases, which are formed via the reaction of isoniazid with organic aldehydes or ketones, are an important family of chelating ligands, and their metal complexes with transition metal ions are of particular interest owing to their importance in biological, industrial, chemical, and pharmaceutical applications. Isoniazid is a medicine with the established therapeutic value that is used to treat a broad range of bacterial infections, including TB, and leprosy [9]. Schiff bases generated from the reaction of pyridine ring containing aldehydes with isoniazid demonstrate stronger antitubercular efficacy than isoniazid [10]. The origin of biological properties of isoniazid-based Schiff bases and their metal complexes is due to the present of (-CO-NH-N=C) unit in their structures. The chelating compounds of aryl hydrazones (such as semicarbazones, thiosemicarbazones etc.) have been shown to function as enzyme inhibitors and are valuable owing to their pharmacological applications [11-13]. It is well known that metal complexes obtained from isoniazid-based Schiff bases exhibit greater antibacterial activity than isoniazid as well as free ligands. The anti-oxidant action of the Schiff base is further improved when it is coordinated with transition metal ions [14].

Nowadays, multidrug-resistant tuberculosis, also known as MDRTB, is a well-known illness. This kind of tuberculosis is caused by an organism that is resistant to both isoniazid and rifampin. These two medications are well-known owing to their widespread usage in the treatment of tuberculosis patients. Therefore, to search a novel drug based on isoniazid is an important research task.

J. N. Yong et al. reported on the Schiff base formed by the reaction of 4-(N, N-dimethylamino)benzaldehyde with isoniazid

(INH) and its antibacterial efficacy against various pathogenic microorganisms. Though the ligand has been published, its metal complexes with transition elements are currently being studied. As a result, there is scope for researchers to continue working on this ligand [15].

In continuation of our work on isoniazid-derived Schiff bases and metal complexes, we will present here the synthesis, characterization, antibacterial, and antioxidant activities of two isoniazid-based Schiff bases and their metal complexes with some divalent transition metal ions.

2. EXPERIMENTAL METHODS

All required chemicals with 99.9% purity were purchased from Merck and Loba chemicals. A METTLER PM 200 electronic balance was used to complete the weighing process. All produced metal complexes' melting or decomposition temperatures were measured using an electrothermal melting point equipment type o.AZ6512. The IR spectra of the produced compounds were acquired using a KBr disc on an FTIR-8400, SHIMADZU, Japan. The complexes' conductivities were measured in DMSO using a Horiba conductivity meter B173 with a set cell constant. The UV-Vis spectra of the ligand and its complexes were measured using a THERMOELECTRON NICOLET evolution 300 UV-Visible Spectrophotometer in DMSO solution (1×10^{-5} M). Sherwood Scientific Magnetic Susceptibility Balance was used in order to determine the values of all complexes' magnetic moments. Elemental analysis was carried out on a LECO(CHNS-932) Elemental Analyzer. Thin Layer Chromatography (TLC) was used to assess the ligand's purity and its metal complexes.

2.1. a. Synthesis of N-(4-Dimethylamino)benzylidene)isonicotinohydrazide Schiff base Ligand (L1)

N-(4-dimethylamino) benzylidene) isonicotinohydrazide, Schiff base Ligand, L1 was synthesized by the conventional condensation reaction (Scheme 1) of 4-(N,N-dimethylamino)benzaldehyde with isoniazid (INH) in an equimolar ratio (i.e., 1:1). An ethanolic solution of INH (1.37 g, 10.00 mmol) was taken in a round bottom flask, and then ethanolic solution of 4-(N,N-dimethylamino)

benzaldehyde (1.49 g, 10.00 mmol) was added to it with continuous stirring. As a catalyst, little amount of glacial acetic acid (2-3 drops) was added dropwise to this mixture. The resultant mixture was allowed to reflux for about 4 hours. TLC monitored the purity of the obtained product throughout the whole reaction. A yellow precipitate of the ligand was produced, which was then filtered and washed several times with cold $\text{CH}_3\text{CH}_2\text{OH}$ solution before being dried in a desiccator over anhydrous CaCl_2 .

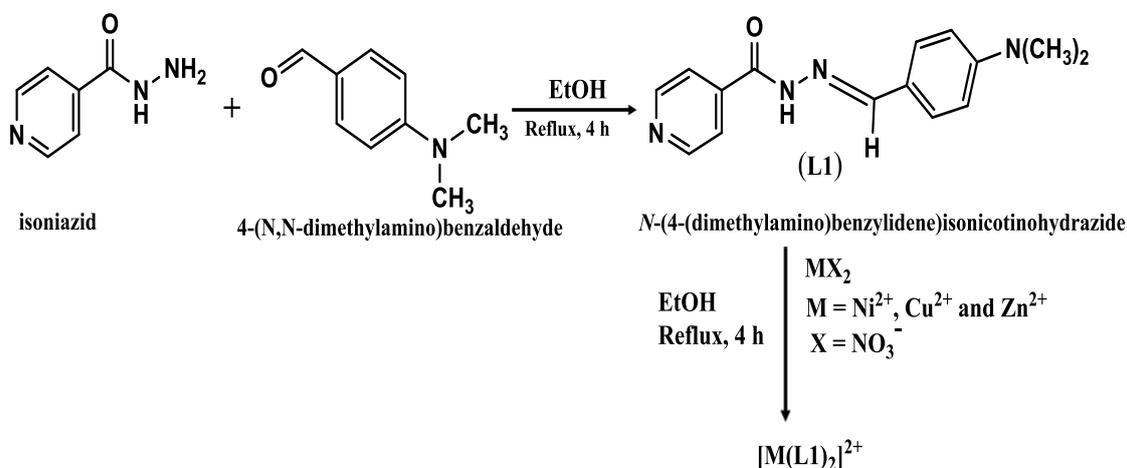
2.1. b. Synthesis of N-(5-nitro-furan-2-yl)methylene)isonicotinohydrazide Schiff base Ligand (L2)

N-(5-nitro-furan-2-yl) methylene) isonicotinohydrazide, Schiff base (L2) was prepared

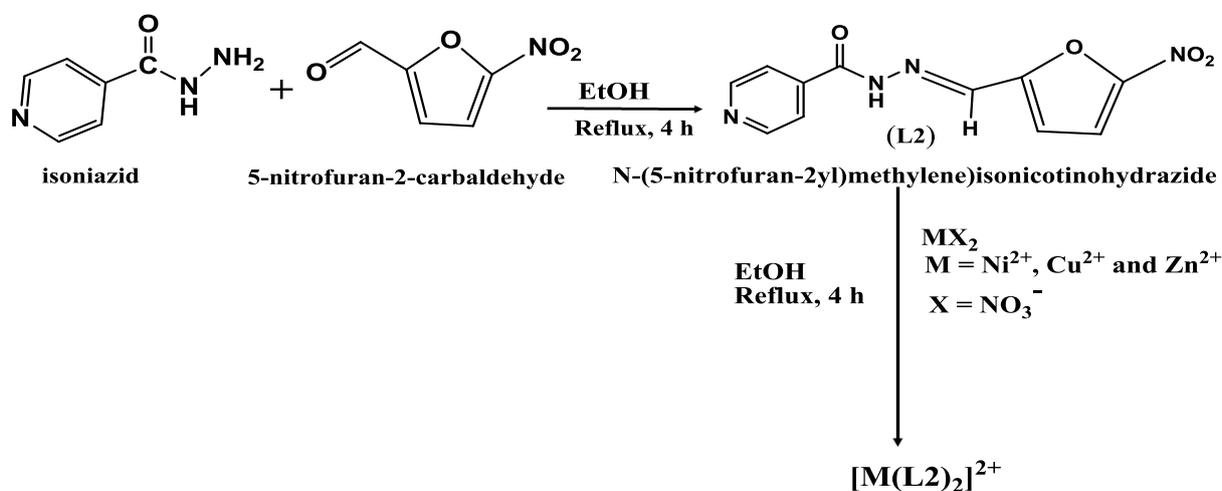
according to the above procedure (scheme 2) from the equimolar ratio of isoniazid and 5-nitro-2-furfuraldehyde. A pale-yellow precipitate was obtained.

2.2 General Procedure for the Synthesis of Metal Complexes with L1 and L2 ligands

15 mL warm ethanolic solutions (1 mmol) of nitrate salts of metal (Zn^{2+} , Ni^{2+} , and Cu^{2+}) were slowly added to the warm ethanolic solution (15 mL) of Schiff base ligand L1 (2 mmol) in a reflux set. The resulting mixture was refluxed for about 4 h. After cooling, the obtained precipitates were filtered and washed with cold $\text{C}_2\text{H}_5\text{OH}$ solution and dried under a vacuum on anhydrous CaCl_2 .



Scheme 1. Synthesis of the Schiff base ligand, L1 and its metal complexes



Scheme 2. Synthesis of the Schiff base ligand, L2 and its metal complexes

Table 1. Physical properties of the ligands (L1 and L2) and their metal complex

Ligand/Complex (Symbol)	Color	M.W	% Yield	M.P/De (°C)	Molar Conductivity (ohm ⁻¹ cm ² mol ⁻¹)	μ_{eff} (B.M)	Elementary Analysis (%)				
							C Found (Calcd.)	H Found (Calcd.)	N Found (Calcd.)	O Found (Calcd.)	M Found (Calcd.)
C ₁₅ H ₁₆ N ₄ O (L1)	Yellow powder	268.30	82	205	NA	NA	67.08 (67.15)	6.05 (6.01)	20.80 (20.88)	5.97 (5.96)	
C ₁₁ H ₈ N ₄ O ₄ (L2)	Pale Yellow powder	260.20	78	185	NA	NA	50.74 (50.77)	3.09 (3.10)	21.48 (21.53)	24.68 (24.60)	
[Ni(L1) ₂](NO ₃) ₂ (NiL1)	Deep Red	719.50	71	>300	121	Dia	50.06 (50.10)	4.45 (4.48)	19.41 (19.47)	17.89 (17.80)	8.19 (8.16)
[Ni(L2) ₂](NO ₃) ₂ (NiL2)	Red	703.30	70	269	128	Dia	37.52 (37.58)	2.24 (2.29)	19.85 (19.92)	31.95 (31.86)	8.41 (8.35)
[Cu(L1) ₂](NO ₃) ₂ (CuL1)	Brown	724.10	73	>300	125	1.90	49.68 (49.76)	4.51 (4.45)	19.28 (19.34)	17.73 (17.67)	8.80 (8.77)
[Cu(L2) ₂](NO ₃) ₂ (CuL2)	Brown	707.90	74	271	121	1.87	37.26 (37.32)	2.27 (2.28)	19.72 (19.78)	31.75 (31.64)	8.95 (8.98)
[Zn(L1) ₂](NO ₃) ₂ (ZnL1)	White	726.00	60	>300	128	Dia	49.68 (49.63)	4.40 (4.44)	19.20 (19.29)	17.68 (17.63)	9.03 (9.01)
[Zn(L2) ₂](NO ₃) ₂ (ZnL2)	White	709.80	71	262	123	Dia	37.18 (37.23)	2.30 (2.27)	19.68 (19.73)	31.60 (31.56)	9.24 (9.21)

Metal complexes of Zn^{2+} , Ni^{2+} , and Cu^{2+} with L2 ligand have synthesized by following the above procedure. Each complex has a distinct color, is soluble in DMF and DMSO but insoluble in common polar solvents.

2.3 Antibacterial Studies

Antimicrobial activity of the L1 and L2 ligands and their metal complexes with Cu^{2+} , Ni^{2+} , and Zn^{2+} ions were performed against *S. aureus*, and *E. coli* in DMSO by disc diffusion approach [16-17]. All pathogenic bacteria under this study were collected from the Department of Pharmacy, University of Rajshahi, Rajshahi-6205, Bangladesh.

2.4 Antioxidant Studies

The DPPH free radical scavenging technique was used to calculate antioxidant activity. The inhibition percentage, which was associated with the compounds' radical scavenging activity, was calculated by using the following formula [18]:

$$\text{DPPH Scavenging Activity (\%)} = \frac{\text{Absorbance of the blank} - \text{Absorbance of the tested sample}}{\text{Absorbance of the blank}} \times 100$$

Calculation of IC_{50} values: In order to get the IC_{50} value, a linear regression was performed between the percentage inhibition and log concentration. Higher antioxidant activity is indicated by a lower IC_{50} value [19].

3. RESULTS AND DISCUSSION

The physical properties of the L1 and L2 and their metal complexes have shown in Table 1.

The molar conductance values of the complexes lie in the range of $121-128 \text{ ohm}^{-1}\text{cm}^2\text{mol}^{-1}$ demonstrating their 1:2 electrolytic character [20-21]. The magnetic moments of the $CuL1$ and $CuL2$ complexes were found to be in the range of 1.87-1.90 B.M, confirming the square planar shape of the Cu^{2+} complexes. On the other hand, these values for the obtained $NiL1$ and $NiL2$ complexes were determined to be 0.41 BM and 0.42 BM, respectively, which supports the diamagnetic character of the Ni^{2+} complexes. All synthesized Zn^{2+} complexes were also diamagnetic due to the d^{10} electronic configuration of the Zn^{2+} ions [22-25].

3.1 IR Spectral Studies

The bands at $(1605) \text{ cm}^{-1}$ and $(1620) \text{ cm}^{-1}$ in the IR spectra, which are caused by the stretching vibration of the azomethine groups ($C=N$) of the L1 and L2 ligands, were shifted to a lower frequency in the spectra of the Cu^{2+} , Zn^{2+} , and Ni^{2+} complexes. This proved that the azomethine group was involved in the coordination through its nitrogen atom (N) [26]. All metal complexes obtained from L1 and L2 ligands display $\nu(C=O)$ band at $1619-1660 \text{ cm}^{-1}$, which is lower than the free ligands value. This clearly suggests the coordination of the carbonyl group with the metal ions through its oxygen atom. New bands around $(523-595) \text{ cm}^{-1}$ and $(413-497) \text{ cm}^{-1}$ detected in the low-frequency area for all complexes (generated from the L1 and L2 ligands) correspond to the frequency of (M-O) and (M-N), respectively [27-28]. All of the IR spectra data for the two ligands (L1 and L2) and their metal complexes are shown in Table 2 and Figs. 1-8.

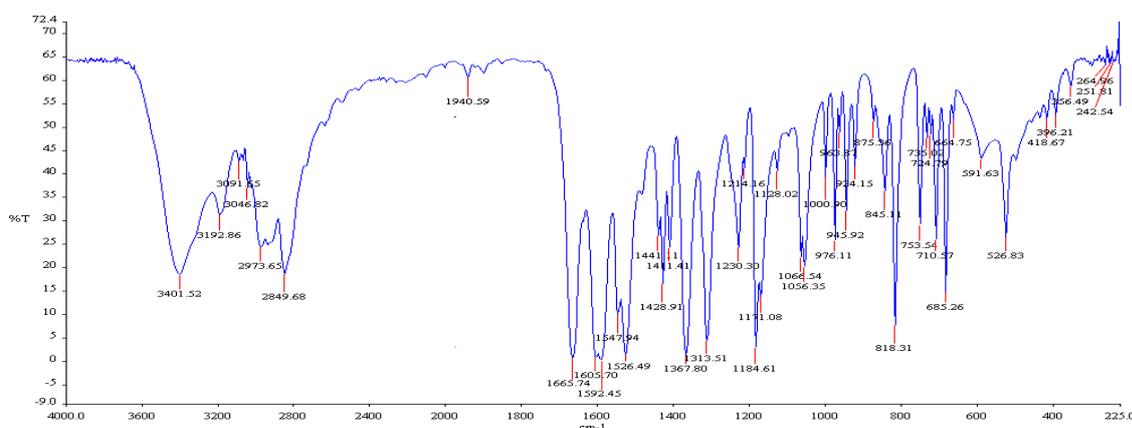


Fig. 1. IR spectrum of L1

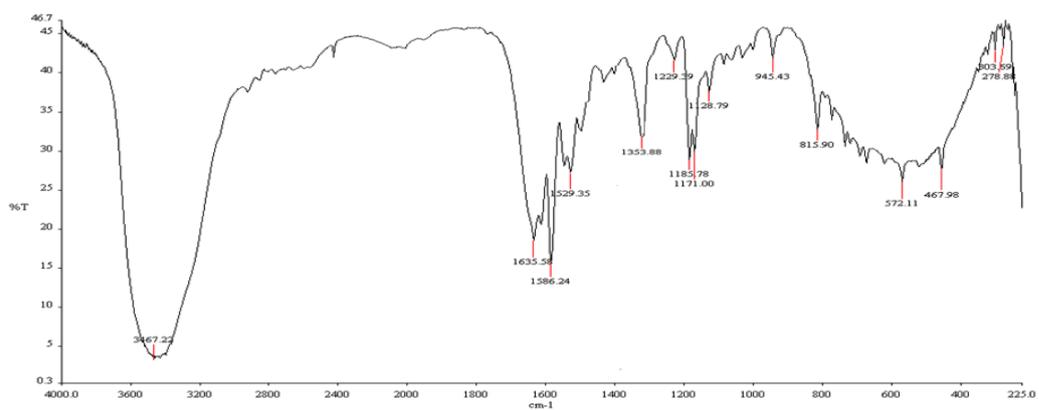


Fig. 2. IR spectrum of NiL1

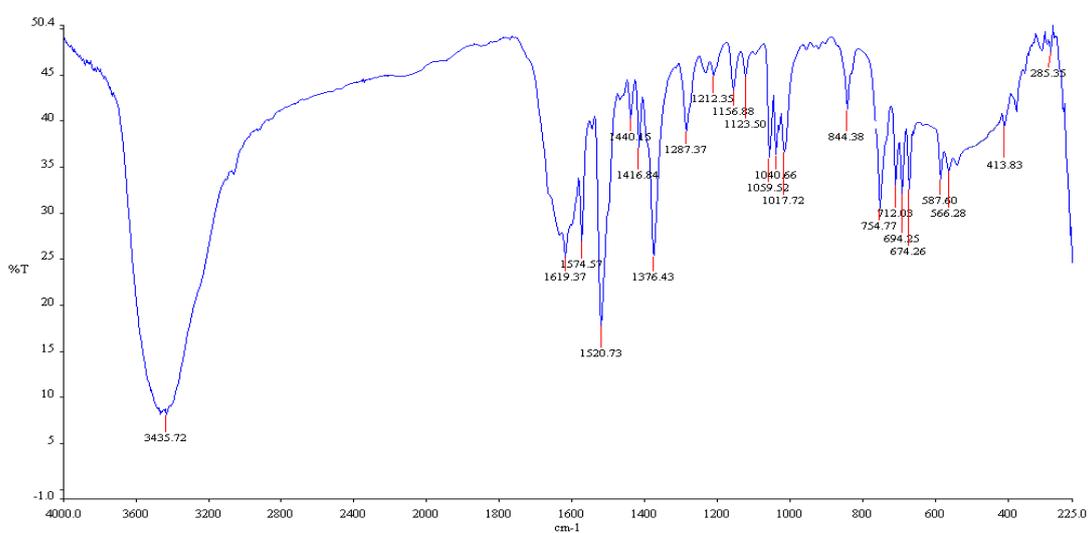


Fig. 3. IR spectrum of CuL1

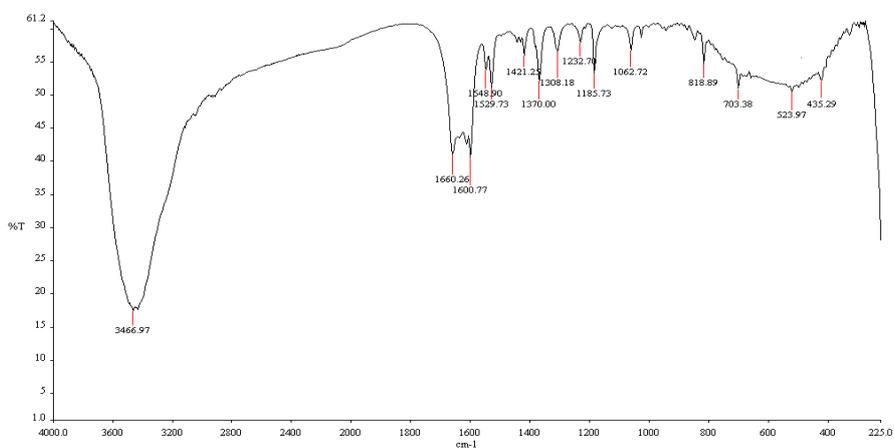


Fig. 4. IR spectrum of ZnL1

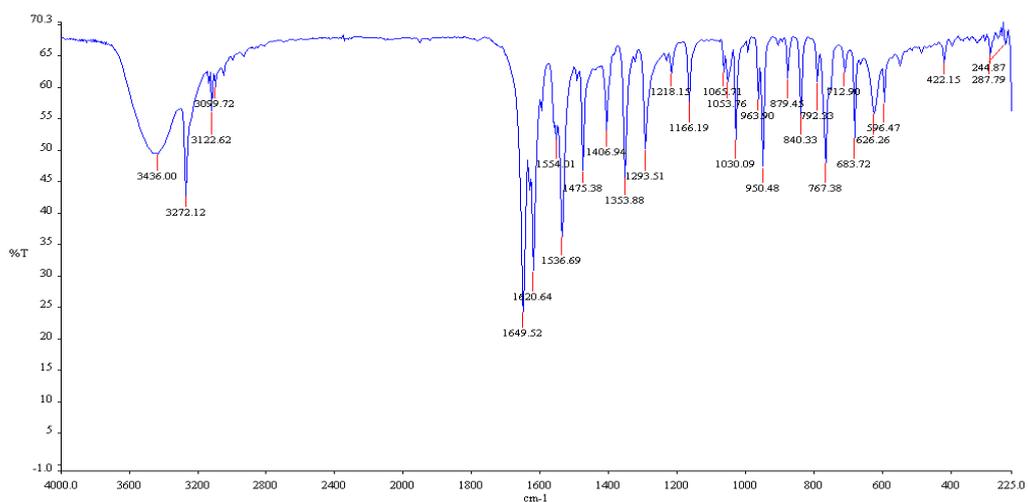


Fig. 5. IR spectrum of L2

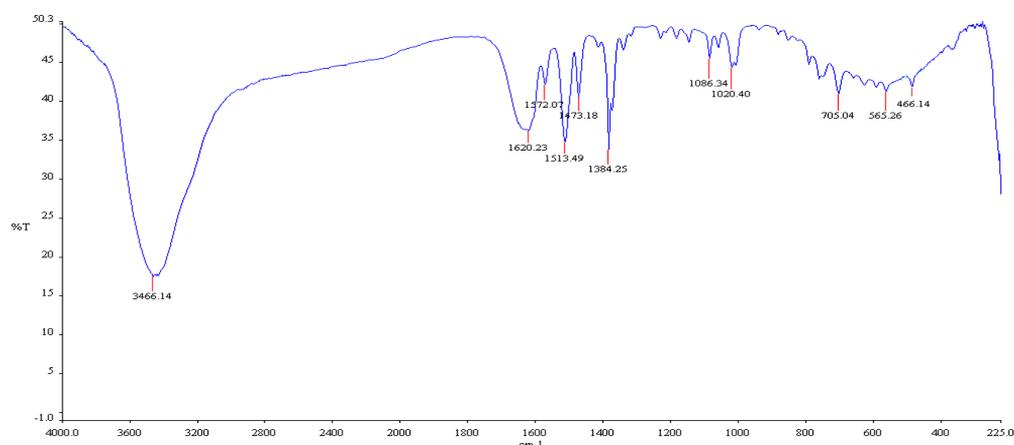


Fig. 6. IR spectrum of NiL2

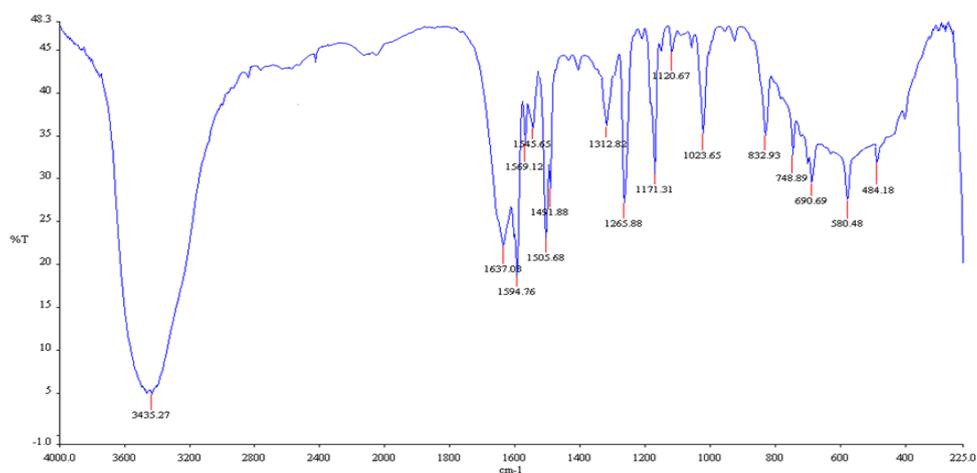


Fig. 7. IR spectrum of CuL2

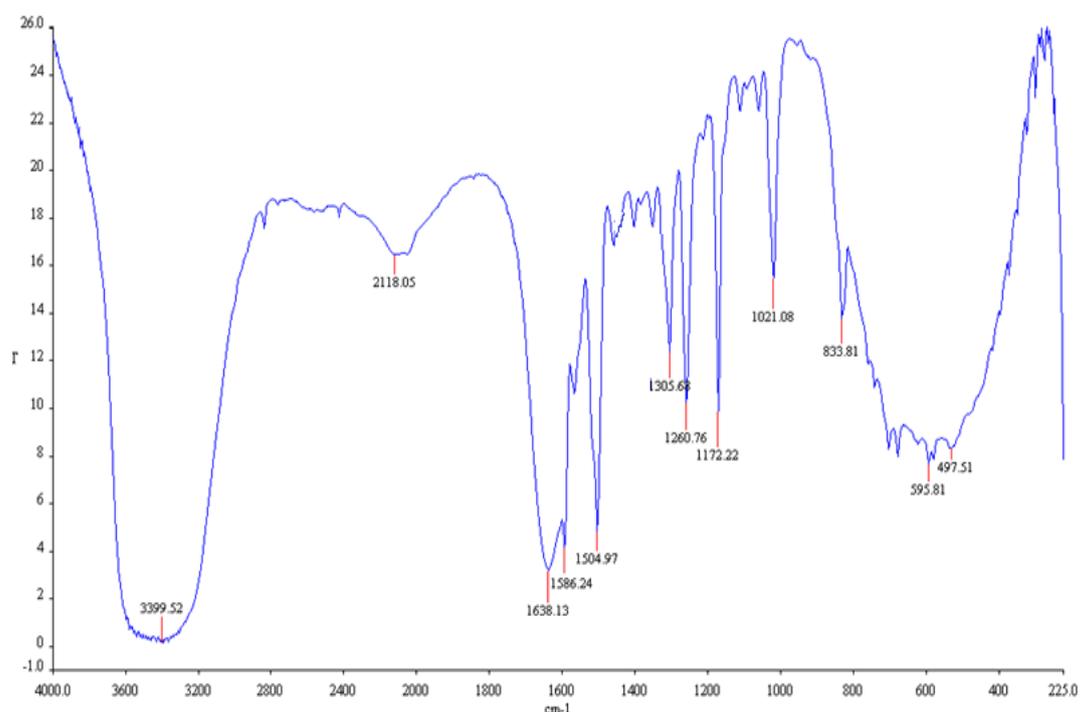


Fig. 8. IR spectrum of ZnL2

Table 2. Key Infrared bands (cm^{-1}) of the ligands (L1 and L2) and their metal complexes

Ligand/ Complexes	$\nu(\text{NH})$	$\nu(\text{C}=\text{O})$	$\nu(\text{C}=\text{N})$	$\nu(\text{M}-\text{O})$	$\nu(\text{M}-\text{N})$
L1	3192	1665	1605	--	--
L2	3272	1649	1620	--	--
NiL1	3467	1635	1586	572	467
NiL2	3466	1620	1572	565	466
CuL1	3435	1619	1574	566	413
CuL2	3435	1637	1594	580	484
ZnL1	3466	1660	1600	523	435
ZnL2	3399	1638	1586	595	497

3.2 Electronic Spectra

The L1 ligand showed two distinct bands at 274 and 323 nm, which were for $\pi-\pi^*$ and $n-\pi^*$ transitions, respectively. Like L1 ligand, all complexes showed these two transitions. The band due to $n-\pi^*$ transition was observed at a longer wavelength which could be due to the involvement of the azomethine group in chelation. The CuL1 and NiL1 complexes exhibit bands at 490 nm and 525 nm. The band located at 490 nm for the CuL1 complex is due to the ${}^2B_{1g} \rightarrow {}^2E_g$ transition whereas the band positioned at 525 nm for the NiL1 complex is for the ${}^1A_{1g} \rightarrow {}^1A_{2g}$ transition [29-30]. The magnetic susceptibility together with UV-Vis spectra

supports the square planar geometry around the CuL1 and NiL1 complexes [22-23]. On the other, the ZnL1 showed a CT band at 374 nm. Like L1, the L2 ligand also exhibits two bands at 266 nm and 330 nm, which are due to $\pi-\pi^*$ and $n-\pi^*$ transitions. All complexes derived from the L2 ligand also showed the same transitions as the L1 derived metal complexes. But the charge transfer (CT) band near at 374 nm was not observed in the case of the ZnL2 complex. However, all characterizations mainly FT-IR, UV-Vis and magnetic susceptibility measurements support the tetrahedral environment of the Zn^{2+} complexes [24-25]. All bands with proper assignments have shown in Table 3 and Figs. 9-10.

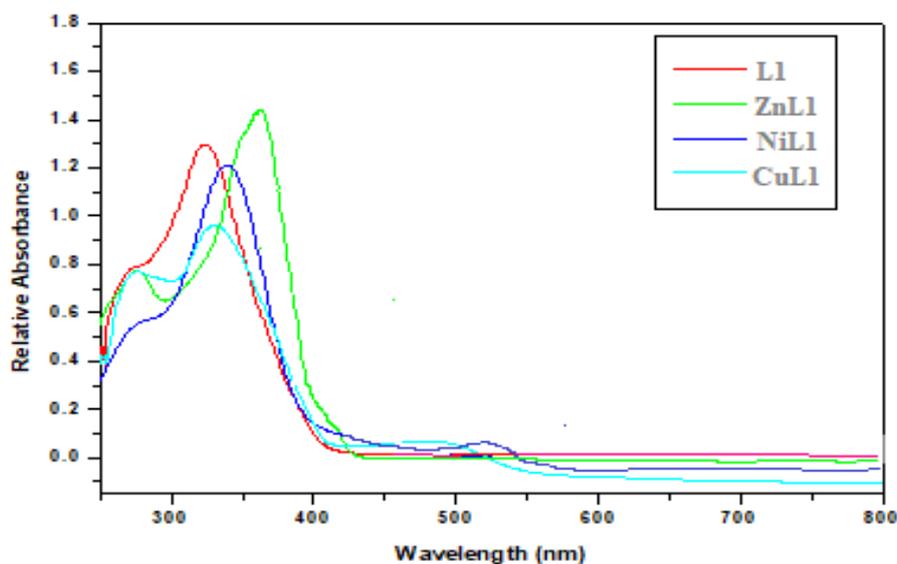


Fig. 9. UV-Vis spectra of L1 and its metal complexes

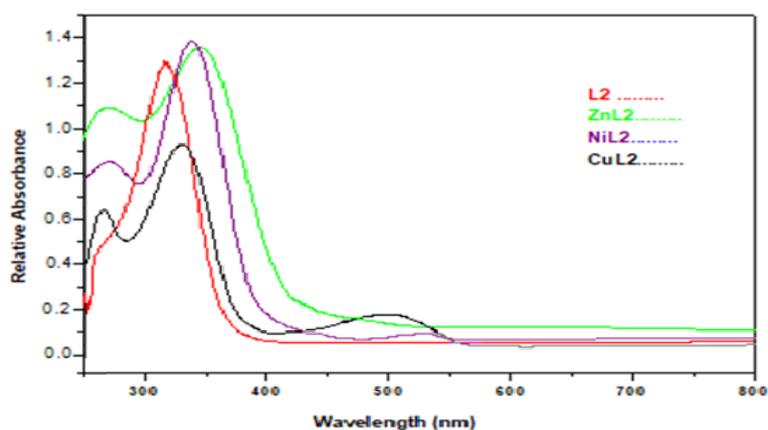


Fig. 10. UV-Vis spectra of L2 and its metal complexes

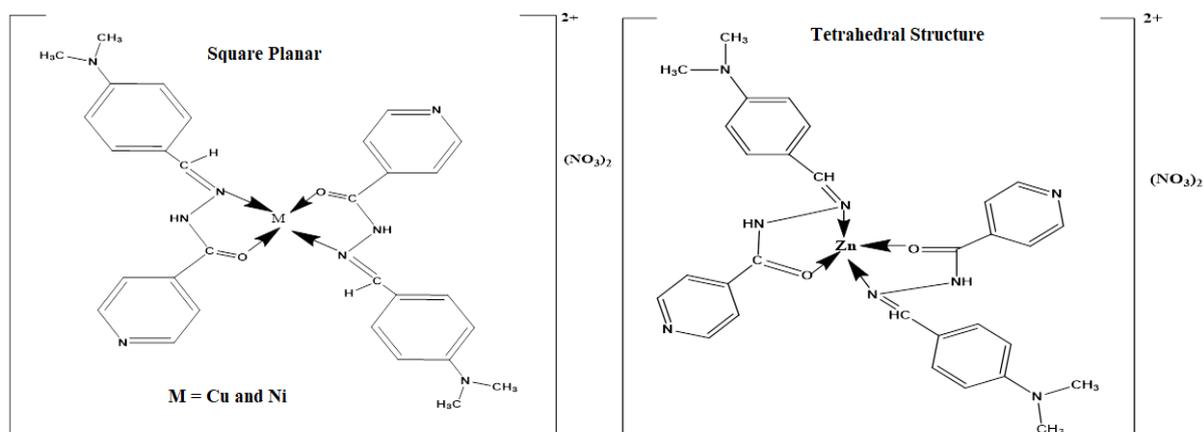
Table 3. Key UV bands (nm) of ligands (L1 and L2) and their metal complexes

Ligand/ Complexes	Band Position (nm)	Assignment	μ_{eff} (BM)	Geometry
L1	274	$\pi \rightarrow \pi^*$		
	323	$n \rightarrow \pi^*$		
L2	266	$\pi \rightarrow \pi^*$		
	330	$n \rightarrow \pi^*$		
NiL1	280	$\pi \rightarrow \pi^*$	Dia	Square planar
	340	$n \rightarrow \pi^*$		
	525	${}^1A_{1g} \rightarrow {}^1A_{2g}$		
NiL2	271	$\pi \rightarrow \pi^*$	Dia	Square planar
	338	$n \rightarrow \pi^*$		
	535	${}^1A_{1g} \rightarrow {}^1A_{2g}$		

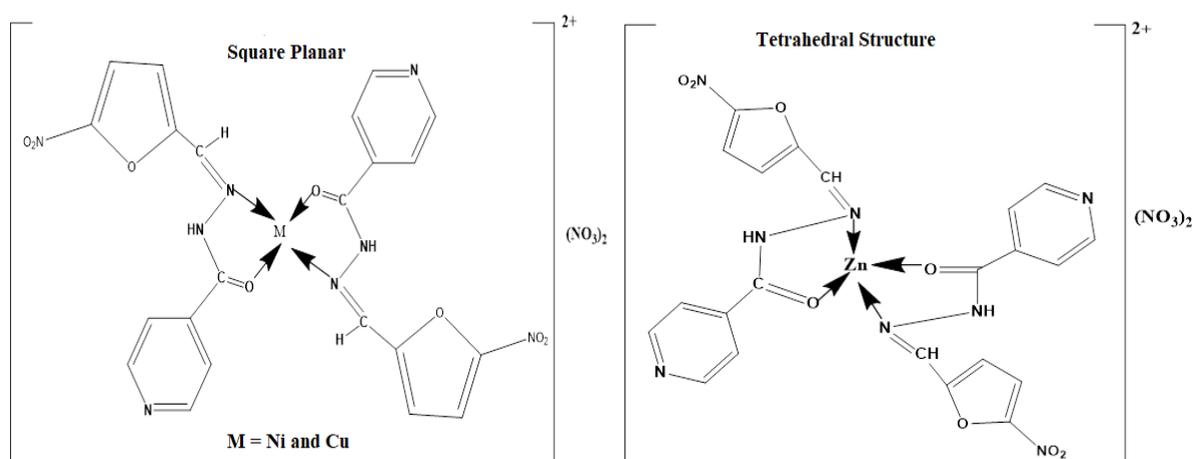
Ligand/ Complexes	Band Position (nm)	Assignment	μ_{eff} (BM)	Geometry
CuL1	276	$\pi \rightarrow \pi^*$	1.90	Square planar
	330	$n \rightarrow \pi^*$		
	490	${}^2B_{1g} \rightarrow {}^2E_g$		
CuL2	270	$\pi \rightarrow \pi^*$	1.87	Square planar
	338	$n \rightarrow \pi^*$		
	500	${}^2B_{1g} \rightarrow {}^2E_g$		
ZnL1	276	$\pi \rightarrow \pi^*$	Dia	Tetrahedral
	353	$n \rightarrow \pi^*$		
	374	CT		
ZnL2	270	$\pi \rightarrow \pi^*$	Dia	Tetrahedral
	345	$n \rightarrow \pi^*$		

Proposed Structure: On the basis of the above characterizations, the following structures can be proposed for the produced metal complexes.

Proposed structures for the complexes, $[M(L1)_2](NO_3)_2$:



Proposed structures for the complexes, $[M(L2)_2](NO_3)_2$:



3.3. Antibacterial Activity

The antibacterial activity of the two ligands (L1 and L2) and their metal complexes against *Escherichia coli* (Gram negative) and *Staphylococcus aureus* (Gram positive) was investigated. The diameter of the inhibitory zone was measured in millimeters, and the results of their antibacterial activity have presented in Table 4. The ligand L1 and its metal complexes did not show any zone of inhibition against *E. coli* (Fig. 11) whereas the L2 and its metal complexes showed good activity against *E. coli* and the following trend is observed: Kanamycin-30 > CuL2 > ZnL2 > NiL2 > L2 (Fig. 12). On the other hand, both ligands and their metal complexes showed good activity against *S. aureus*. The ZnL1 complex among all metal complexes synthesized from the L1 ligand, showed the highest antibacterial activity against *S. aureus*. In the case of the L2 derived metal complexes, the CuL2 complex exhibited better antibacterial activity against *S. aureus* than that of Kanamycin-30. The following trend is observed: CuL2 > Kanamycin-30 > NiL2 > ZnL2 > L2. J. N. Yong has earlier documented the antibacterial activity of ligand L1 against *E. coli* and *S. aureus*

bacteria. According to their findings, the L1 ligand had excellent action against *E. coli* but no zone of inhibition against *S. aureus*. When compared to our findings, their acquired results are completely contrary [15]. Several ideas have been proposed to explain the biological activity of different transition metal coordination complexes. Increased antibacterial activity of metal (II) complexes may be a result of the metal ion's influence on the normal condition of the bacterial cell process. Several studies have revealed that the structural components with extra (C=N) bonds to nitrogen and oxygen donor systems decrease enzyme activity because of metal coordination. Chelation increases the lipophilicity of the central metal ion, hence enhancing the hydrophobicity and liposolubility of the complex. This makes it more likely that the complex substance will penetrate the lipid layers of the cell membrane of the microorganisms. As soon as the complexes enter the cell, they begin to obstruct the metal-binding sites that are present in the enzymes of the bacteria. In turn, this disrupts the cell's respiration process by inhibiting protein synthesis, which limits the organism's growth [31-35].

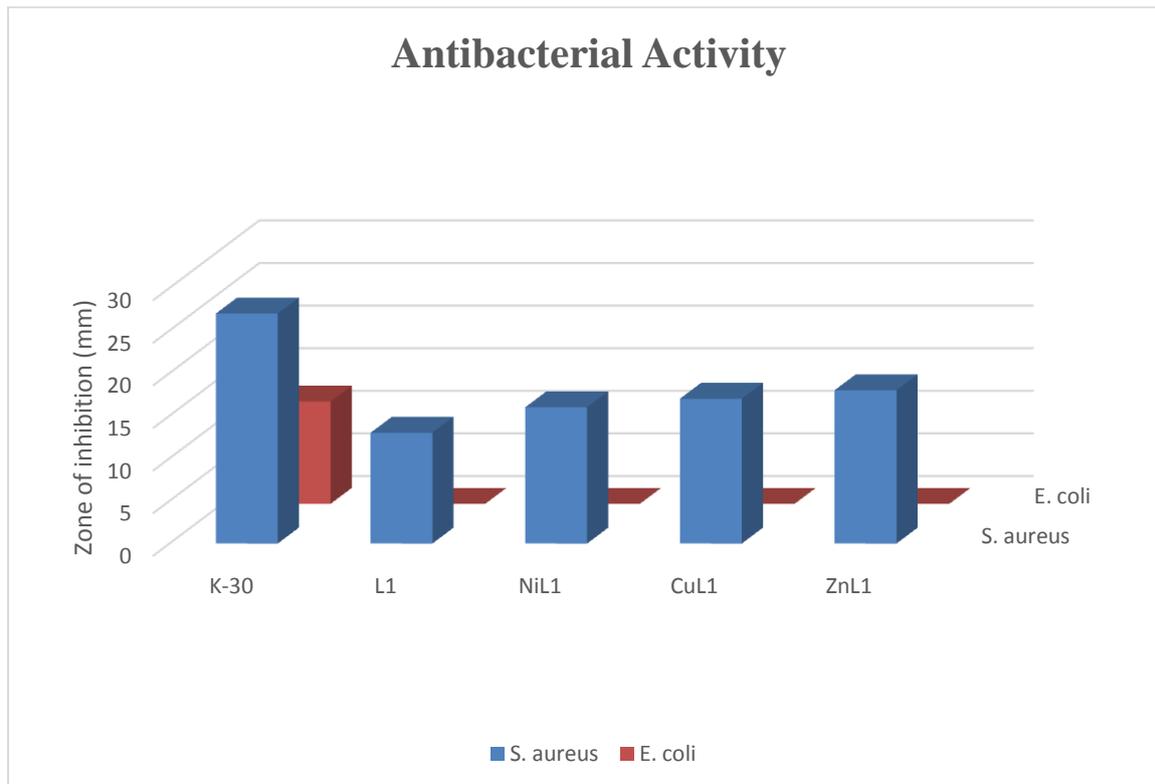
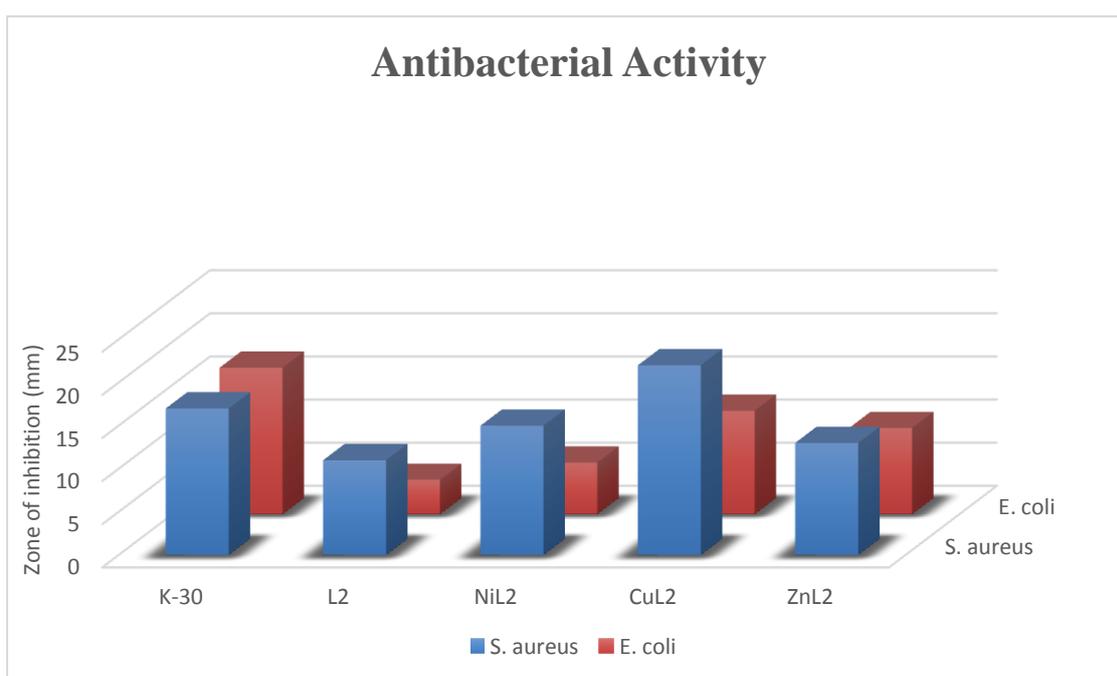


Fig. 11. Graphical representation of antibacterial activity of ligand L1 and its metal complexes against mentioned bacteria with standard Kanamycin-30 (K-30)

Table 4. Antibacterial activities of the two ligands (L1 and L2) and their metal complexes

Diameter of Zone of Inhibition (mm) of tested compounds (100µg/disc)		
Compounds	Gram Negative	Gram Positive
	<i>Escherichia coli</i>	<i>Staphylococcus aureus</i>
Kanamycin (30 µg/disc)	12	27
Ligand (L1)	-ve	13
NiL1	-ve	16
CuL1	-ve	17
ZnL1	-ve	18
Ligand (L2)	04	11
NiL2	06	15
CuL2	12	22
ZnL2	10	13
Kanamycin (30 µg/disc)	17	17

**Fig. 12. Graphical representation of antibacterial activity of ligand L2 and its metal complexes against mentioned bacteria with standard Kanamycin-30 (K-30)**

3.4 Antioxidant Activity

The antioxidant properties of L1 and its metal ion complexes were evaluated using the free radical molecule 1, 1-Diphenyl-1-picryl hydrazyl (DPPH). Table 5 displays the percentage of DPPH radical scavenging activity of L1, metal complexes, as well as BHT (butylated hydroxytoluene) as a reference. According to the findings, all of the metal complexes showed moderate DPPH radical scavenging activity (Figs. 13-14). The order can be expressed as BHT > CuL1 > NiL1 > ZnL1 > L1. Same trend was also observed in the case of the metal complexes derived from the L2 ligand. Both cases the Cu²⁺ complexes have

higher antioxidant activity than other synthesized complexes. DPPH scavenging activity of the metal complexes obtained from the ligand (L1 or L2) is much greater than that of the free ligand (L1 or L2), suggesting that complexes are good free radical scavengers and antioxidants than free ligand (L1 or L2) but lower when compared to standard BHT. The radical scavenging activity of the standard BHT, as well as the metal complexes, was shown to increase in a dose-dependent way. The chelation of the ligands with transition metal ions resulted in a considerable enhancement in the antioxidant capabilities of the ligands. The oxidizing potentials (OP) of the complexes are associated with the presence of

chemicals that exert their effects by breaking the chain of free radicals via the contribution of hydrogen atoms [32, 36]. So, the outcomes of this study imply that the CuL1 and CuL2 complexes may be employed to treat

pathological illnesses induced by oxidative stress. The IC₅₀ value of all mentioned compounds in combination with standard BHT has been calculated and shown in Tables 5-6.

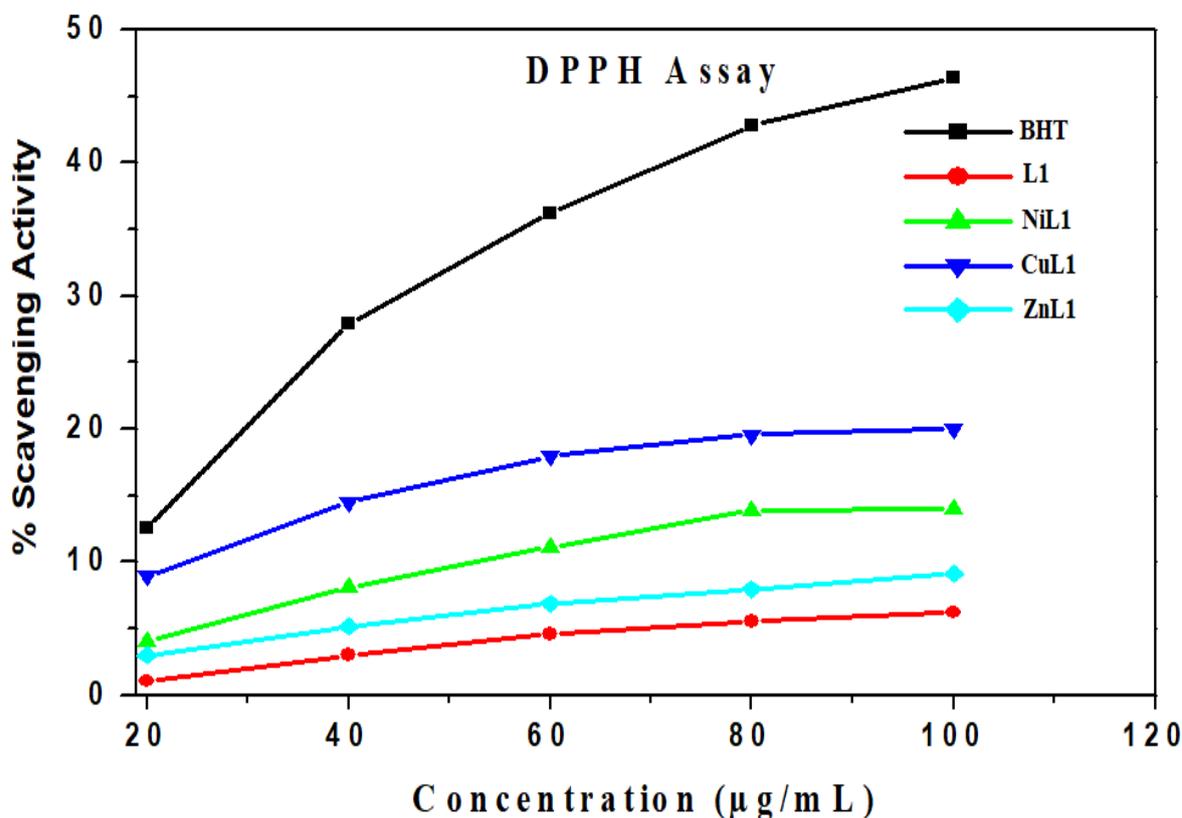


Fig. 13. DPPH radical scavenging activity of the L1 and its metal ions complexes at different concentrations (20, 40, 60, 80, and 100 µg/mL) with standard BHT

Table 5. % of Scavenging activity of BHT, ligand L1, and its metal complexes

Conc. (µg/mL)	% BHT	% L1	% NiL1	% CuL1	% ZnL1
20	12.54	1.04	4.03	8.96	3.01
40	27.88	2.99	8.11	14.54	5.15
60	36.21	4.61	11.14	17.93	6.89
80	42.76	5.54	13.89	19.56	7.95
100	46.38	6.21	14.04	20.00	9.11
IC ₅₀ Value:	100.81	771.92	368.20	309.46	641.04

Table 6. % of Scavenging activity of BHT, ligand L2, and its metal complexes

Conc. (µg/mL)	% BHT	% L2	% NiL2	% CuL2	% ZnL2
20	13.29	2.03	7.21	10.02	3.80
40	31.97	3.88	10.29	22.25	6.71
60	41.20	4.03	12.23	27.03	8.00
80	45.23	5.16	14.03	28.26	9.86
100	46.36	6.29	15.65	28.75	9.73
IC ₅₀ Value:	96.25	993.10	429.72	182.98	624.27

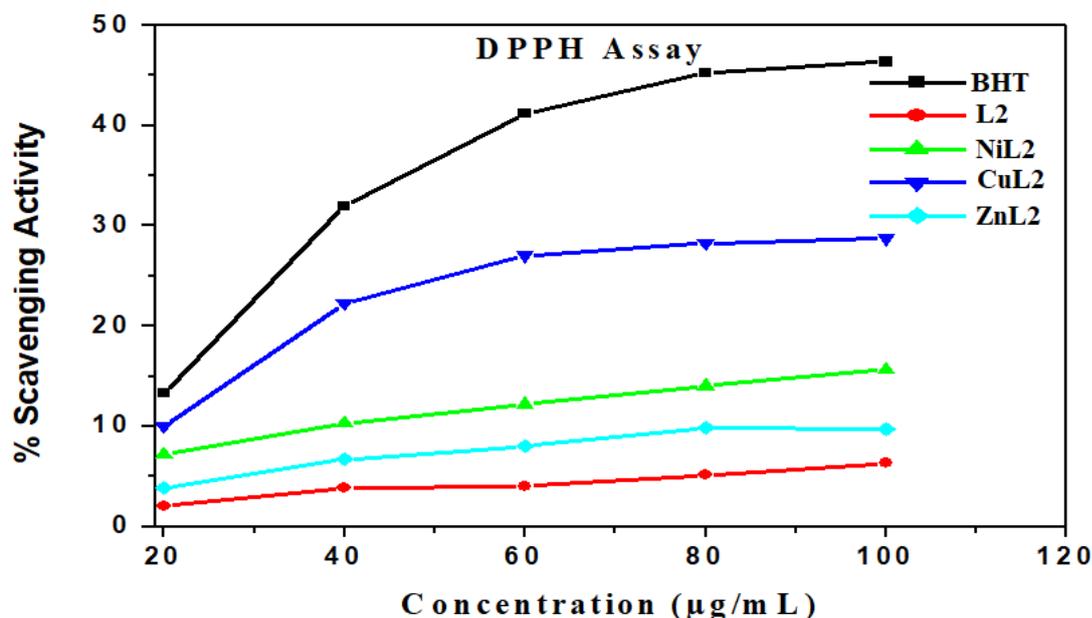


Fig. 14. DPPH radical scavenging activity of the L2 and its metal ions complexes at different concentrations (20, 40, 60, 80, and 100 µg/mL) with standard BHT

4. CONCLUSION

Isoniazid based two bidentate Schiff base ligands (L1 and L2) and their divalent metal complexes were successfully synthesized and also characterized. The L1 and L2 ligands coordinated to the central metal (II) ions through carbonyl oxygen (O) and azomethine nitrogen (N) donor atoms. No inhibition zone was observed in the case of the L1 ligand and its metal complexes against *E. coli* (Gram negative). But all complexes showed good antibacterial activity against *S. aureus*. The ZnL1 complex among all metal complexes synthesized from the L1 ligand, showed the highest antibacterial activity against *S. aureus*. On the other hand, the CuL2 complex exhibited better antibacterial activity against *S. aureus* than that of Kanamycin-30. For the both ligands, the Cu²⁺ complexes exhibited the highest antioxidant efficacy. Before considering copper complexes as potentially useful antibacterial treatments for people, there has to be sufficient research conducted on the toxicity of these compounds to humans.

ACKNOWLEDGEMENTS

The authors are thankful to the Chairman, Department of Chemistry, University of Rajshahi, Bangladesh for the laboratory Facilities.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Witkop B, Ramachandran LK. Progress in non-enzymatic selective modification and cleavage of proteins, *Metabolism*, 1964, 13(10): 1016-1025.
2. Morton RA, Pitt GA. Studies on rhodopsin. 9. pH and the hydrolysis of indicator yellow. *Biochemical Journal*. 1955 Jan;59(1):128.
3. Fridovich I, Westheimer FH. On the mechanism of the enzymatic decarboxylation of acetoacetate. II. *Journal of the American Chemical Society*. 1962 Aug;84(16):3208-9.
4. Hammes GG, Fasella P. A kinetic study of glutamic-aspartic transaminase. *Journal of the American Chemical Society*. 1962 Dec;84(24):4644-50.
5. Radfard R, Abedi A. Synthesis and characterization of new Schiff bases of ethylenediamine and benzaldehyde derivatives, along with their iron complexes. *Journal of Applied Chemical Research*. 2015 May 1;9(2):59-66.

6. Obasuyi EI, Iyekowa O. Synthesis, Characterization and Antimicrobial of Schiff Base from 5-Bromo-Salicylaldehyde and P-Toluidine. *Journal of Applied Sciences and Environmental Management*. 2018;22(11):1733-6.
7. Rao VK, Reddy SS, Krishna BS, Naidu KR, Raju CN, Ghosh SK. Synthesis of Schiff's bases in aqueous medium: a green alternative approach with effective mass yield and high reaction rates. *Green Chemistry Letters and Reviews*. 2010 Sep 1;3(3):217-23.
8. Saadeh HA, Shaireh EA, Mosleh IM, Al-Bakri AG, Mubarak MS. Synthesis, characterization and biological activity of Schiff bases derived from metronidazole. *Medicinal Chemistry Research*. 2012 Oct;21(10):2969-74.
9. Singh NK, Singh DK, Singh SB. Synthesis, Characterization, And Biological Studies On Cobalt (II), Nickel (II), Copper (II), And Zinc (II) Complexes With N-Picol Inoyl-N'-Thiobenzoyl Hydrazine. Synthesis and reactivity in inorganic and metal-organic chemistry. 2002 May 28;32(4):703-20.
10. Sharma RP, Kothari AK, Sharma NK. Acneform eruptions and antitubercular drugs. *Indian Journal of Dermatology, Venereology and Leprology*. 1995 Jan 1;61(1):26-7.
11. Dilworth JR. The coordination chemistry of substituted hydrazines. *Coordination Chemistry Reviews*. 1976 Oct 1;21(1):29-62.
12. Merchant JR, Chothia DS. Antituberculous Schiff bases. *Journal of Medicinal Chemistry*. 1970 Mar;13(2):335-6.
13. Biradar NS, Havinale BR. Dimeric square planar complexes of Cu (II) with aroyl hydrazones. *Inorganica Chimica Acta*. 1976 Jan 1;17:157-60.
14. Ashrafuzzaman MD, Camellia FK, Mahmud AA, Pramanik MD, Nahar K, HAQUE M. Bioactive Mixed Ligand Metal Complexes Of Cu (II), Ni (II), And Zn (II) Ions: Synthesis, Characterization, Antimicrobial And Antioxidant Properties. *Journal of the Chilean Chemical Society*. 2021 Sep;66(3):5295-9.
15. Yong JN, Mainsah EN, Ntum SJ, Ndifon P. Synthesis, characterization and antibacterial studies of some isoniazid-derived schiff bases. *International Research Journal of Pure and Applied Chemistry*. 2016;12(1):1-8.
16. Hossain MS, Islam MA, Zakaria CM, Haque MM, M. A. Mannan, M. K. Zahan. Synthesis, spectral and thermal characterization with antimicrobial studies on Mn(II), Fe(II), Co(II) and Sn(II) complexes of tridentate N,O coordinating novel Schiff base ligand, *J. Chem. Bio. Phy. Sci*. 2016, 6(1): 041-045.
17. Shiraj-U-Ddaula M, Islam MA, Aktar S, Islam MK, Al-Bari MA, Haque MM, Kudrat-E-Zahan M. Synthesis, characterization and antimicrobial activity of Cd (II), Ni (II), Co (II) and Zr (IV) metal complexes of Schiff Base Ligand Derived from Diethylenetriamine and Isatin. *Asian Journal of Research in Chemistry*. 2014 Jul 1;7(7):1.
18. Bingöl M, Turan N. Schiff base and metal (II) complexes containing thiophene-3-carboxylate: Synthesis, characterization and antioxidant activities. *Journal of Molecular Structure*. 2020 Apr 5;1205:127542.
19. Leaves L, Leaves L. Antioxidant activity by DPPH radical scavenging method of *ageratum conyzoides*. *American Journal of Ethnomedicine*. 2014;1(4):244-9.
20. Ali I, Wani WA, Saleem K. Empirical formulae to molecular structures of metal complexes by molar conductance. Synthesis and reactivity in inorganic, metal-organic, and nano-metal chemistry. 2013 Oct 21;43(9):1162-70.
21. Dianu ML, Kriza A, Stanica N, Musuc AM. Transition metal M (II) complexes with isonicotinic acid 2-(9-anthrylmethylene)-hydrazide. *J. Serb. Chem. Soc*. 2010 Jan 1;75(11):1515-31.
22. Raman N, Dhaweethu Raja J, Sakthivel A. Synthesis, spectral characterization of Schiff base transition metal complexes: DNA cleavage and antimicrobial activity studies. *Journal of Chemical sciences*. 2007 Jul;119(4):303-10.
23. Chandra S, Gupta LK, Jain D. Spectroscopic studies on Mn (II), Co (II), Ni (II), and Cu (II) complexes with N-donor tetradentate (N4) macrocyclic ligand derived from ethylcinnamate moiety. *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*. 2004 Aug 1;60(10):2411-7.
24. Mitu L, N. Mohamed, S. Iqbal, N. Raman, I. Muhammad I, S. K. Sharma. Template Synthesis, Characterization and Biological Activity of Cu(II), Ni(II), Co(II), Zn(II)

- Complexes with Isonicotinoylhydrazone. E- J. Chem. 2010;7(1):227-233.
25. Afsan F, Dalia SA, S. Hossain, S. Sarker, K. E. Zahan. Synthesis, Spectral and Thermal Characterization of Selected Metal Complexes Containing Schiff Base Ligands with Antimicrobial Activities, Asian J. Chem. Sci. 2018;4(3):1-19.
 26. Yadav M, Sharma S, Devi J. Designing, spectroscopic characterization, biological screening and antioxidant activity of mononuclear transition metal complexes of bidentate Schiff base hydrazones. Journal of Chemical Sciences. 2021 Mar;133(1):1-22.
 27. Burns GR. Metal complexes of thiocarbonylhydrazide. Inorganic Chemistry. 1968 Feb;7(2):277-83.
 28. Khalil MM, Ismail EH, Mohamed GG, Zayed EM, Badr A. Synthesis and characterization of a novel schiff base metal complexes and their application in determination of iron in different types of natural water. Open Journal of Inorganic Chemistry. 2012 Apr 1;2(2):13.
 29. Abd-Elzaher MM. Synthesis, characterization, and antimicrobial activity of cobalt (II), nickel (II), copper (II) and zinc (II) complexes with ferrocenyl Schiff bases containing a phenol moiety, Appl. Organometall. Chem. 2004;18:149-155.
 30. Lever AP. Inorganic electronic spectroscopy. Studies in physical and theoretical chemistry. 1984;33..
 31. Patel MN, Pansuriya PB, Parmar PA, Gandhi DS. Synthesis, characterization, and thermal and biocidal aspects of drug-based metal complexes. Pharmaceutical chemistry journal. 2008 Dec;42(12):687-92.
 32. Al-Amiery AA, Al-Majedy YK, Ibrahim HH, Al-Tamimi AA. Antioxidant, antimicrobial, and theoretical studies of the thiosemicarbazone derivative Schiff base 2-(2-imino-1-methylimidazolidin-4-ylidene) hydrazinecarbothioamide (IMHC). Organic and medicinal chemistry letters. 2012 Dec;2(1):1-7.
 33. Jesmin M, Ali MM, Salahuddin MS, Habib MR, Khanam JA. Antimicrobial activity of some schiff bases derived from benzoin, salicylaldehyde, aminophenol and 2, 4 dinitrophenyl hydrazine. Mycobiology. 2008 Mar 1;36(1):70-3.
 34. El-Sherif AA, Eldebss TM. Synthesis, spectral characterization, solution equilibria, in vitro antibacterial and cytotoxic activities of Cu (II), Ni (II), Mn (II), Co (II) and Zn (II) complexes with Schiff base derived from 5-bromosalicylaldehyde and 2-aminomethylthiophene. Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy. 2011 Sep 1;79(5):1803-14.
 35. Bagihalli GB, Avaji PG, Patil SA, Badami PS. Synthesis, spectral characterization, in vitro antibacterial, antifungal and cytotoxic activities of Co (II), Ni (II) and Cu (II) complexes with 1, 2, 4-triazole Schiff bases. European journal of medicinal chemistry. 2008 Dec 1;43(12):2639-49.
 36. Hernandez JA, Jiménez A, Mullineaux P, Sevilla F. Tolerance of pea (*Pisum sativum* L.) to long-term salt stress is associated with induction of antioxidant defences. Plant, cell & environment. 2000 Aug;23(8):853-62.

© 2022 Camellia et al.; This is an Open Access article distributed under the terms of the Creative Commons Attribution License (<http://creativecommons.org/licenses/by/4.0>), which permits unrestricted use, distribution, and reproduction in any medium, provided the original work is properly cited.

Peer-review history:
The peer review history for this paper can be accessed here:
<https://www.sdiarticle5.com/review-history/88447>