Investigating the Coordination Behavior of (E)-2-(((furan-2-ylmethyl) imino) methyl)phenol with Mercury(II) Ion: Synthesis, Characterization, and Biological Evaluation

Mudassar Alvi[1], Muhammad Uzair Ashraf[1], Aqsa Nisar[2], Muhammad Jhangir[1], Muhammad Ahsan Javed[3], Hammad Shoukat[1], Mohammad Munir Akbar[3], Mohsin Mubarik[1], Anum Sehar[4], Kulsoom Ghulam Ali[*1], Saboor Badshah[5]

[1]Department of Chemistry, Government College University, Faisalabad, Punjab, Pakistan

[2]Department of Biochemistry, Government College University, Faisalabad, Punjab, Pakistan

[3]Department of Chemistry, University of Education, Faisalabad Campus, Punjab, Pakistan

[4]Department of Chemistry, University of Agriculture Faisalabad, Punjab, Pakistan

[5]Department of Botany, Kohat University of Science and Technology Kohat, KPK, Pakistan

Abstract

Advances in inorganic chemistry have resulted in the development of metal complexes with organic ligands, potentially serving as medicinal agents. A novel schiff base (E)-2-(((furan-2-ylmethyl)imino)methyl)phenol was synthesized by refluxing 2-furylmethylamine and salicylaldehyde and its Hg(II) complex have also been synthesized. Their structures were demonstrated based on their spectral analysis of Fourier transform infrared, ^{1}H nuclear magnetic resonance, and UV-visible spectroscopy. The elemental analysis and physical characteristics of a newly synthesized ligand and its metal complex with mercury were also evaluated. Strains of bacteria and fungus were used in vitro to investigate their antibacterial and antifungal properties. It was found that the Hg(II) metal complex of newly synthesized ligand showed more antibacterial and antifungal activity.

Keywords: Metal complexes, Hg (II), Biological activity, Schiff base

1. Introduction

Schiff bases are highly effective ligands in coordination chemistry due to their easy synthesis and ability to form chelates with diverse metal ions (Boulechfar et al., 2023; Ghanghas et al., 2021;). They can readily and regularly create stable compounds with most transition metals (El-Gammal et al., 2021). The formula RC=NR is a versatile equation that can be used to characterize Schiff bases, which are chemical compounds synthesized by the condensation reaction between an amine and either a ketone or an aldehyde (Raczuk et al., 2022). These Schiff bases can act as donor ligands with varying coordination capacities, such as bidentate, tridentate, tetradentate, or hexadentate (Soroceanu & Bargan, 2022). This is primarily because of their simple synthesis, high solubility, various structures, and magnetic, spectroscopic, redox, and catalytic properties in typical solvents (Ahmed & Mohamed, 2022). Because of their variety in structure and wide range of possible uses including anticancer (Parveen, 2020), anti-convulsant (Osman et al., 2021), antitumor, antifungal (Frei et al., 2021), antibacterial (Ceramella et al., 2022), anti-tuberculous (Cordeiro & Kachroo, 2020) antioxidant (Xing et al., 2022), antimalarial (Meena & Kumar, 2023), anti-inflammatory (Sandhu et al., 2023), and their DNA binding and cleavage capabilities, Schiff bases and their metal complexes received considerable interest. They can be utilized in sensors, solar cells, energy storage tools, and corrosion protection techniques (Al Awadh, 2023).

The Schiff base derivatives of furfurylamine are very advantageous biochemical compounds with biological characteristics (Venkateswarlu et al., 2021). Furtrethonium is a cholinergic medication derived from furfurylamine. Schiff base ligands containing imine groups (HC=N-) that can coordinate with metal ions offer numerous benefits, including antitumor, antibacterial, antifungal, and herbicidal properties, as well as anticancer, anti-HIV, anti-parasitic effects, corrosion inhibitors, and biosensor applications (Kumar et al., 2023). The synthesis of metal complexes necessitates the synthesis of a new Schiff base ligand, which is a pivotal step. Salicylaldehyde, also known as 2-hydroxybenzaldehyde, is the primary carbonyl compound used to create Schiff bases (Iftikhar et al., 2018). Nitrogen and oxygen-containing compounds that act as ligands serve as accurate models for intricate biological processes. They combine with metal ions and produce coordination complexes, which give rise to Schiff base metal complexes with a variety of geometries (Ghanghas et al., 2021).

Transition metals have distinctive features not typically found in organic compounds, which can boost their potential for biological activity (Rafique et al., 2010). A diversity of coordination spaces and geometries, ligand activation and dissociation, and redox chemistry are among these properties (Karges et al., 2021). These complexes exhibit a variety of activities, including anti-diabetic, anti-inflammatory, and anti-infective characteristics (Scarim et al., 2021). Significant endeavors are dedicated to the advancement of transition metal complexes for medicinal purposes. Despite several drawbacks and adverse effects, transition metal complexes remain the predominant chemotherapeutic agents and play a significant role in medical treatments (Sodhi & Paul, 2019). The objective of the study was to synthesize previously unreported furfuryamine-based Schiff bases and their metal complexes. The newly synthesized metal complexes were characterized using FT-IR, UV-Vis, ^{1}H NMR, and elemental analyzer. The biological activities of newly synthesized metal complexes were also assessed.

2. Material and Methods

2.1 Materials

All of the utilized compounds and reagents were of analytical grade and required no additional purification. The compounds 1-(2-Furylmethylamine), salicylaldehyde, methanol, metal salt, and mercury(II) chloride were obtained from Sigma Aldrich. Solvents like ethanol, methanol, chloroform, acetone, and dimethyl sulfoxide (DMSO) were of Sigma Aldrich.

2.2 Synthesis of the ligand

1-(2-Furylmethylamine) (0.143 ml) and salicylaldehyde (0.17 ml) were mixed in methanol (30 ml). After stirring for some time acetic acid was added. The resulting solution was stirred using a magnetic stirrer and then put through reflux for 5 hours, as a result Schiff base was formed. The resultant product obtained was dried and recrystallized from methanol.

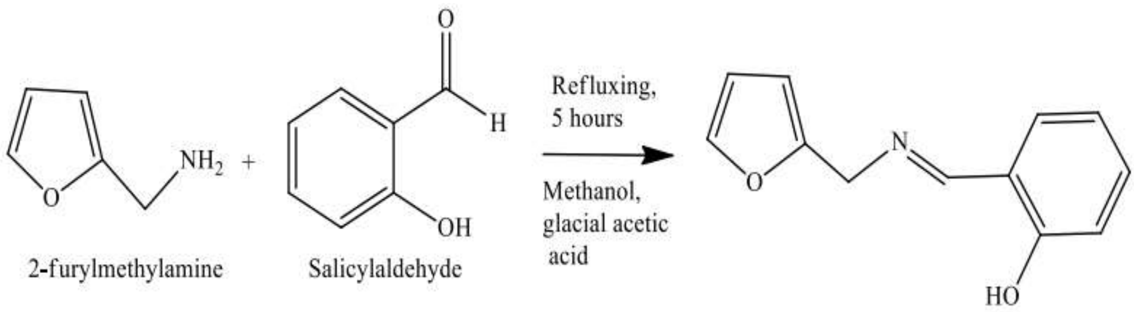

Figure 1: Synthesis of the Schiff base ligand

2.3 Synthesis of the [HgL2] complex

1-(2-Furylmethylamine) (0.143 ml) and salicylaldehyde (0.17 ml) were mixed together in (30 ml) methanol. Glacial acetic acid added after some time while stirring. The resultant solution was magnetically stirred and refluxed for 5 hours as the result Schiff base is formed. Sodium metal (0.018 g) was added in methanolic solution of Schiff base which react with methanol to form sodium methoxide which act as base. A solution of Hg(II) chloride (0.25 g) in methanol was prepared. The metal salt was then added to the solution of Schiff base in a molar ratio of 1:2 (metal: ligand). The mixture was refluxed for duration of 7 hours. The product obtained was air dried and recrystallized at room temperature.

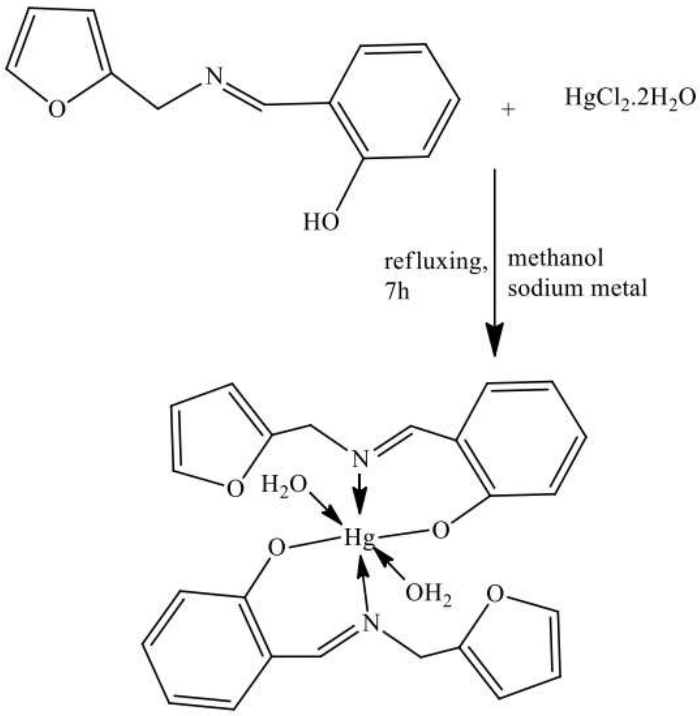

Figure 2: Synthesis of the Hg(II) complex

3. Results and Discussion

3.1 Metal complexes synthesis

The reaction of 1-(2-Furylmethylamine) (0.143 ml) with salicylaldehyde (0.17 ml) in methanol (30 ml) results in the synthesis of Schiff base. After agitating briefly, approximately 2-3 drops of glacial acetic acid were introduced into the solution. Subsequently, the synthesized combination endured reflux for 5 hours. A solution of Schiff base solvent was made and metal salts (M= Hg(II)) were added in a molar ratio of 1:2 (metal: ligand) and resulting solution was then refluxed for a duration of 7-8 hours. Mercury(II) used as a chloride while zinc(II) was used in form of acetate salt. The product obtained after removal of solvent was air dried and recrystallized at 25 ^{o}C temperature. The synthesized compounds exhibited air stability and solubility in several solvents such as dimethyl sulfoxide, methanol, and ethanol.

3.2 Physical properties

The Schiff base ligand and its metal complexes were found to be in a solid state with a melting point ranging from 95 to 22 ℃. Furthermore, they exhibited stability at room temperature (25 ℃). They were obtained at high yield in the range of 71 to 83 %. These complexes were soluble in solvents like chloroform, methanol, dimethyl sulfoxide, and ethanol. Elemental analysis was performed to check the percentage of carbon, nitrogen and hydrogen atoms, values of these atoms are given in the Table 1. The elemental analysis has experimental and theoretical values as well. For the ligand and the associated metal(II) complexes, Table 2 lists the molecular formula, molecular weight, melting temperature, % yield, and solubility data.

Table 1: Elemental analysis information of metal complexes (II) and ligand

Complex	%C		%H		%N	
	Experimental	Theoretical	Experimental	Theoretical	Experimental	Theoretical
Schiff Base	79.98	80.13	6.40	6.52	6.79	7.03
Hg(II) Complex	47.64	47.88	3.43	3.52	4.51	4.65

Table 2: Physical characteristics of metal complexes (II) and ligand

Complex	Molecular Formula	Molecular Weight	Melting Point (°C)	Yield (%)	Solubility
Schiff base	$C_{13}H_{13}NO$	199.25	95	79	DMSO, Ethanol, Methanol, Chloroform
Hg(II)	$C_{24}H_{21}HgN_2O_4$	602.02	161	71	DMSO, Ethanol, Methanol, Chloroform

3.3 FT-IR Analysis

The peak ranges of the ligand and the complexes in the infrared (IR) were determined. Both an absorption band at 2953 cm-1 related to the O-H group and an absorption band at 1639 cm-1 relating to the C=O group are visible in the infrared spectra of the free ligand. When the v(OH) band of the unbound ligand vanished at about 2950 cm-1, the spectra of the complexes showed that the Schiff base had deprotonated before coordination. The IR spectra of the complex exhibited a downward shift in the (C=N) band towards a lower frequency, in contrast to the free ligand band at 1662 cm-1. The origin of the non-ligand bands detected inside the 425-454 cm-1 range was identified to be the v(M-N) stretch. The occurrence of bands within the 532 to 549 cm-1 range offers conclusive proof of the interaction between oxygen and metal ions (Refat et al., 2008). Hg(II) complex coordination of nitrogen with metal is indicated by 426 cm^{-1}, which confirms that metal(II) nitrogen bond is formed in the synthesized complex.

Table 3: FTIR spectrum data of the ligand and it's Hg(II) complex

Complex	*v*(OH)	*v*(CH)	*v*(C=N)	*v*(M-O)	*v*(M-N)
HL	2953	3292.5	1662.57	-	-
Hg(II)	-	2941.23	1608.06	549.87	425.78

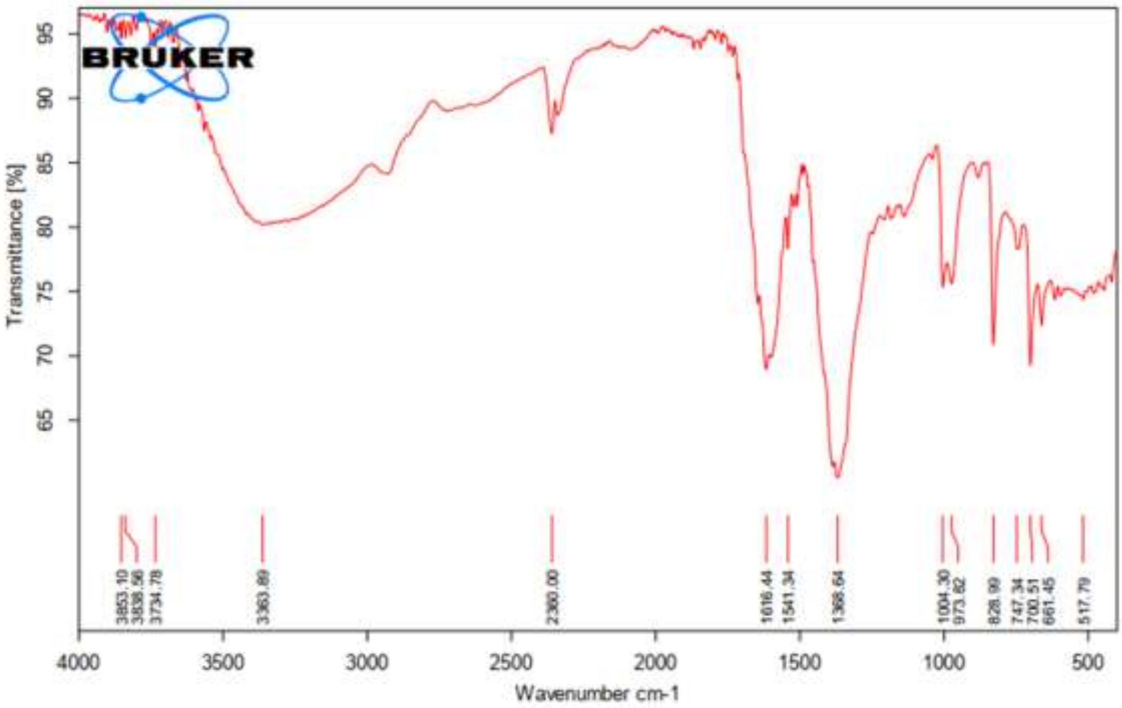

Figure 3: FTIR spectra of ligand

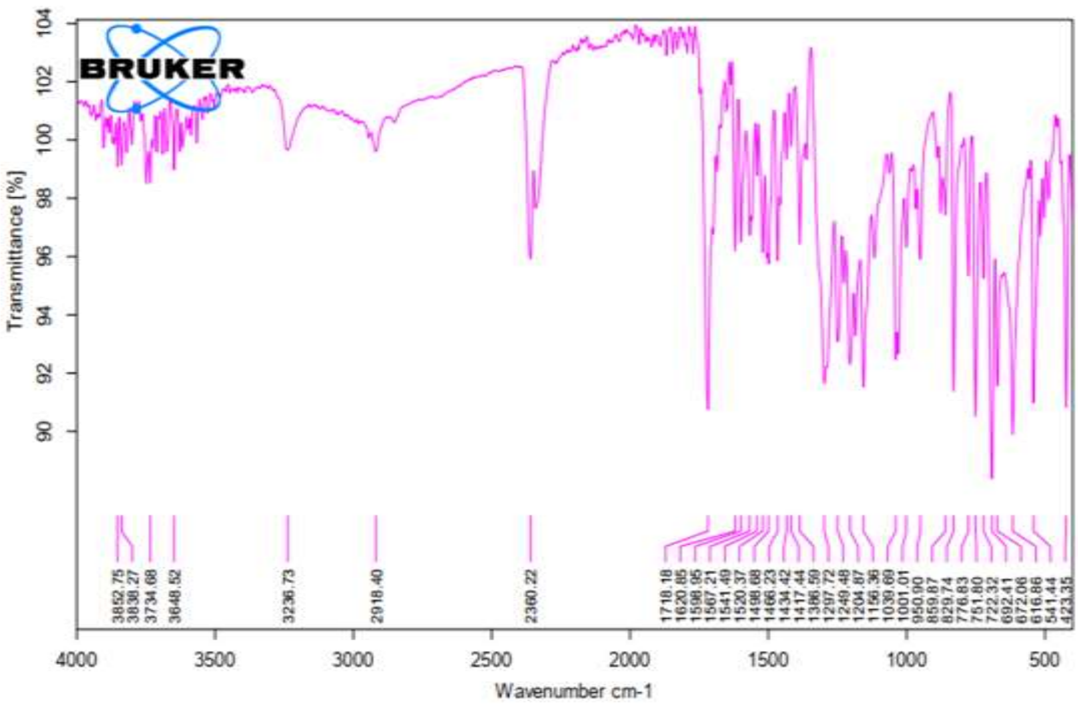

Figure 4: FTIR spectra of Hg-complex

3.4 UV-visible spectroscopy

The UV-visible spectroscopy of metal complexes was conducted in a methanol solution with a wavelength range of 200-400 nm at a temperature of 25°C. Observations were made on the electronic spectra of the synthesized ligand (HL) and the Mercury(II) complex. The spectrum data allows for the observation of many types of transitions in both the ligand and its synthesized metal(II) complex. The electronic spectra of the Hg(II) complex showed that the intra-ligand observation band in the range of the 200-250 nm, which is consider as π-π* transition. While the metal to ligand charge transfer peak appeared at 320 nm and consider as a n-π* transition. The appearance of the third band at 420 nm in the Hg(II) complex is attributed to ligand to metal charge transfer, specifically a π-π* charge transfer transition (Mahmoud et al., 2017).

Table 4: UV-Visible spectrum data of metal complexes and ligands

Complex	**Intra- ligand transition(nm)**	**LMCT ⅄ max**
HL(II)	280 (3.53), 320 (3.47)	-----
Hg(II)	320 (4.98)	420 (4.157)

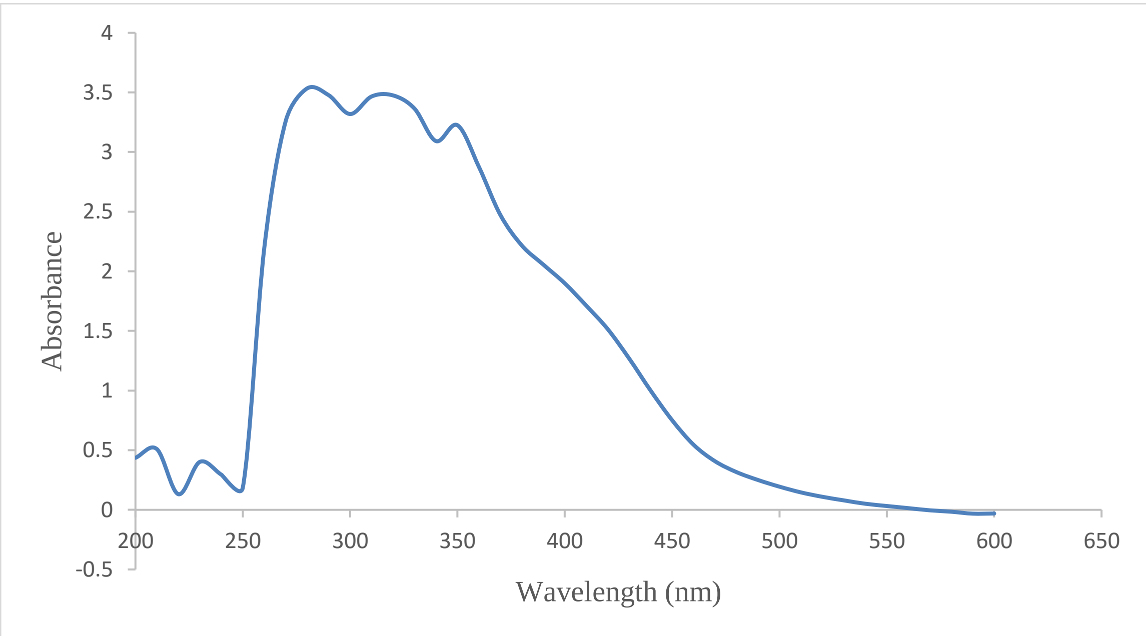

Figure 5: UV-Visible spectra of the ligand [HL]

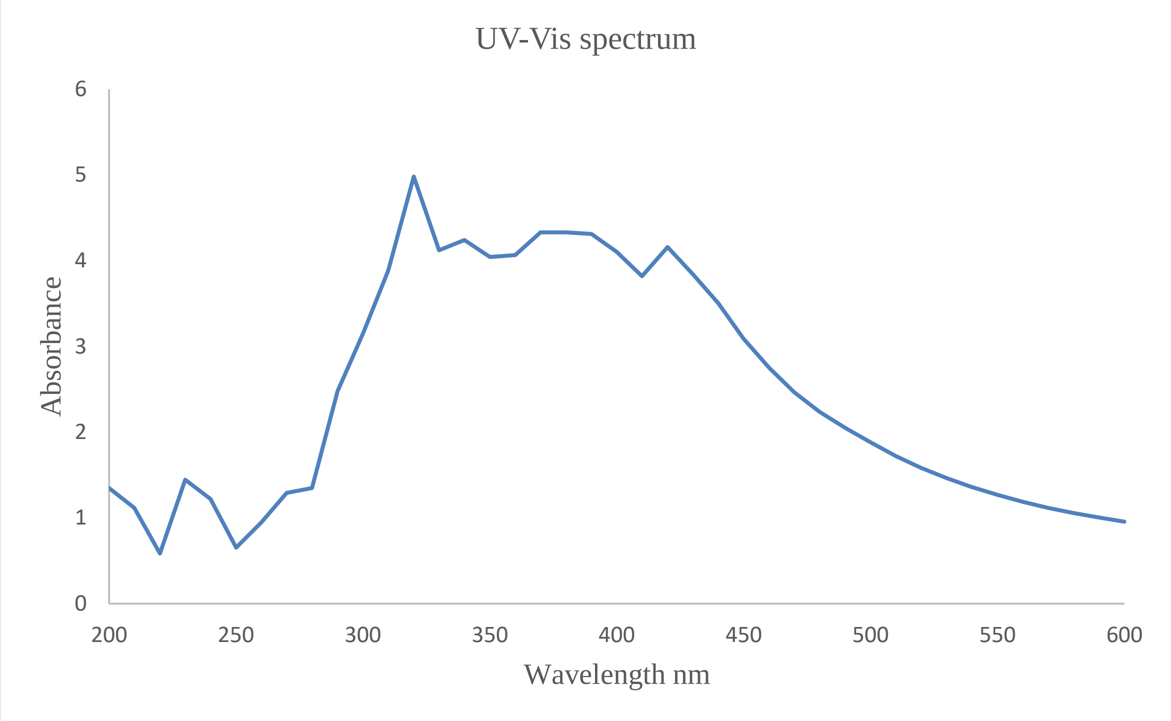

Figure 6: UV-Visible spectra of the Hg metal complex

3.5 ^{1}H NMR spectroscopy

The ligand and metal complexes' ^{1}H NMR spectra's distinctive signal was captured in the DMSO. At room temperature, tetramethylsilane is utilized as an internal reference. With the help of the proton estimated using the incremental technique, every proton present in the ligand & complexes of metals were identified in position and number. On complexation with the metals Hg(II) this signal is shifted to the downfield at (9.76 ppm), which is an indication for the bonding of azomethine group to the metal. The appearance of the singlet at 8.12 ppm in the ^{1}H NMR spectrum of the Schiff base (HL) is the conformation for the presence of the azomethine in the spectra of the ligand and complexes a singlet appear in range of the ∂ 1.99-2.60 ppm. These are due to the CH_3 protons which are directly attached to the Carbon atoms. In the spectra of ligand and the complexes the phenyl proton of ligand appeared in the region of the 6.13-7.32 ppm.

The complexes' 1H NMR spectra showed that there is no NH proton signal, which suggests that the ligand's nitrogen ring has been deprotonated and that metal coordination has followed (Behest et al., 2021). The highest point is observed at 13.46 ppm in the spectra of the ligand, which corresponds to the peak of the OH group. Nevertheless, the lack of that prominent peak in the given metal complex spectra suggests that the metal is bonded to the ligand via the oxygen atom of OH group found in the synthesized ligand (Lupascu et al., 2021).

Table 5: ^{1}H-NMR data of Schiff base (HL) and metal (II) complexes

Complexes	OH (ppm)	CH (Ar) ppm	HC=N (ppm)
HL	13.460	6.12-7.30	8.12
Zn(II) complex	--------------	8.16	9.76

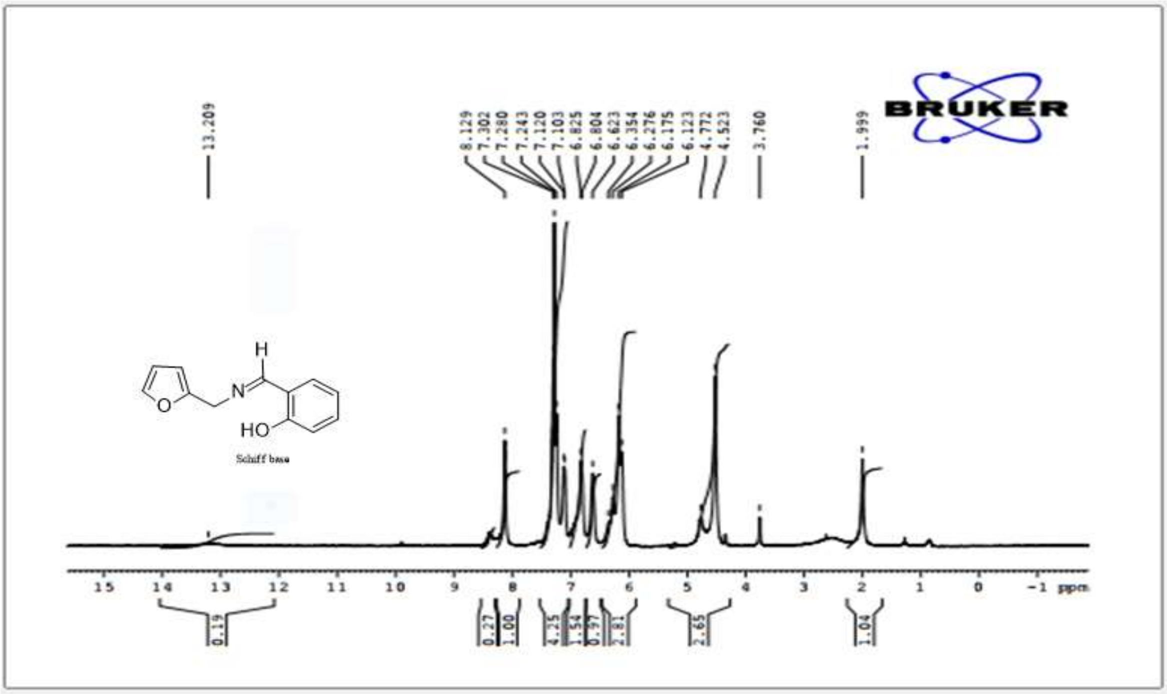

Figure 7: ^{1}H NMR spectra of Schiff base

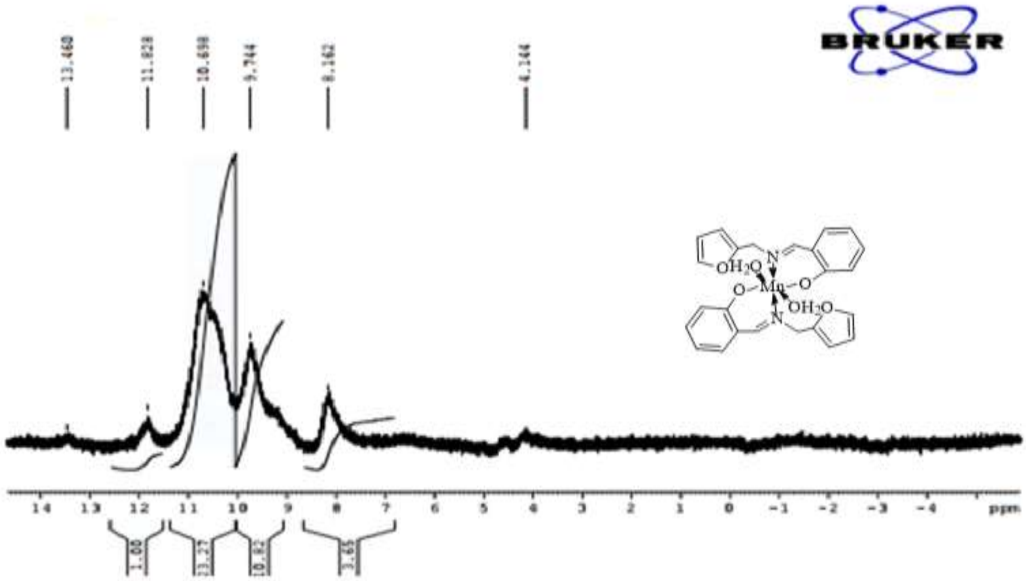

Figure 8: ^{1}H NMR Spectra of metal complex

3.6 Biological activities

The prepared ligand and its metal complexes with the Hg(II) complexes was checked for antibacterial activity against two different strain bacteria. One of them was the gram positive *(Bacillus substilus)* and the other was gram negative bacteria *(Escherichia coli)* the Disc Diffusion method was used to check their activity. The sample solution with a concertation of 1mg/ml prepared in DMSO and introduced into the petri dish the results are given in the Table 6**.** From the data summarized in the Table 6 ligand (HL) show less antibacterial activity with respect to metal complexes. While the standard drug used has higher antibacterial activity against G-positive and G-negative bacteria. However, the complexes show higher or almost comparable antibacterial activity than ligand. The higher inhibition zone recorded in the Hg(II) complex against the *(Bacillus substilus) and (Escherichia Coli).*

Antifungal strain was cultivated at 28 °C on potato dextrose sugar medium. The Schiff base ligand and metal complexes showed good antifungal activity (Table 6). The antifungal activity of the Schiff base ligand and its complexes was assessed by measuring the zone of inhibition. The ligand HL demonstrated inhibitory effects on *C. albicans* at a distance of 7 mm and on *A. flavus* at a distance of 6 mm. The Hg(II) complex exhibited superior antifungal activity, resulting in a 12 mm zone of inhibition against *C. albicans* and 11 mm against *A. flavus*. The antifungal activity of the metal complex was similar to that of ciprofloxacin. The enhance antifungal activity is due to coordination of the ions of metal with nitrogen of azomethine. Due to increase in chelation lipophilic character increase due to which metal penetrate into the lipid membrane of fungus cell and block the metal coordination site of enzyme and cause death of fungal cell. Results of antifungal activity are shown in table 6.

Table 6: Antimicrobial activities of the ligand and synthesized complexes

Complex no	Bacterial zone of inhibition (mm)		Fungal zone of inhibition (nm)	
	B. substilis	***E. coli***	***C. albicans***	***A. flavus***
HL	13	12	7	6
Hg(II) complex	18	20	12	11
S.D (Ampicillin)	19	21	-	-
S.D (Ciprofloxacin)	-	-	18	14

4. Conclusion

Schiff bases and metal complexes are extensively utilized in biomedical medicines for various purposes such as antibacterial, antimalarial, anticancer, antiviral, anti-inflammatory, antioxidant, anticonvulsant, anti-anthelmintic activities, as well as in bioprinting, tissue regeneration, enzyme inhibition, and drug transport. In this research work a novel furylamine based Schiff base and its complex with Hg(II) have been synthesized. Their structure and physical properties were also assessed. The synthesized ligand and its Hg(II) metal complex were evaluated for their antibacterial and antifungal activities. The results demonstrated that the Hg(II) metal complex shown more effectiveness in comparison to the ligand (L).

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