

**COMMISSIONERATE OF COLLEGIATE EDUCATION
GOVERNMENT OF TELANGANA**

JIGNASA - STUDENT STUDY PROJECT

**Synthesis, Spectral Characterization Of Mononuclear Copper (II)
Complex And Antimicrobial Studies With 2-((E)-(5-Cyclohexyl-2-
Methoxyphenylimino)Methyl)Phenol**

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(Re-Accredited by NAAC with 'A' grade]

HANAMKONDA, WARANGAL(U)

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Date: 24.01.2020

CERTIFICATE

Certified that the work embodied in this study project entitled "**Synthesis, spectral characterization of mononuclear copper (II) complex and antimicrobial studies with 2-((E)-(5-cyclohexyl-2-methoxyphenylimino)methyl) phenol**" has been carried out by **G. Nikhil Krishna, MPC-III, G. Uday Kiran, BtBZC-III, M. Roshini, MZC-II, CH. Om Shireesh, MPC-II, M. Pravalika, MPC-I and G. Vinay, MBC-I** under the supervision of **K. Jagadesh Babu and K. Suneetha** in the Department of Chemistry, Kakatiya Government College, Hanamkonda.

PRINCIPAL

Synthesis, spectral characterization of mononuclear copper (II) complex and antimicrobial studies with 2-((E)-(5-cyclohexyl-2-methoxyphenylimino)methyl) phenol

Introduction

The interaction of small molecules, especially metal complexes, with biomolecules such as nucleic acid and proteins, due to their application in drug design has become prominent area of interest. Cancer is a major public health issue in many parts of the world. If recent global trends in the occurrence of cancer and population growth continue in the future, it is expected that there will be 23.6 million reports of new cancer diagnoses worldwide each year by 2030 [1]. Similarly the metal complexes have their own characteristic geometrical designs. It is believed that the type of coordinated ligands and the geometrical orientation of the ligands are crucial factors in promoting the interaction of a given metal complex with DNA[2, 3]. In general, the metal complexes of Schiff bases play a key role in understanding the coordination chemistry of transition metals. Particularly, the imine ($-C=N-$) group of Schiff base provides an opportunity for the splendid biological activities such as antimicrobial, antitumor and herbicidal activities[4-10]. The above facts and features help us to focus on designing a series of biologically active metal complexes such as, copper complex derived from 2-((E)-(5-cyclohexyl-2-methoxyphenylimino) methyl) phenol in the present investigation.

Materials and Instrumentation

All the starting materials (aldehyde and amine) are procured from Sigma-Aldrich Chemical Pvt. Ltd., with high purity and were used directly. Solvents used such as methanol, petroleum ether, acetone and chloroform were purchased from Merck and Hi media Ltd., and purified by standard procedures. Magnetic moments of the complexes were determined on a Gouy balance model 7550 using $Hg[Co(NCS)_4]$ as standard. Metal content of the complexes was estimated by atomic absorption spectroscopy using GBC Avanta 1.0 AAS. FT-IR spectra were recorded in the range $4000-250\text{ cm}^{-1}$ on Shimadzu IR Prestige-21 using KBr pellets. NMR spectra of the Schiff bases were recorded on Bruker 400 MHz NMR instrument using TMS as internal reference. ESI

mass spectra of all compounds were recorded on VG AUTOSPEC mass spectrometer. Melting points of the compounds were determined on a Polmon instrument (model No: MP-96). Electronic spectra were recorded on a Shimadzu UV-Vis 2600 spectrophotometer using DMSO as solvent.

Synthesis of Schiff baseligand

The synthesis of ligand was described in **Scheme 1**. Methanolic solution of 2-((E)-(5-cyclohexyl-2-methoxyphenylimino)methyl)phenol (10 mM) was magnetically stirred in a round bottom flask to which a drop wise addition of salicylaldehyde (10 mM) in 1:1 molar ratio. The reaction mixture was refluxed at 50–60 °C with constant stirring for 3-5 h and the purity of the compounds was tested by thin layer chromatography (TLC) using different solvent mixtures.

2-((E)-(5-cyclohexyl-2-methoxyphenylimino)methyl)phenol,

(C₂₀H₂₃NO₂), (HL^I): Yield: 75 %. IR (KBr): $\nu_{(\text{O-H})}$ 3430, $\nu_{(\text{CH=N})}$ 1613, $\nu_{(\text{C-O})}$ 1196 (Fig. 1). UV-Vis; $\lambda_{\text{max}}/\text{nm}$ (cm⁻¹): 260(38461), 343 (29154), 438 (22831) (Fig. 2). ¹H-NMR (400MHz, CDCl₃) (δ): 13.97 (s, 1H); 8.71 (s, 1H); 7.39-6.88 (Ar, 10H); 3.86 (s, 4H); 2.48 (1H); 1.87-1.41 (6H) (Fig. 3). ESI-MS (m/z): 310 [M+H]⁺ (Fig. 4). MP: 71°C.

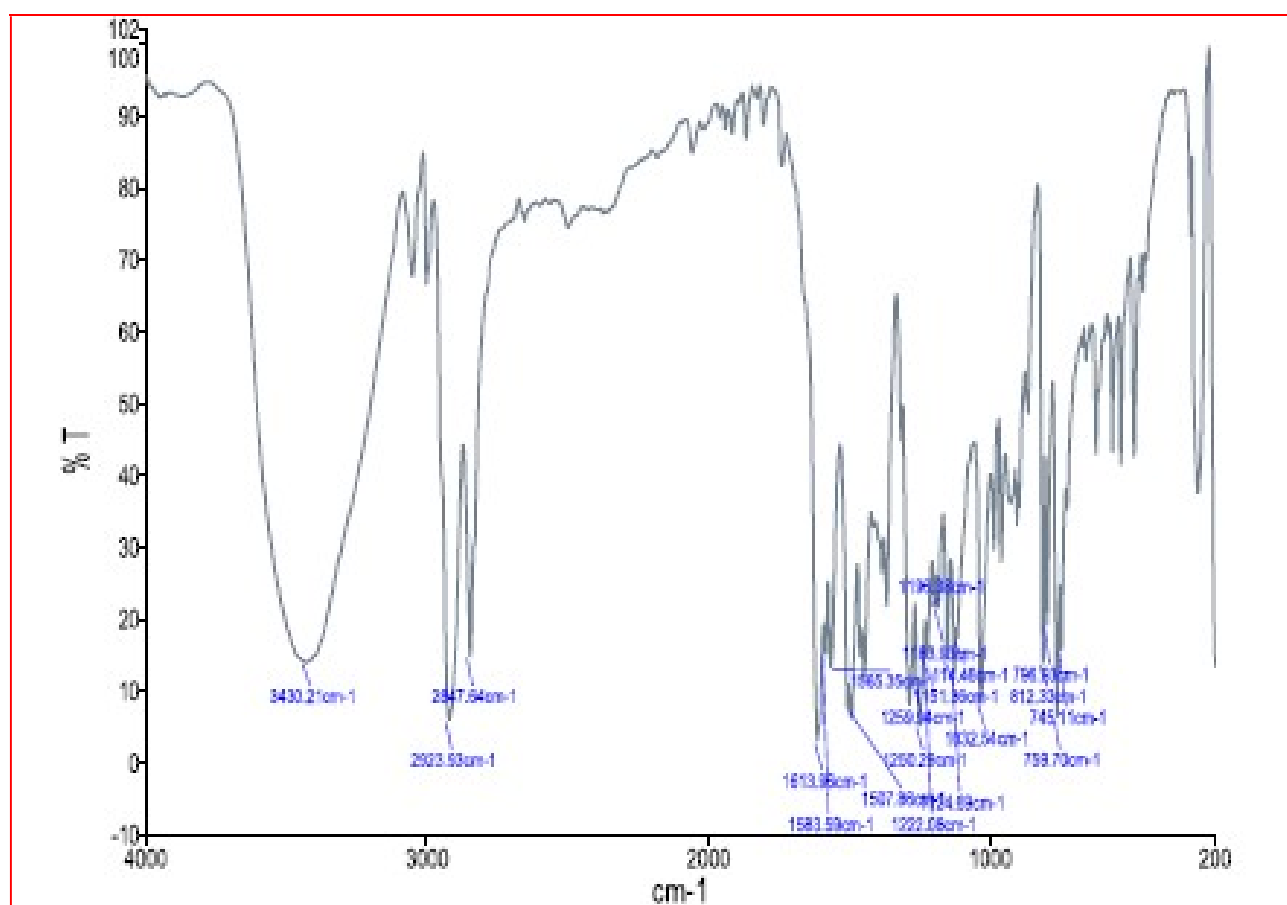


Fig. 1. FT-IR spectrum of ligand HL¹

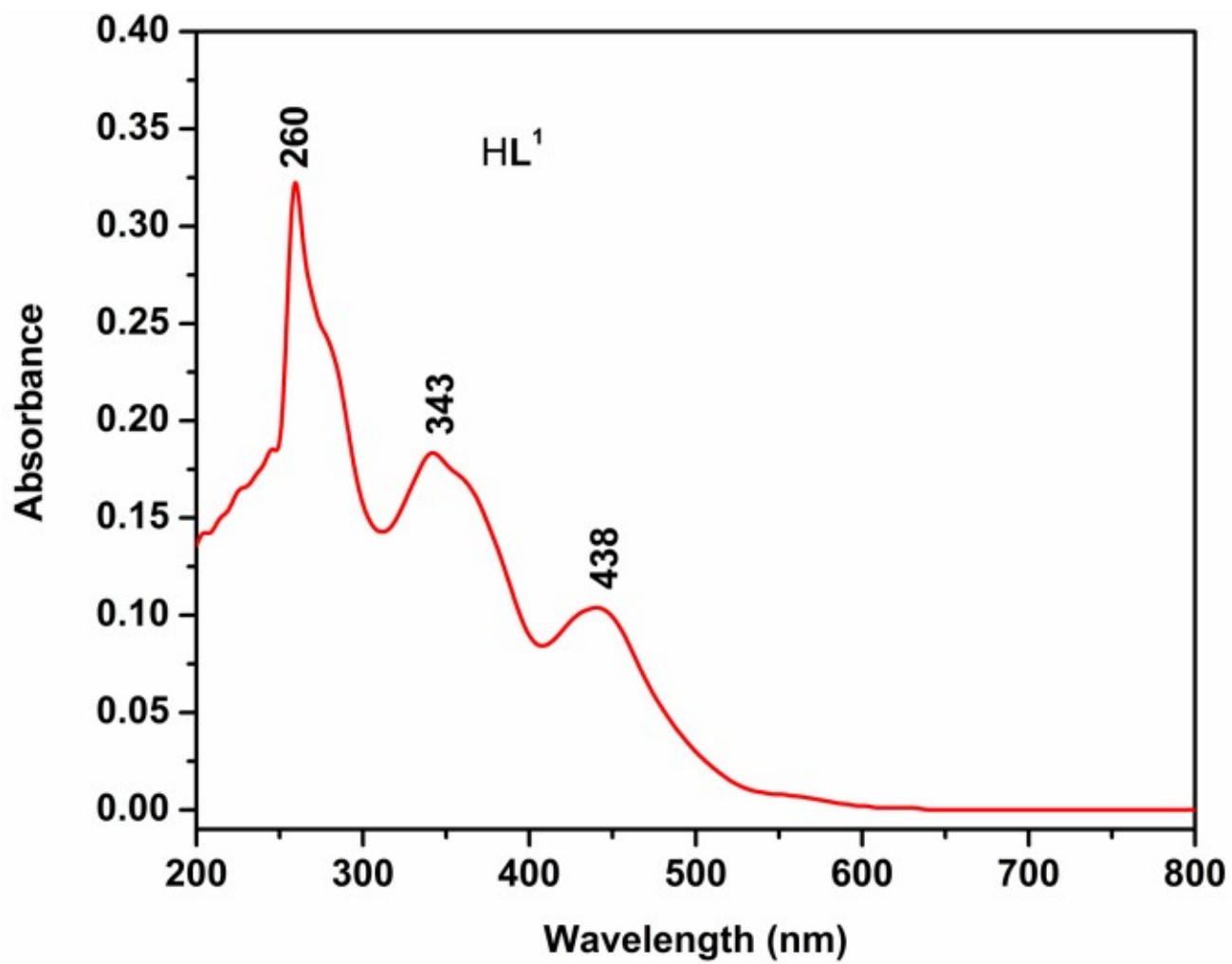


Fig. 2. UV-Vis spectrum of ligand HL¹

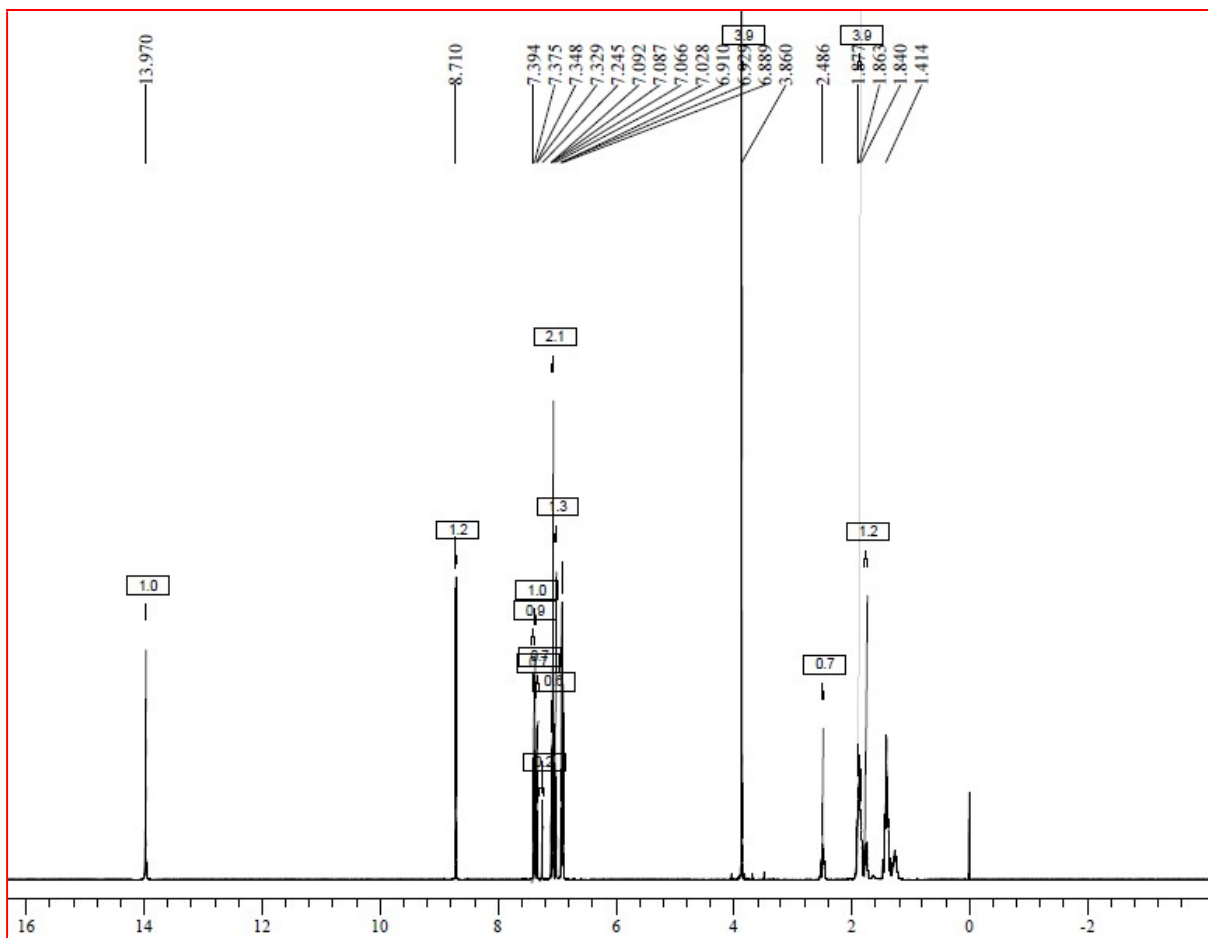


Fig.3. $^1\text{H-NMR}$ spectrum of ligand **HL**¹

Sample Name : DSB-CM-620
 Data File : 23012020.59.lcd
 Date Acquired : 1/23/2020 5:50:37 PM
 Batch File : 22012020.lcb

MS Spectrum
 D:\DATA\JAN-2020\23012020.59.lcd

Averaged ESI Positive+
 Spectrum Mode: Averaged 0.072-0.253(27-93)

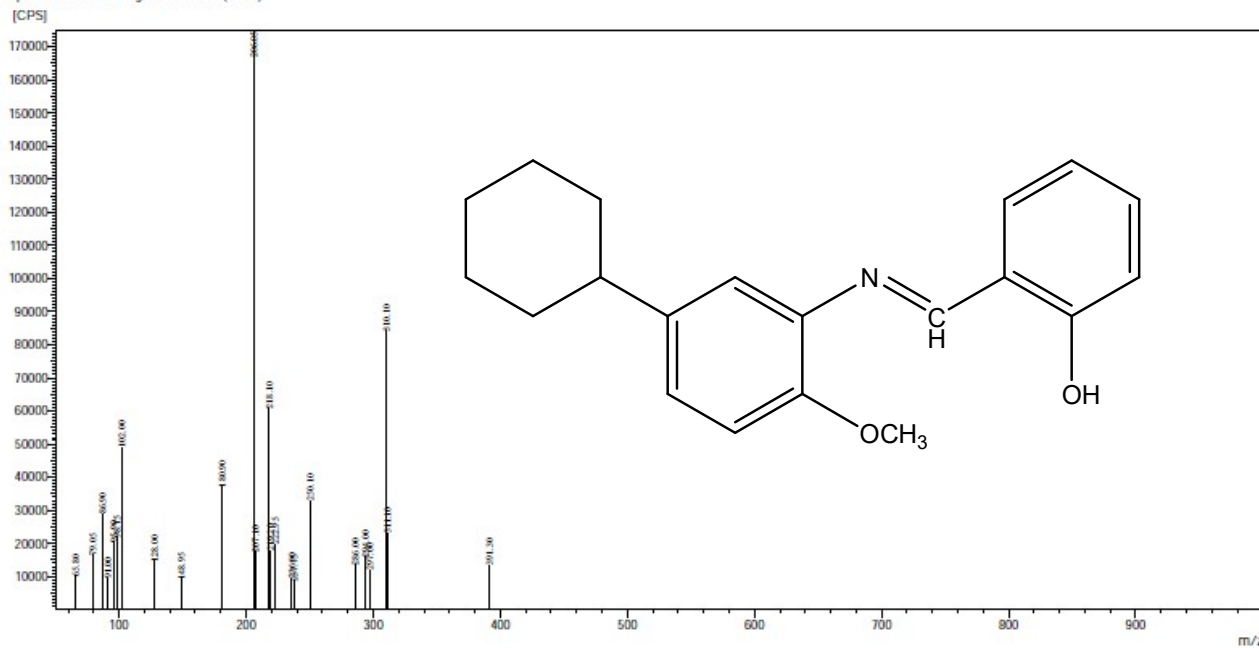


Fig. 4. Mass spectrum of ligand **HL**¹

Synthesis of binary metal complex

A hot methanolic solution (10 mM) of copper acetate monohydrate $[\text{Cu}(\text{CH}_3\text{COO})_2 \cdot \text{H}_2\text{O}]$ was added drop wise to a stirred hot methanolic solution of Schiff base ligand **HL**¹ (20mM) taken in 1:2 molar ratio. After addition, the solution turned into colour. After that, the reaction mixture was refluxed with stirring at 60–70 °C for 4-5 h. The obtained solid product was isolated, filtered and washed with petroleum ether and methanol. The metal complexes were dried in vacuum desiccators over anhydrous CaCl_2 . The synthetic procedure of Schiff base ligand and its binary metal complex was shown in **Scheme 1**.

$[\text{Cu}(\text{L}^1)_2] (\text{C}_{40}\text{H}_{44}\text{CuN}_2\text{O}_4) (\mathbf{1a})$:

Yield: 75 %. IR (KBr): $\nu_{(\text{CH}=\text{N})}$ 1616, $\nu_{(\text{C}-\text{O})}$ 1116, $\nu_{(\text{M}-\text{O})}$ 530, $\nu_{(\text{M}-\text{N})}$ 450 (Fig. 5). UV-Vis (DMSO) $\lambda_{\text{max}}/\text{nm}$ (cm^{-1}): 277(36101), 407(24570), 601(16638). (Fig. 6). μ_{eff} (BM): 1.71. ESI-MS (m/z): 681 $[\text{M}+\text{H}]^+$ (Fig. 7). MP: 180°C.

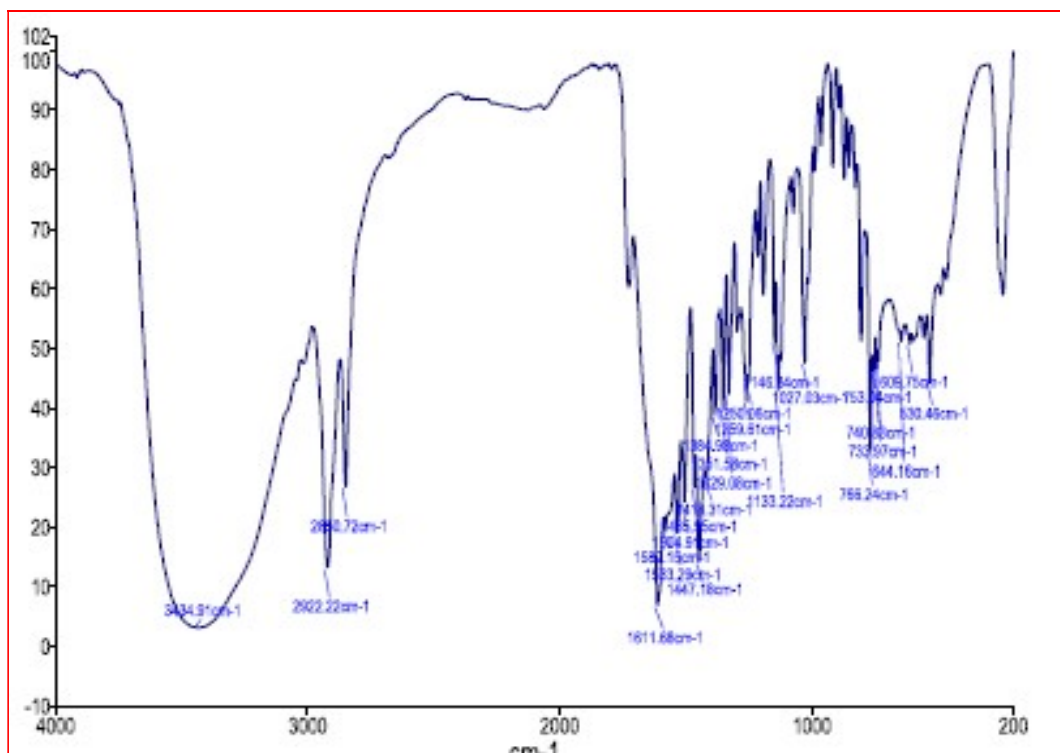


Fig. 5. FT-IR spectrum of complex 1a

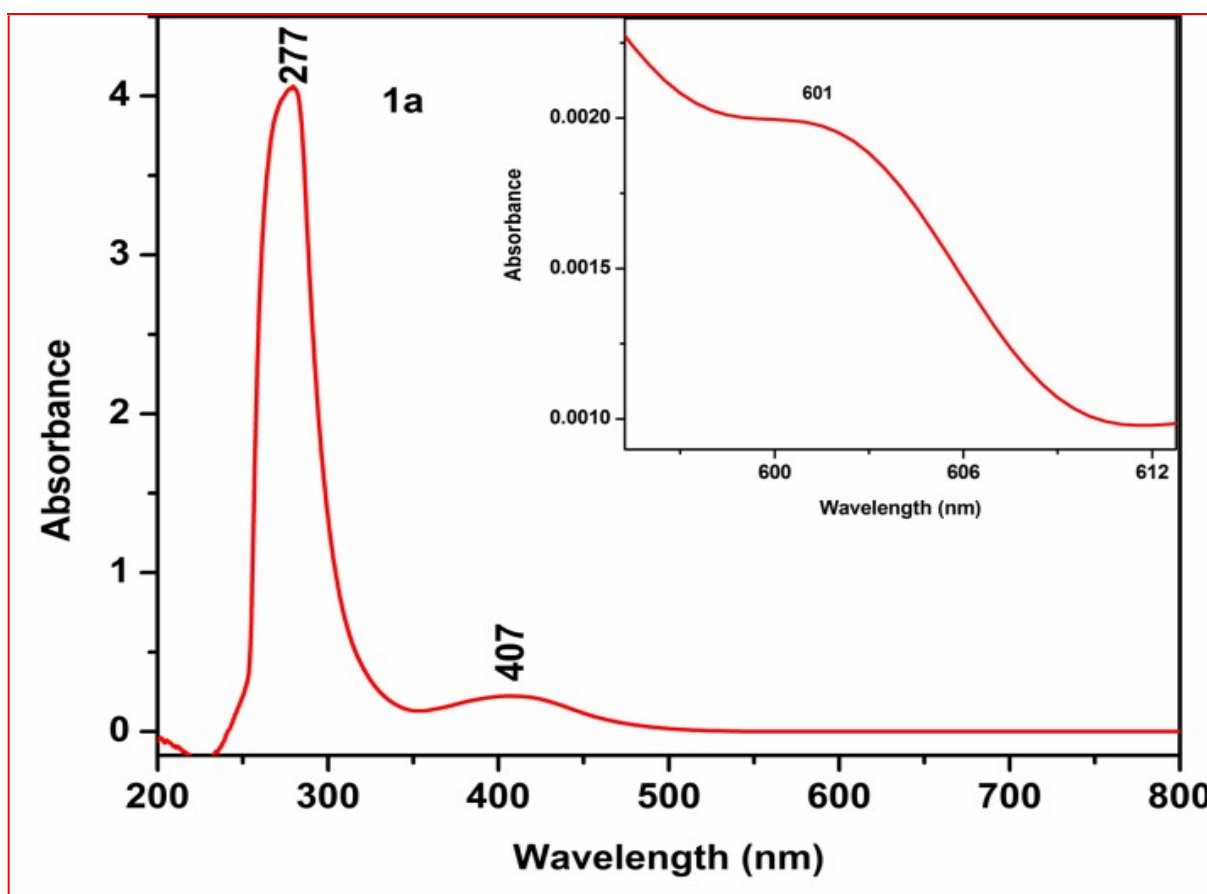


Fig. 6. UV-Vis spectrum of complex 1a

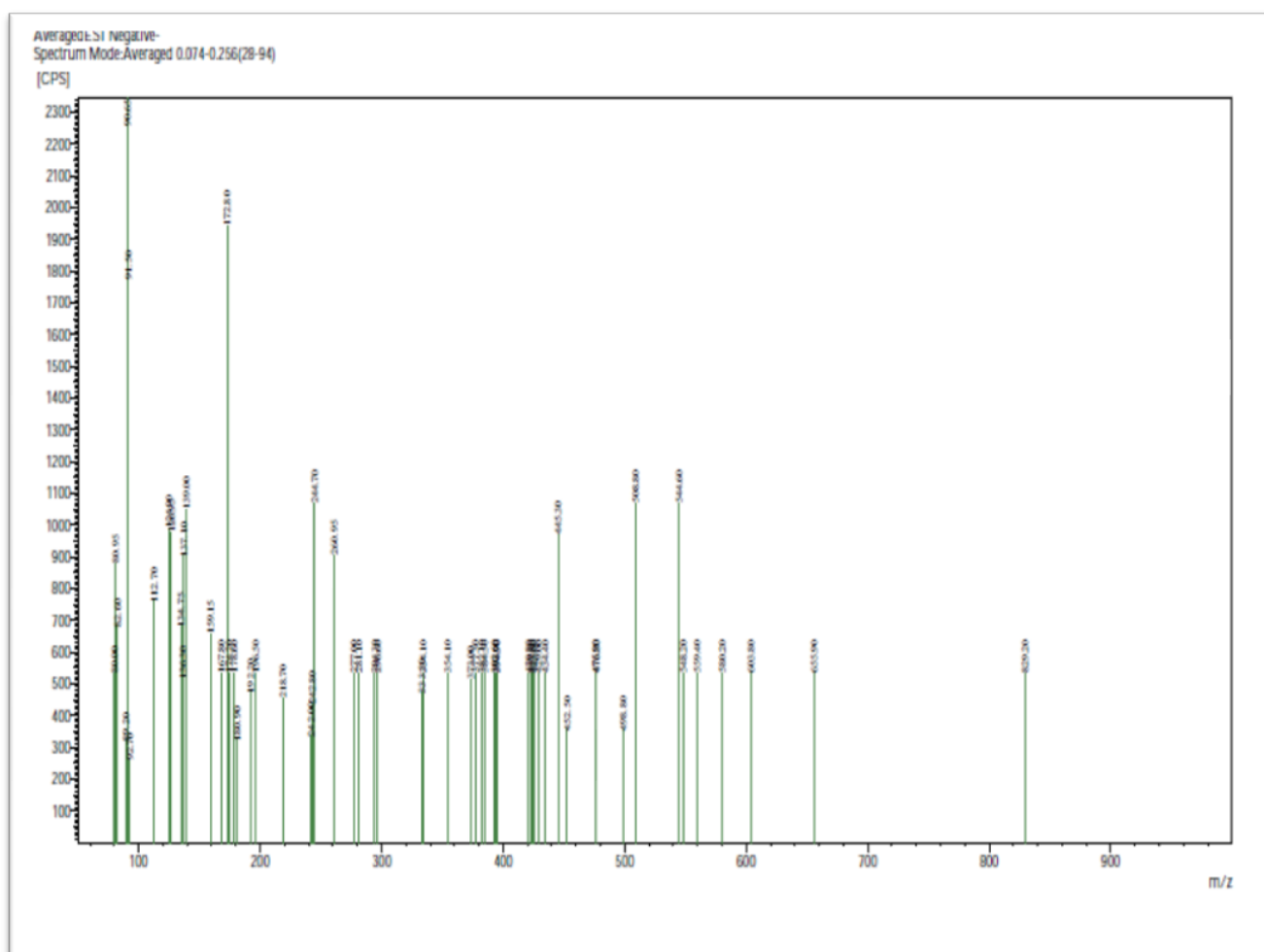
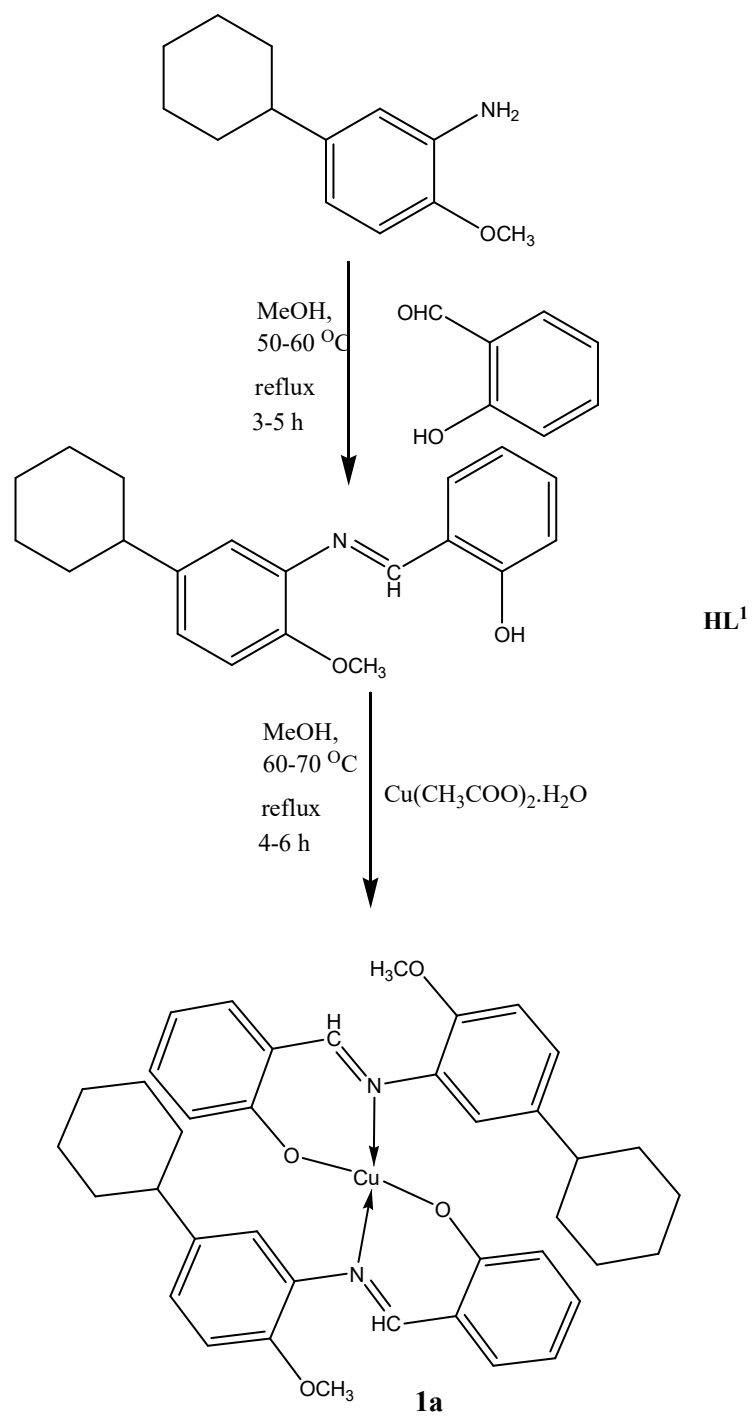


Fig. 7. Mass spectrum of complex **1a**



Scheme 1. Synthesis of ligand (**HL¹**) and its binary Cu(II) complex (**1a**).

Results and discussion

Schiff base and its metal complex (Scheme 1) are coloured, highly stable at room temperature and non-hygroscopic. Both, ligand and its complex are soluble in DMF, DCM, DMSO and other organic solvents like methanol, acetonitrile and chloroform etc., while insoluble in water. The analytical data of synthesized complex is in good agreement with the calculated stoichiometric ratios of metal to ligand (1:2).

FT-IR spectra

The coordination mode of the ligand towards the metal centers has been explored by the comparison of an infrared spectrum of the free ligand with corresponding metal complex, shown in Fig. 1 and 5. The ligand HL¹ showed a characteristic strong band at 1613, due to the azomethine group of Schiff base, this band is shifted in complex to a lower wave number indicating that the coordination occurred through the azomethine nitrogen atom of Schiff bases [16-20]. A band at 3430 cm⁻¹ due to phenolic -OH group of Schiff base is not found in complex, indicating the coordination to central metal ion by deprotonation. In addition, the two non-ligand bands appeared in the complex due to $\nu(\text{M-O})$ and $\nu(\text{M-N})$ bands further supported the coordination occurred through the phenolic oxygen and azomethine nitrogen atoms, respectively.

Electronic spectra and Magnetic moments

The UV-Visible spectra of the ligand and its metal(II) complex were recorded in DMSO solution at room temperature. The absorption spectrum of ligand exhibited two bands at 260 and 343 nm are assigned to $\pi\text{-}\pi^*$ transition of phenyl ring and $n\text{-}\pi^*$ transitions of azomethine (-C=N-) group, respectively. On comparison of the spectra of free ligand with the complex it was observed that a slight shift in the position and intensity of these bands. This might be due to coordination of metal ion with ligand. In addition, an absorption characteristic broad band observed in the complex due to d-d transition. The copper complex showed the band at 601 nm for (1a) due to ${}^2\text{B}_{1g} \rightarrow {}^2\text{A}_{1g}$ transition [11] compatible with square planar geometry around copper centers.

Antimicrobial activity

The antimicrobial activity of the ligand and its metal complex are evaluated by paper disc technique using nutrient agar as the medium [12, 13] and results are presented in **Table 1**. From the results, the ligand either exhibited no activity or having low to moderate activity against bacterial and fungal strains. But its metal complex showed moderate to good activity compared to the standard antibiotics. In evaluation, the activity of all the strains in the presence of ligand increased when coordinated with metal(II) ion. Most of the literature reports reveal that, inactive or less active compounds become more active upon coordination/complexation [14]. The increase in antimicrobial activity of the complex may be due to the high lipophilicity of metal complex and can be explained on the basis of Overtone's concept and Tweedy's chelation theory [15]. The chelation reduces the polarity of the metal ion considerably by the partial sharing of its positive charge with the donor atoms as well as π -electron delocalization on the entire chelating ring. This process, in turn, increases the lipophilic nature of the metal centre, which favours the metal permeation effectively through the lipid layer of the cell membrane thus destroying them more aggressively [16, 17]. Moreover, the Overtone's concept of cell permeability tells that the lipid membrane that surrounding the organism cell favors the passage of only the lipid-soluble materials; therefore, the lipophilic property controls the antimicrobial activity.

Table 1. Zone of inhibition (mm) of the Schiff base and its metal complex and free metal salt 500 μ g/mol concentration.

Compound	Bacteria (mm)				Fungi (mm)	
	Gram positive		Gram negative		<i>S. rolfii</i>	<i>M. phaseolina</i>
	<i>B. amyloliquefaciens</i>	<i>S. aureus</i>	<i>E. coli</i>	<i>K. pneumoniae</i>		
HL^I	01±0.2	02±0.3	0	01±0.1	0	01±0.4
1a	26±0.2	23±0.4	21±0.3	22±0.2	20±0.2	21±0.2
Cu(CH ₃ COO) ₂ ·H ₂ O	1±0.1	1±0.2	0	1±0.3	0	0
<i>Ampicillin</i>	30±0.2	31±0.2	30±0.2	30±0.2	-	-
<i>Mancozeb</i>	-	-	-	-	30±0.2	31±0.2

(±) Standard deviation

Conclusion

Schiff base ligand and its metal(II) complex were synthesized and physicochemically characterized by means of spectroscopic, electrochemical and magnetic measurements. The analytical and spectral data concluded that the copper complex owned a square planar geometry with 1:2 (metal:ligand) stoichiometry. In addition, the antimicrobial activity results showed that the complex exhibited higher antimicrobial activity than the corresponding Schiff base but somewhat lower activity than the standard antibiotics. These investigations will be useful in developing the new metal based drugs for the treatment of bacterial infections.

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Action photos of students in Chemistry Laboratory







