

## Antimicrobial Assay of Newly Synthesised Copper Complex Derived from Tolyamine

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### Abstract

An attempt has been made to synthesise the Schiff base ligand (E)-4-bromo-2-((p-tolylimino)methyl)phenol by the condensation of tolyamine and 5-bromosalicylaldehyde and the coordination behavior its copper complex has been explored by various spectroscopic techniques like UV-Vis., IR, <sup>1</sup>H NMR, MS and elemental analysis. The investigative information of the unpredictable demonstrates the arrangement of 1:2 Copper to ligand proportion with the formula [CuL<sub>2</sub>]. The ligand and the copper chelate have been screened for their antimicrobial activities utilizing disc dissemination technique against gram positive and gram negative bacterial species like *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumonia* and parasitic species like *Candida* and *Aspergillus*.

**Keywords:** Schiff bases; Amino acid derivatives; Metal-Schiff base complexes; Antimicrobial activities

### Introduction

The exploration enthusiasm dealing Schiff base metal edifices is wide due to a limited extent to their potential notice for various interdisciplinary zones that incorporate bio-inorganic science, catalysis and microbial exercises [1]. These metal complexes have attracted substantial and growing interest owing to the role they play in facilitating an understanding of the molecular processes occurring in biochemistry, materials science, catalysis, encapsulation, activation, transport, separation phenomena and hydrometallurgy [2]. Schiff bases metal edifices have likewise been appeared to display a wide scope of biological activities, including antifungal, antibacterial, antimalarial, anti-proliferative, anti-inflammatory, antiviral, and antipyretic properties [3]. Imine or azomethine groups are present in various natural, natural-derived, and non-natural compounds. The imine group present in such compounds has been shown to be critical to their biological activities [4]. The highlight of the most significant examples of compounds belonging to this class, which exhibit antimalarial, antibacterial, antifungal, and antiviral activities have been reported in numerous literature. The relationship between Schiff bases and other pharmacological activities, such as ant proliferative activities have also been well documented [5]. In this article, the synthesis of the Schiff bases ligand and its copper chelate has been discussed. Both the ligand and the copper chelate have been characterized by various spectroscopic techniques like UV-Vis., IR, <sup>1</sup>H NMR and elemental analysis. Also, the synthesized complexes has been screened for their antimicrobial activities using disc diffusion method against various gram-positive and gram negative bacterial species like *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumonia* and fungal species like *Candida* and *Aspergillus*.

### Experimental

#### Materials

All the chemicals used were of analytical grade purchased from Aldrich chemical Company and were used without further purification.

#### Physical measurements

IR spectra (KBr pellets) were recorded in the region 4000-400 cm<sup>-1</sup> on an FT-IR spectrum BX-II spectrophotometer. <sup>1</sup>H NMR spectrum was recorded with a model Bruker Advance DPZ-300 spectrometer

operating at 300 MHz using DMSO-d<sub>6</sub> as a solvent and TMS as an internal standard. Electronic spectra were recorded on Perkin Elmer LS25 spectrophotometer using ethanol as a solvent. The mass spectra were recorded on a GCMS-QP2010 Shimadzu mass spectrometer with DI (direct inlet) and CI (Chemical Ionization).

#### Preparatory procedure of Schiff base ligand [L]

The Schiff base (E)-4-bromo-2-((p-tolylimino)methyl)phenol [L] used was prepared [6] by the condensation reaction of a solution of 1.7614 g (0.01mol) of 5-Bromo salicylaldehyde in (20 ml) of ethanol was added 1.0717 g (0.01mol) of Para-toluidine in the same volume of ethanol in drop wise through dropping funnel. The resulting reaction mixture was then refluxed with stirring at 40°C for 3-4 hours. The response of the reaction was observed by TLC. After completion of the reaction, reaction blend was cooled and the dissolvable evacuated utilizing a Buchi rotating evaporator until the aggregate volume of the response blend was decreased to one-fourth of the underlying volume. On cooling to 5°C, dark golden yellow colour precipitates of the desired compound were obtained. It was filtered, recrystallized from ethanolic solution and dried at room temperature with 90.1% yield.

#### Preparatory procedure of Schiff base-copper complex [CuL<sub>2</sub>]

The Schiff base copper complex under investigation has been prepared [6] by the condensation reaction of Schiff base ligand [L], 2.95 g in (25 ml) of ethanol to which was added (25 ml) of an aqueous solution of Copper nitrate hexahydrate in the molar ratio of 2:1. The obtained mixture was then refluxed with stirring at 50°C for 3-4 hours and then kept overnight to ensure the complete reactions. Then it was

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allowed to cool at 5°C. Evaporated one-third of reaction mixture to get the dark yellow solid was filtered and washed with ethanol several times followed by drying under vacuum for 2 hr. The formation of the complex was determined by either the way of color changes or else IR spectroscopy.

### In-vitro antimicrobial studies

The newly prepared Schiff base and its copper chelate were screened for *in-vitro* antimicrobial activity according to the disc diffusion method. The antimicrobial assay was carried out against gram negative, gram positive bacteria including, *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumonia* and fungal species like *Candida* and *Aspergillus* [7,8]. The stock solution (1 mgmL<sup>-1</sup>) of the test chemical was prepared in DMF solution. The stock solution was further diluted with sterilized distilled water to 60, 40 and 20 µgmL<sup>-1</sup> dilutions. The test chemicals of various concentrations were added to clean clear antimicrobial susceptibility discs. The microbes were sub refined in supplement agar medium or potato dextrose agar (PDA) for organisms and the circles were kept onto the same. The Petri dishes were brooded for 24 h at 37°C for microscopic organisms and for 72 h at 28°C for growths. The standard antimicrobial medications Amikacin for microbes and Ketoconazole for parasites were additionally screened under comparative conditions for examination. The outcomes were recorded by measuring the zones of development restraint encompassing the plates. The mean esteem gotten from three autonomous repeats was utilized to figure the zone of development restraint of each specimen. Keeping in mind the end goal to clear up the impact of solvent (DMF) on the antimicrobial screening, DMF alone was added to separate discs and utilized as control, and it demonstrates no action against microbial strains.

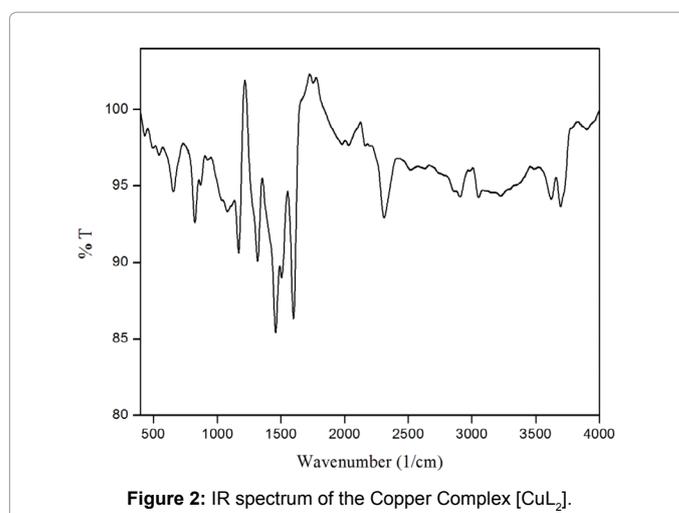
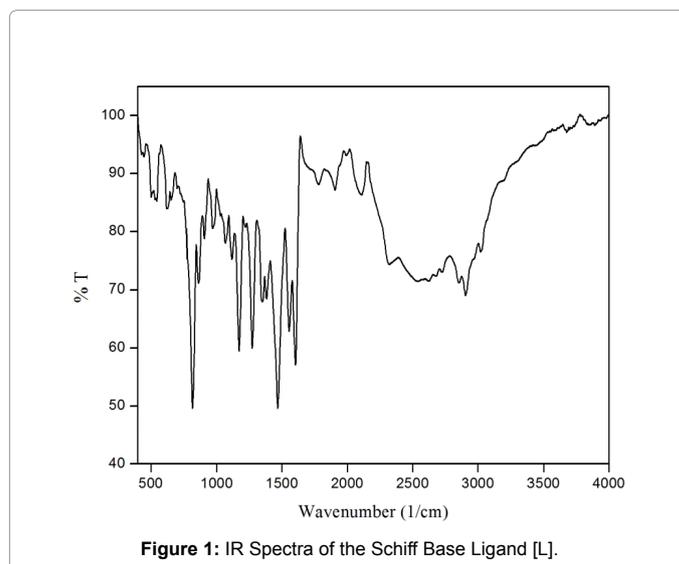
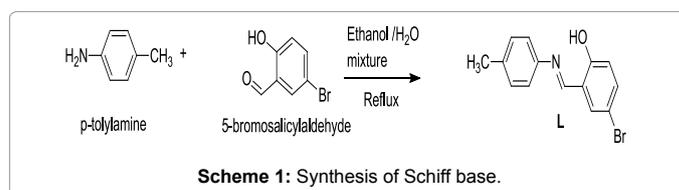
## Results and Discussion

### Analytical data and physical properties

The analytical data and some physical properties of the metal complexes are collected in Table 1 and the scheme of synthesis of the complex is given in Scheme 1. The complex is steady in air, dissolvable in water and regular natural solvents. The nearness of leucine and 5-Bromo-salicylaldehyde in the copper complex has been affirmed by the TLC after hydrolysis of the metal complex.

### IR spectra

The most critical IR assignments of the metal edifices have been dictated via careful correlation with the spectra of Schiff base ligand gotten from leucine and 5-bromo-salicylaldehyde. IR spectra of the Schiff base ligand indicates band around 1610 cm<sup>-1</sup> allocated to the azomethine gathering, this affirms the buildup between the amino gathering of leucine and the aldehyde gathering of 5-bromo-salicylaldehyde in the development of the Schiff base [9]. The medium force pinnacle of retention in the Schiff base ligand around 3000 cm<sup>-1</sup> because of the phenolic hydroxyl gathering of the Schiff base ligand and this pinnacle of assimilation vanishes while chelation with the metal particle. This affirms the coordination through phenolic -OH and the focal metal particle [10]. The azomethine ingestion band experiences a negative move of 1612 cm<sup>-1</sup> in the mind-boggling, which might be ascribed to the coordination of the nitrogen iota of azomethine gathering to the metal particle [11]. The IR range of the ligand and the Cu complex is given in Figures 1 and 2.



### Electronic spectra

The electronic range of the ligand and the delegate Cu (II) Schiff base complex is given in Figures 3 and 4 separately and the phantom information has been given in Table 2. The retention of the ligand L is described by four primary assimilation groups in the locales 200-500 nm. The band at  $\lambda_{max}=229$  nm and  $\lambda_{max}=271$  nm is ascribed to  $\pi \rightarrow \pi^*$  move [12,13]. The band at  $\lambda_{max}=349$  nm attributed to the  $\pi \rightarrow \pi^*$  transition of the azomethine gathering and  $\lambda_{max}=372$  nm is credited to the  $n \rightarrow \pi^*$  transition-related with the azomethine mass with intra sub-atomic charge transfer [14]. The electronic range of the [CuL<sub>2</sub>] complex demonstrates the shoulder of charge transfer shift at 255 nm and wide d-d transition band focused at 360 nm, because of 2B1g  $\rightarrow$  2E1g. This progress proposes the mutilated octahedral geometry for the metal complex [15,16].

Compound	Molecular Formula	Molecular Wt.	Cal. (Exp.) %			Color	Yield (%)
			C	H	N		
L	C <sub>14</sub> H <sub>12</sub> ONBr	290.16	57.95(57.92)	4.17(4.14)	4.13(4.11)	Golden Yellow	89
CuL <sub>2</sub>	C <sub>28</sub> H <sub>22</sub> O <sub>2</sub> N <sub>2</sub> Br <sub>2</sub> Cu	638.93	52.40(52.39)	3.45(3.43)	4.36(4.32)	Yellow	92

Table 1: Analytical data and some physical properties of the ligand and metal complexes.

Compound	$\lambda_{\max}$ (nm)	Band assignment
L	229, 271, 349	$\pi \rightarrow \pi^*$
	372	$n \rightarrow \pi^*$
CuL <sub>2</sub>	243, 298	$\pi \rightarrow \pi^*$
	360	$n \rightarrow \pi^*$

Table 2: UV-Vis Spectral Data  $\lambda_{\max}$  (nm) for the ligand and the complexes.

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

The <sup>1</sup>H NMR Spectra of Schiff base ligand in DMSO-d<sub>6</sub> demonstrates flag of multiplets at 2.4 ppm proportional to the 6H of two methyl gatherings. Singlet at 1.3 ppm compares to the methine protons related with two methyl gatherings. Multiplets at 2.3 ppm are expected to the, methylene hydrogen molecule related with azomethine gathering. The multiplets in  $\delta$  7.0-8.1 ppm area are doled out to the protons of benzylidenimine ring gatherings. The singlet at  $\delta$  6.7 ppm is because of the free hydroxyl gathering and the solid singlet at  $\delta$  8.7 ppm is doled out for the azomethine proton. The <sup>1</sup>H NMR Spectra of Schiff base ligand appears in Figure 5.

### Antimicrobial activity

The Schiff base ligand and its Cu (II) Schiff base buildings were tried for their inhibitory consequences for the development of *Escherichia coli*, *Staphylococcus aureus*, *Bacillus subtilis*, *Klebsiella pneumonia* microscopic organisms since microorganisms can accomplish imperviousness to anti-infection agents through biochemical and morphological changes [17]. They have likewise been tried on *Canadida* and *Aspergillus* organisms. The antimicrobial action was tried by utilizing the circle dispersion strategy. The antimicrobial movement of the new mixes is displayed in Table 3. The nearness of hydroxyl gathering in the Schiff base ligand assumes a critical part for its antimicrobial movement [18], and furthermore the nearness of imine gathering which imports in explaining the component of change response in organic frameworks [7].

The copper complex was found to repress more contrasted and the parent Schiff base ligand against the same miniaturized scale life forms and under the indistinguishable test conditions. The expansion in an organic shift of the metal chelates might be because of the impact of the metal particle on the ordinary cell handle. A conceivable method of poisonous quality increment might be considered in the light of Tweedy's chelation hypothesis [8]. Chelation impressively diminishes the extremity of the metal particle as a result of halfway imparting of its positive charge to the contributor gathering and conceivable  $\pi$  electron delocalization inside the entire chelate ring framework that is shaped amid coordination. Such chelation could improve the lipophilic character of the focal metal iota and thus expanding the hydrophobic character and lipo dissolvability of the complex supporting its penetration through the lipid layers of the cell film along these lines deactivates breath handle in the microorganisms. Moreover, the method of activity of the mixes may include the arrangement of a hydrogen bond through the azomethine nitrogen particle (>C=N) with the dynamic focuses of cell constituents, bringing about impedance with the typical cell system [19].

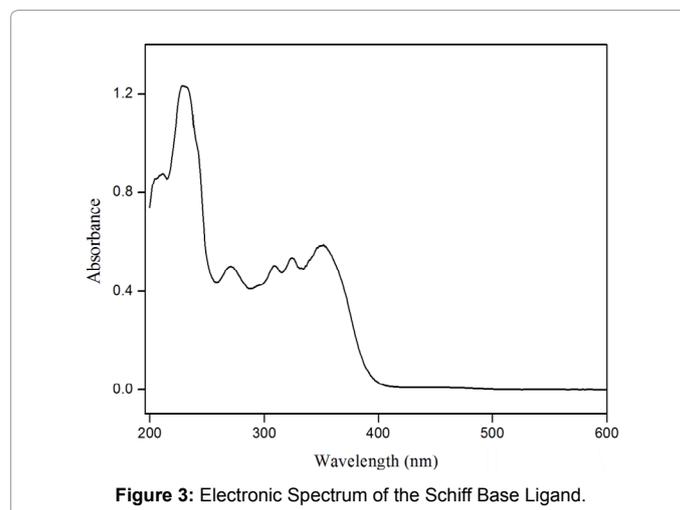


Figure 3: Electronic Spectrum of the Schiff Base Ligand.

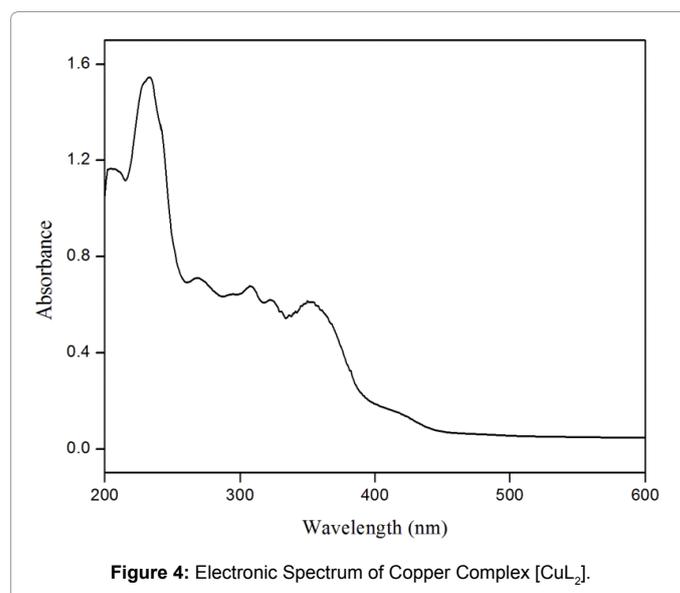


Figure 4: Electronic Spectrum of Copper Complex [CuL<sub>2</sub>].

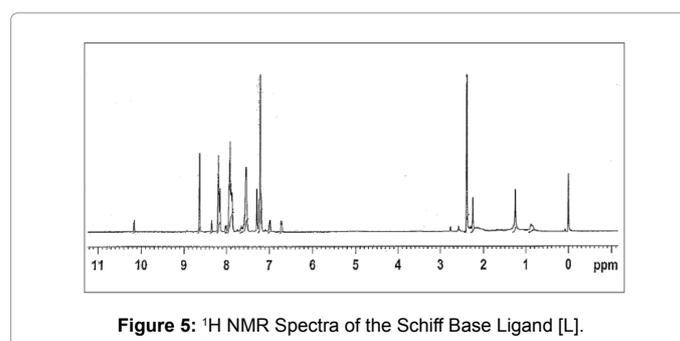


Figure 5: <sup>1</sup>H NMR Spectra of the Schiff Base Ligand [L].

Compounds	Diameter of inhibition zone (in mm)					
	<i>E. coli</i>	<i>Staphylococci</i>	<i>Bacillus</i>	<i>Klebsiella</i>	<i>Candida</i>	<i>Aspergillus</i>
L	15	10	14	11	11	11
[CuL <sub>2</sub> ]	18	14	17	13	14	13
Control	-	-	-	-	-	-
Standard	20	17	20	17	17	15

**Table 3:** Antimicrobial activity. Control: DMSO; Standard: Bacteria - Amikacin, Fungus - Ketoconazole.

## Conclusion

The present work uncovers the blend of the Schiff base ligand [L] and its copper complex CuL<sub>2</sub> edifice. The integrated ligand and the buildings were fundamentally described by phantom systems like IR, UV and <sup>1</sup>H NMR. The logical information of the edifices demonstrates the development of 1:2 Metals to Ligand proportion of the general recipe ML<sub>2</sub>, where M speaks to Cu (II) particle, while L speaks to the Schiff base. The ghastly reviews demonstrate that the ligand is composed of the metal particle in a tridentate way through azomethine-N phenolic-oxygen and carboxylic oxygen gatherings. The metal edifice has been relegated octahedral geometry. The ligand and the metal chelates have been screened for their antimicrobial exercises; the outcome demonstrates that the metal edifices have upgraded inhibitory movement than the Schiff base ligand under indistinguishable conditions.

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