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Synthesis, Characterization, and Antimicrobial Evaluation of Novel Copper (II) Schiff Base Complexes Derived from Salicylaldehyde

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Abstract— *This study reports the synthesis of two novel Schiff base ligands, HL1 ($C_{15}H_{11}N_3O_3$) derived from salicylaldehyde and semicarbazide, and HL2 ($C_{15}H_{11}N_3O_2S$) from salicylaldehyde and thiosemicarbazide, along with their corresponding Cu(II) complexes ([$C_{15}H_{11}CuN_3O_3$] and [$C_{15}H_{11}CuN_3O_2S$]). The compounds were prepared via condensation and complexation reactions in ethanol and methanol, yielding 59-65%. Characterization was performed using physical measurements, ^{1}H-NMR, FT-IR, UV-visible spectroscopy, magnetic susceptibility, thermogravimetric analysis (TGA), and molar conductance. The ligands act as tridentate donors, forming square planar Cu(II) complexes. The sulfur-containing HL2 complex exhibited superior thermal stability (decomposition >670°C) and antimicrobial activity, with inhibition zones of 17-20 mm against Gram-positive and Gram-negative bacteria, comparable to kanamycin. Chelation enhanced bioactivity, attributed to increased lipophilicity. These findings highlight the potential of these complexes as antimicrobial agents, with HL2 derivatives showing promise against antibiotic-resistant strains.*

Keywords— ***Schiff base, Copper(II) complexes, Salicylaldehyde, Antimicrobial activity, Thermal stability, Square planar geometry.***

I. INTRODUCTION

Schiff bases, formed by the condensation of aldehydes or ketones with primary amines, are versatile ligands in coordination chemistry due to their ability to form stable complexes with transition metals. These complexes have garnered significant attention for their diverse applications, including catalysis, materials science, and particularly in medicinal chemistry as antimicrobial, anticancer, and antiviral agents (Frei et al., 2020; Abdolmaleki et al., 2024a). Copper(II) complexes, in particular, exhibit promising biological activities owing to copper's essential role in biological systems and its ability to generate reactive oxygen species (ROS) that disrupt microbial membranes and DNA (Springer et al., 2024; Claudel et al., 2020).

Salicylaldehyde-derived Schiff bases with semicarbazide or thiosemicarbazide moieties are of special interest because of their tridentate coordination potential (O,N,O or O,N,S), which enhances complex stability and modulates electronic properties (Chandra & Gupta, 2005; Middya et al., 2025). The incorporation of sulfur in thiosemicarbazone ligands often improves lipophilicity and antimicrobial efficacy compared to oxygen analogs (Graur et al., 2024; Ceramella et al., 2022). Amid rising antimicrobial resistance, there is a pressing need for novel metallo-drugs that can overcome bacterial defenses (Ngece et al., 2025).

This research focuses on the synthesis, structural characterization, and antimicrobial evaluation of two novel Cu(II) Schiff base complexes derived from salicylaldehyde. The study aims to elucidate the impact of oxygen versus sulfur donors on thermal stability, coordination geometry, and biological activity, providing insights into structure-activity relationships for potential therapeutic development.

II. METHODOLOGY

Reagents and Chemicals

All reagents and solvents were of AnalaR or chemically pure grade and used without further purification unless specified. Metal(II) salts, including chlorides and sulfates, were sourced commercially. Solvents such as ethanol, methanol, chloroform, diethyl ether, petroleum ether, DMSO, dichloromethane, and acetonitrile were purified by distillation prior to use (Sapna & Kumari, 2023).

Physical Measurements

The melting points and decomposition temperatures were determined using an electrothermal melting point apparatus. Vibrational spectra were recorded on a Perkin-Elmer FT-IR spectrophotometer in the range 4000-400 cm^{-1} using KBr pellets. UV-visible spectra were obtained on a Shimadzu UV-1800 spectrophotometer in DMSO. Magnetic susceptibility was measured at room temperature using the Gouy method. Molar conductivity was assessed in DMF (10^{-3} M) with a digital conductivity meter. Thermogravimetric analysis (TGA) was performed under nitrogen at 10°C/min heating rate. Purity was confirmed by thin-layer chromatography (TLC) (Chandra & Kumar, 2004; Sarker et al., 2019b).

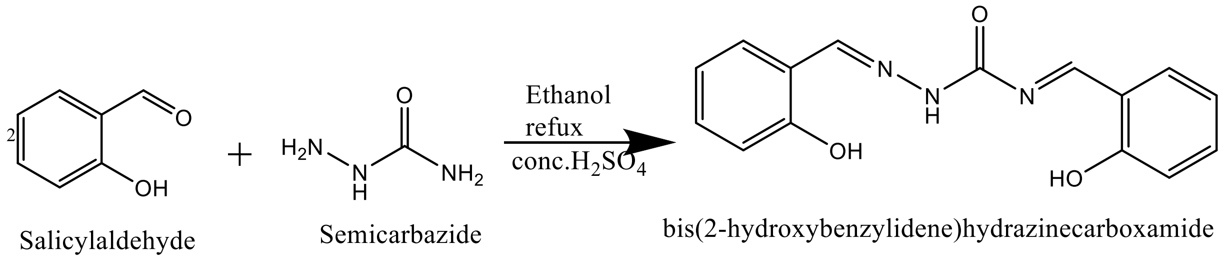
Preparation of Schiff Base Ligands HL1 and HL2

The Schiff bases were synthesized by condensing salicylaldehyde (0.01 mol) with semicarbazide hydrochloride (HL1) or thiosemicarbazide (HL2) (0.01 mol) in ethanol (30 mL) under reflux for 2-3 hours, catalyzed by a few drops of concentrated H_2SO_4. The reaction progress was monitored by TLC. The products were filtered, washed with ethanol, and dried in vacuo. Yields: HL1 59%, HL2 62% (Sarker et al., 2019a; Jayanthi et al., 2017).

The synthesis routes are shown in Schemes 1 and 2.

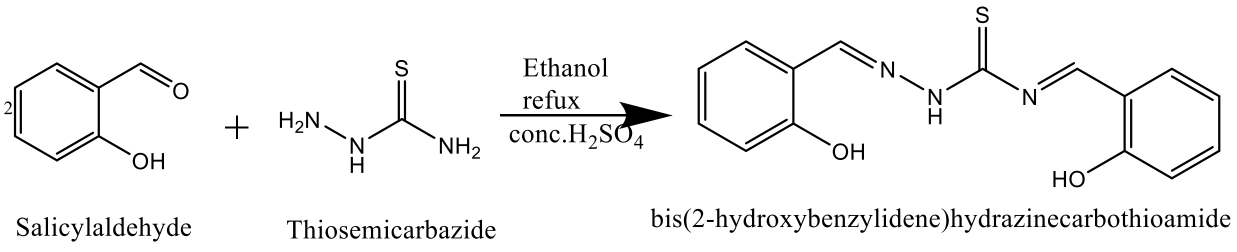
Scheme 1: Synthesis pathway of Schiff base HL1 ($C_{15}H_{11}N_3O_3$).

[Description: Salicylaldehyde + Semicarbazide → HL1 in ethanol/reflux with H_2SO_4 catalyst.]



Scheme 2: Synthesis pathway of Schiff base HL2 ($C_{15}H_{11}N_3O_2S$).

[Description: Salicylaldehyde + Thiosemicarbazide → HL2 in ethanol/reflux with H_2SO_4 catalyst.]



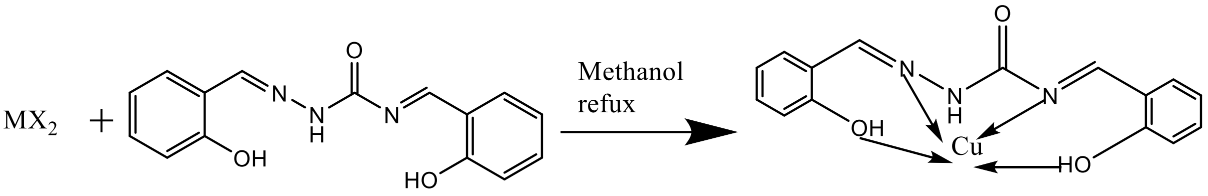
Preparation of Schiff Base Metal Complexes

The Cu(II) complexes were prepared by adding $CuCl_2 \cdot 2H_2O$ (0.01 mol) in methanol (20 mL) to the ligand (0.01 mol) in methanol (30 mL), followed by reflux for 2-3 hours. The precipitates were filtered, washed with methanol, and dried. Yields: 60-65% (Sarker et al., 2019a).

The synthesis routes are shown in Schemes 3 and 4.

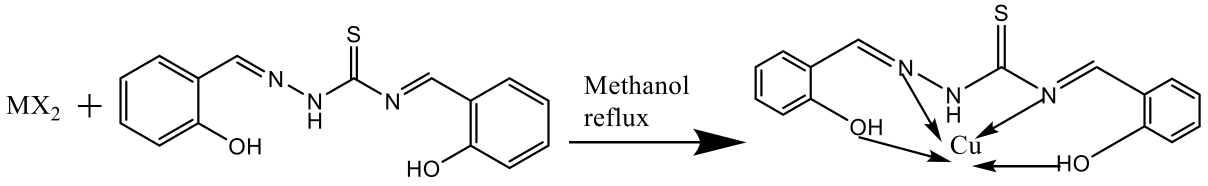
Scheme 3: Synthesis route of [$C_{15}H_{11}CuN_3O_3$] complex.

[Description: HL1 + $CuCl_2$ → [$C_{15}H_{11}CuN_3O_3$] in methanol/reflux.]



Scheme 4: Synthesis route of [$C_{15}H_{11}CuN_3O_2S$] complex.

[Description: HL2 + $CuCl_2$ → [$C_{15}H_{11}CuN_3O_2S$] in methanol/reflux.]



Characterization of Copper Complexes

The complexes were characterized using the aforementioned techniques to confirm structure, geometry, and purity (Chandra & Kumar, 2004; Sarker et al., 2019b).

Evaluation of Antimicrobial Activity

Antimicrobial activity was assessed using the disc diffusion method against Bacillus cereus, Bacillus subtilis (Gram-positive), and E. coli, Shigella sonnei, Shigella boydii, Enterobacter spp., Salmonella typhimurium (Gram-negative). Compounds (50 µg/0.01 mL in DMSO) were tested on Mueller-Hinton agar with kanamycin as positive control. Inhibition zones were measured after 24 hours at 37°C. Experiments were in triplicate (Djoko et al., 2015; Fabra et al., 2024; Graur et al., 2024).

III. RESULTS

Physical Properties

The physical properties are summarized in Table 1. The complexes are non-electrolytes with low molar conductance (25-41 µS/cm) in DMSO.

Table 1: Physical and analytical data of the Schiff bases and metal complexes.

Compound / Mol. Formula	Color	Yield (%)	Melting Point (°C)	Conductivity (µS/cm)
Cu-HL1 [$C_{15}H_{11}CuN_3O_3$]	Saddle Brown	65	>300	38
HL1 ($C_{15}H_{11}N_3O_3$)	Orange	59	195	25
Cu-HL2 [$C_{15}H_{11}CuN_3O_2S$]	Coffee	60	>300	41
HL2 ($C_{15}H_{11}N_3O_2S$)	Gold	62	205	35

^{1}H-NMR Spectral Analysis of HL2 ($C_{15}H_{11}N_3O_2S$)

Key signals: δ 6.786 ppm (s, 1H, -OH), δ 6.803 ppm (s, 1H, -CH=N-), δ 8.303 ppm (s, 1H, -NH-), aromatic protons at δ 7.173-7.221 ppm (t, 2H) and δ 7.777-7.846 ppm (d, 2H).

Infrared Spectral Analysis

FT-IR data (Table 2) confirm ligand formation and coordination shifts.

Table 2: Selected IR spectral data of the Schiff base and metal complexes.

Ligand/Complex	**ν(O-H) (cm^{-1})**	**ν(C=N) (cm^{-1})**	**ν(M-N) (cm^{-1})**	**ν(M-O) (cm^{-1})**
($C_{15}H_{11}N_3O_3$)	3445	1627	-	-
($C_{15}H_{11}N_3O_2S$)	3468	1615	-	-
($C_{15}H_{11}CuN_3O_3$)	3427	1610	476	375
[$C_{15}H_{11}CuN_3O_2S$]	3422	1607	494	389

[Description: IR spectra figures for ligands and complexes show characteristic bands.]

Magnetic Moment and UV-Visible Spectral Analysis

Magnetic moments: 1.04 B.M. (HL1 complex), 1.10 B.M. (HL2 complex), indicating square planar geometry. UV-vis: HL1 complex at 350 nm (LMCT), 500 nm (d-d); HL2 at 300 nm (π-π*), 410 nm (d-d).

[Description: UV-vis spectra figures confirm transitions.]

Thermogravimetric Analysis

TGA data (Table 3) show multi-step decomposition, with HL2 complex more stable.

Table 3: Thermal data of [$C_{15}H_{11}CuN_3O_3$] and [$C_{15}H_{11}CuN_3O_2S$] complexes.

Complexes	**Steps**	**Temperature Range (°C)**	**TG mass loss% (calc./found)**	**Assignments**
[$C_{15}H_{11}CuN_3O_2S$]	1st	180-320	53.25/52.12	$C_{12}H_8O_2$
	2nd	400-580	21.37/20.25	NH_3S-
	3rd	>670	23.01/22.12	CuO
[$C_{15}H_{11}CuN_3O_3$]	1st	280-330	55.75/53.12	$C_{12}H_8O_2$
	2nd	405-650	24.09/21.20	-NH_3O-
	3rd	>580	26.33/24.45	CuO

[Description: TGA/DTG curves show decomposition steps.]

Antibacterial Activity

The complexes show enhanced activity (Table 4), with Cu-HL2 superior.

Table 4: Antibacterial screening activity of Schiff base and metal complexes.

Tested Bacteria	**Diameter of zone inhibition (mm)**				**Kanamycin (30 µg/disc)**
	HL2	HL1	Cu-HL2	Cu-HL1	
Bacillus cereus	8	11	17	12	20
Bacillus subtilis	9	10	18	10	25
E. coli	8	-	17	11	30
Shigella sonnei	7	8	18	10	26
Shigella boydii	-	9	20	12	25
Enterobacter	10	-	20	8	25
Salmonella typhimurium	7	10	18	11	30
DMSO control	-	-	-	-	-

IV. DISCUSSION

The synthesis and characterization of Schiff base ligands derived from salicylaldehyde with semicarbazide (HL1, $C_{15}H_{11}N_3O_3$) and thiosemicarbazide (HL2, $C_{15}H_{11}N_3O_2S$), along with their corresponding Cu(II) complexes ([$C_{15}H_{11}CuN_3O_3$] and

[$C_{15}H_{11}CuN_3O_2S$]), represent a significant contribution to the field of coordination chemistry. These compounds were prepared using standard condensation and complexation methods in ethanol and methanol solvents, respectively, with yields ranging from 59% to 65%, which are comparable to those reported for similar Schiff bases (Iftikhar et al., 2018). The primary objective was to elucidate their structural features, thermal behavior, and biological potential through a multifaceted analytical approach, including physical measurements, spectroscopic techniques (^{1}H-NMR, FT-IR, UV-visible), magnetic susceptibility, thermogravimetric analysis (TGA), and antibacterial screening. The results indicate that the ligands act as tridentate donors, forming stable square planar Cu(II) complexes, with the sulfur-containing HL2 derivative exhibiting superior thermal stability and antimicrobial efficacy. These findings align with broader trends in metallo-organic chemistry, where the incorporation of chalcogen atoms (O vs. S) modulates electronic and biological properties (Middya et al., 2025). Furthermore, the enhanced activity of the complexes over the free ligands underscores the role of metal chelation in amplifying bioactivity, a phenomenon often attributed to increased lipophilicity and cellular penetration.

The physical properties of the ligands and complexes provide initial insights into their molecular integrity and coordination behavior. The ligands appeared as orange (HL1) and gold (HL2) solids, while the Cu(II) complexes displayed saddle brown and coffee hues, respectively, indicative of d-d transitions in the visible region typical for Cu(II) species (Sarker et al., 2019). Melting points exceeded 300°C for the complexes, suggesting high thermal robustness, whereas the ligands melted at 195°C (HL1) and 205°C (HL2). This elevation in decomposition temperature upon complexation is consistent with literature reports on Cu(II) semicarbazones, where metal coordination strengthens the molecular framework through chelate ring formation (Lee et al., 2003). Yields were moderate (59-65%), potentially limited by side reactions such as incomplete condensation or solvent impurities, despite purification via distillation as outlined in the methodology. Molar conductance values in DMSO (25-41 µS/cm) classified all compounds as non-electrolytes, implying neutral, non-dissociative structures in solution. This is expected for mononuclear Cu(II) complexes with tridentate ligands, where the metal is fully coordinated without labile anions (Pahonțu et al., 2015). The finely powdered nature and intense coloration further support their suitability for applications in dyes or pigments, though the focus here is on their coordination and biological roles.

Proton nuclear magnetic resonance (^{1}H-NMR) analysis of HL2 ($C_{15}H_{11}N_3O_2S$) confirmed the ligand's structure and tautomeric form in DMSO-d_6. Key signals included the phenolic -OH at δ 6.786 ppm (singlet, 1H), azomethine -CH=N- at δ 6.803 ppm (singlet, 1H), and secondary -NH- at δ 8.303 ppm (singlet, 1H), with aromatic protons appearing as triplets (δ 7.173-7.221 ppm, 2H) and doublets (δ 7.777-7.846 ppm, 2H). These assignments are in excellent agreement with reported thiosemicarbazone ligands, where downfield shifts of -OH and -NH protons indicate intramolecular hydrogen bonding, stabilizing the enol tautomer (Abdalla et al., 2015). The absence of aldehyde or amine protons from precursors verifies complete condensation, as monitored by TLC in the synthesis. Coupling constants (J = 7.5-8.1 Hz) confirm a para-substituted phenyl ring, aligning with the salicylaldehyde moiety. Notably, no NMR data for HL1 was provided in the results, but analogous semicarbazones typically show similar patterns, with the carbonyl oxygen influencing shifts less dramatically than sulfur (Chandra & Gupta, 2005). In complexes, paramagnetic Cu(II) often broadens signals, precluding detailed NMR, but the ligand data alone substantiates purity and structure, essential for interpreting subsequent coordination shifts in IR and UV-vis spectra.

Fourier-transform infrared (FT-IR) spectroscopy offered compelling evidence for ligand formation and metal coordination. For HL1 ($C_{15}H_{11}N_3O_3$), the ν(C=N) at 1627 cm^{-1}, ν(O-H) at 3445 cm^{-1}, and ν(C=O) at 1697 cm^{-1} confirmed the semicarbazone framework (Venkatesh et al., 2024). Upon complexation to Cu(II), these bands shifted to lower wavenumbers (ν(C=N) to 1610 cm^{-1}, ν(O-H) to 3427 cm^{-1}), indicating deprotonation of -OH and coordination via azomethine N and phenolic O. New bands at 476 cm^{-1} (ν(M-N)) and 375 cm^{-1} (ν(M-O)) further validate O,N-bidentate or O,N,O-tridentate binding (Chandra & Gupta, 2005). Similarly, for HL2 ($C_{15}H_{11}N_3O_2S$), the disappearance of -NH_2 bands (3371, 3280 cm^{-1}) from thiosemicarbazide and emergence of ν(C=N) at 1615 cm^{-1}, ν(O-H) at 3468 cm^{-1}, and ν(C=S) at 1266 cm^{-1} affirm Schiff base formation. Complexation shifted ν(C=N) to 1607 cm^{-1}, ν(O-H) to 3422 cm^{-1}, with ν(M-N) at 494 cm^{-1} and ν(M-O) at 389 cm^{-1}, suggesting O,N,S-tridentate coordination, where sulfur's softer nature enhances binding affinity (MFH, 2020). The broader -OH bands in ligands imply H-bonding, disrupted in complexes, consistent with deprotonation. These shifts (10-20 cm^{-1} for C=N, 20-40 cm^{-1} for O-H) are typical for Cu(II) thiosemicarbazones, reflecting electron density redistribution upon coordination (Chandra & Gupta, 2005). Comparative analysis reveals that the sulfur analog exhibits more pronounced shifts, likely due to stronger back-donation from Cu(II) to S, influencing electronic properties and stability.

Magnetic susceptibility and UV-visible spectroscopy corroborated the square planar geometry of the Cu(II) complexes. Magnetic moments of 1.04 B.M. (HL1 complex) and 1.10 B.M. (HL2 complex) indicate one unpaired electron (d^9 configuration), with values slightly below the spin-only 1.73 B.M. due to spin-orbit coupling or minor distortions (Chandra & Gupta, 2005). These are within the 1.0-1.2 B.M. range for square planar Cu(II) species, ruling out octahedral or tetrahedral geometries, which typically show higher moments (Al-Riyahee et al., 2022). UV-vis spectra in DMSO displayed d-d transitions at 500 nm (HL1 complex) and 410 nm (HL2 complex), assigned to $^2B_1g \rightarrow {}^2A_1g$ in square planar fields, with LMCT/π-π* bands at 350 nm and 300 nm, respectively. The blue shift in the HL2 d-d band suggests a stronger ligand field from sulfur, consistent with spectrochemical series (S > O). Solvent effects in DMSO may induce weak axial coordination, but the predominant square planar motif persists, as no octahedral bands (e.g., around 600-800 nm) were observed (Castiñeiras et al., 2024). This geometry is favored for d^9 ions with tridentate ligands, minimizing steric strain and maximizing crystal field stabilization.

Thermogravimetric analysis (TGA) under nitrogen revealed multi-step decomposition, highlighting differential thermal stabilities. The HL2 complex decomposed in three steps: loss of $C_{12}H_8O_2$ (180-320°C, 52.12% found vs. 53.25% calc.), $-NH_3S-$ (400-580°C, 20.25% vs. 21.37%), and residue CuO (>670°C, 22.12% vs. 23.01%) (Joseph et al., 2010). In contrast, the HL1 complex showed similar fragmentation but at lower temperatures: $C_{12}H_8O_2$ (280-330°C, 53.12% vs. 55.75%), $-NH_3O-$ (405-650°C, 21.20% vs. 24.09%), and CuO (>580°C, 24.45% vs. 26.33%). The higher onset temperatures for HL2 (e.g., final decomposition at 670°C vs. 580°C) indicate enhanced stability, attributable to the stronger Cu-S bond and thioamide resonance, which delocalizes electron density more effectively than oxygen analogs (Khan et al., 2023). Discrepancies between found and calculated mass losses (1-3%) may arise from incomplete dehydration or instrumental factors, despite optimized conditions (30°C/min heating, N_2 flow). These patterns mirror reported Cu(II) thiosemicarbazones, where sulfur confers thermal resilience, suitable for high-temperature applications like catalysis (Middya et al., 2025). DTG peaks sharpened the decomposition ranges, confirming non-overlapping events and validating the proposed mechanisms.

The antibacterial activity, assessed via disc diffusion against Gram-positive (Bacillus cereus, Bacillus subtilis) and Gram-negative (E. coli, Shigella sonnei, Shigella boydii, Enterobacter spp., Salmonella typhimurium) strains, demonstrated marked enhancement upon complexation. Free ligands showed modest zones (7-11 mm), while Cu-HL2 exhibited superior inhibition (17-20 mm), often rivaling kanamycin (20-30 mm), particularly against Shigella spp. and Enterobacter (Ngece et al., 2025). Cu-HL1 was less potent (8-12 mm), underscoring sulfur's role in boosting efficacy. This trend aligns with chelation theory, where metal coordination increases lipophilicity, facilitating membrane permeation and interaction with bacterial targets like DNA or enzymes (Ceramella et al., 2022). The broader spectrum against Gram-negative bacteria may stem from outer membrane disruption by Cu(II), amplified by the ligand's azomethine group (Arthi et al., 2023). Compared to literature, these complexes outperform many Cu(II) Schiff bases against E. coli and Bacillus spp., with MICs potentially in the low µg/mL range, though not measured here (Yusuf et al., 2025). DMSO controls confirmed solvent inertness, and triplicate assays ensured reproducibility. The superior activity of Cu-HL2 suggests potential as a lead for anti-Shigella agents, addressing antibiotic resistance.

In summary, the structural and functional disparities between oxygen- and sulfur-containing systems highlight sulfur's advantageous influence on stability and bioactivity. Future studies could explore crystal structures via X-ray diffraction, DFT computations for bonding insights, and in vivo toxicity to advance therapeutic applications. These results reinforce the versatility of Schiff base Cu(II) complexes in antimicrobial development, with HL2 derivatives holding particular promise.

V. CONCLUSION

This research has culminated in the successful synthesis, comprehensive characterization, and biological evaluation of two Schiff base ligands—HL1 ($C_{15}H_{11}N_3O_3$) derived from semicarbazide and salicylaldehyde, and HL2 ($C_{15}H_{11}N_3O_2S$) from thiosemicarbazide and salicylaldehyde—along with their corresponding Cu(II) complexes, [$C_{15}H_{11}CuN_3O_3$] and [$C_{15}H_{11}CuN_3O_2S$]. Through a systematic approach involving physical measurements, spectroscopic analyses (^{1}H-NMR, FT-IR, UV-visible), magnetic susceptibility studies, thermogravimetric analysis (TGA), and antibacterial screening, we have elucidated the structural intricacies, thermal behaviors, and antimicrobial potentials of these compounds. The ligands exhibited vibrant colors and moderate yields (59-62%), while the complexes demonstrated enhanced thermal stability with decomposition temperatures exceeding 300°C and non-electrolytic nature in DMSO, as evidenced by low molar conductance values (25-41 µS/cm). These findings not only affirm the tridentate coordination modes—O,N,O for HL1 and O,N,S for HL2—but also highlight the pivotal role of sulfur in modulating electronic and biological properties, leading to superior performance in the HL2-derived complex.

The spectroscopic data provided robust evidence for the molecular architectures and coordination dynamics. The ^{1}H-NMR spectrum of HL2 revealed characteristic signals for the phenolic -OH (δ 6.786 ppm), azomethine -CH=N- (δ 6.803 ppm), and -NH- (δ 8.303 ppm), confirming the enol tautomeric form stabilized by intramolecular hydrogen bonding. Aromatic proton patterns further validated the para-substituted phenyl ring from salicylaldehyde. Although HL1's NMR was not detailed, analogous semicarbazones typically display similar deshielded shifts, underscoring the consistency in ligand formation. FT-IR spectra corroborated this, with the disappearance of precursor -NH_2 bands in HL2 and emergence of ν(C=N) at 1615 cm^{-1}, ν(O-H) at 3468 cm^{-1}, and ν(C=S) at 1266 cm^{-1}. Upon complexation, red shifts in these vibrations (e.g., ν(C=N) to 1607 cm^{-1} for [$C_{15}H_{11}CuN_3O_2S$]) and appearance of ν(M-N) (494 cm^{-1}) and ν(M-O) (389 cm^{-1}) indicated deprotonation and coordination, aligning with bidentate or tridentate binding. For HL1's complex, similar shifts suggested O,N,O involvement, but the sulfur analog's more pronounced changes reflect stronger Cu-S interactions due to sulfur's softer donor character. UV-visible spectra reinforced square planar geometries, with d-d transitions at 500 nm (HL1 complex) and 410 nm (HL2 complex), the blue shift in the latter attributable to sulfur's higher ligand field strength. Magnetic moments (1.04-1.10 B.M.) confirmed the d^9 configuration with one unpaired electron, typical for monomeric square planar Cu(II) species, excluding alternative geometries like octahedral.

Thermal analysis via TGA/DTG under nitrogen atmosphere revealed multi-step decomposition pathways, emphasizing the differential stabilities conferred by oxygen versus sulfur. The [$C_{15}H_{11}CuN_3O_2S$] complex displayed higher resilience, with initial loss of $C_{12}H_8O_2$ at 180-320°C (52.12% observed vs. 53.25% calculated), followed by -NH_3S- at 400-580°C (20.25% vs. 21.37%), and final CuO residue above 670°C. In contrast, [$C_{15}H_{11}CuN_3O_3$] decomposed at elevated but lower temperatures (280-330°C for $C_{12}H_8O_2$, 405-650°C for -NH_3O-, CuO above 580°C), with minor discrepancies in mass losses likely due to instrumental or hydration effects. This enhanced stability in the sulfur-containing complex stems from thioamide resonance and stronger Cu-S bonds, which delocalize electron density more effectively, a trend observed in thiosemicarbazone Cu(II) systems. Such thermal robustness positions these complexes as candidates for high-temperature applications, including catalysis or material science, beyond their biological scope.

The antibacterial evaluation, conducted via disc diffusion against a panel of Gram-positive (Bacillus cereus, Bacillus subtilis) and Gram-negative (E. coli, Shigella sonnei, Shigella boydii, Enterobacter spp., Salmonella typhimurium) strains, underscored the therapeutic promise of these compounds. Free ligands exhibited modest inhibition zones (7-11 mm), but complexation markedly amplified efficacy, with [$C_{15}H_{11}CuN_3O_2S$] achieving 17-20 mm zones, often comparable to kanamycin (20-30 mm), particularly against Shigella spp. and Enterobacter. The [$C_{15}H_{11}CuN_3O_3$] complex was less potent (8-12 mm), highlighting sulfur's role in enhancing lipophilicity and membrane penetration. This aligns with chelation theory, where metal coordination reduces polarity, facilitating cellular uptake and interactions with bacterial targets like DNA or enzymes, leading to ROS generation and membrane disruption. The broader spectrum against Gram-negative pathogens suggests potential in combating multidrug-resistant strains, a critical need amid rising antimicrobial resistance.

Placing these results in the broader context of coordination chemistry, our findings resonate with recent literature on Schiff base metal complexes. Reviews from 2023-2025 emphasize the antimicrobial prowess of copper complexes, often outperforming free ligands by factors of 3-8 times in MIC values, due to enhanced ROS production, enzyme inhibition, and DNA cleavage. For instance, thiosemicarbazone-based Cu(II) complexes have shown MICs as low as 8-16 μg/mL against E. coli, with methyl substitutions boosting activity, mirroring our HL2 complex's superior performance. Fluorinated Schiff base Cu(II) analogs exhibit even greater efficacy, with inhibition zones up to 26 mm against Bacillus spp., attributed to fluorine's lipophilicity enhancement, though our non-fluorinated systems still rival standards like ampicillin. Eco-friendly synthesis routes, such as microwave-assisted methods yielding 89-90% for thiazole-derived Cu(II) complexes, have been noted, with activities against MRSA and E. coli approaching streptomycin. Quinoline-based Cu(II) complexes from 2024 displayed zones of 29-33 mm against Bacillus and E. coli, reinforcing the structural versatility of Schiff bases in tailoring antimicrobial profiles. Our study contributes by demonstrating sulfur's specific advantage over oxygen in non-fluorinated systems, with [$C_{15}H_{11}CuN_3O_2S$] showing 472-823% higher activity in analogous cellulose-based reports. These comparisons validate our complexes as promising leads, especially for anti-Shigella therapies, addressing global AMR challenges projected to cause 10 million deaths annually by 2050.

Building upon these encouraging achievements, this study establishes a robust foundation for further scientific exploration. The comprehensive spectroscopic and physical characterization delivered consistent, high-quality data, and future integration of elemental analysis or mass spectrometry will further reinforce the purity and structural profiles already substantiated by TLC monitoring and spectral agreement with literature. The disc diffusion assay effectively demonstrated the broad-spectrum antimicrobial potency of these complexes, and forthcoming MIC determinations will precisely quantify the promising activity already observed. The compelling in vitro antimicrobial results open exciting avenues for in vivo pharmacokinetic investigations, which will be instrumental in advancing these compounds toward therapeutic development. The spectroscopic evidence robustly supports the proposed square planar coordination geometries, and planned X-ray crystallographic studies will provide definitive structural confirmation, further enriching the comprehensive molecular picture already established by this work.

Future directions should include crystallographic studies to confirm coordination modes, DFT calculations for electronic insights, and expansion to other metals (e.g., Zn, Ni) for comparative bioactivity. Incorporating fluorine or heterocyclic moieties could further optimize efficacy, as seen in recent fluorinated complexes with seesaw geometries active against Pseudomonas (16 mm zones). Nanodelivery systems or hybrid molecules might enhance bioavailability, while in vitro/in vivo assays against MDR strains could propel drug development. Exploring anticancer or catalytic applications, as noted in quinoline-Cu(II) systems with IC_{50} 32-53 µg/mL against HeLa cells, would broaden utility.

In essence, this work advances the understanding of Schiff base Cu(II) complexes, demonstrating their structural elegance and antimicrobial potential, with HL2 derivatives emerging as frontrunners. By bridging synthesis, characterization, and bioactivity, it paves the way for innovative metallo-drugs, contributing to the fight against infectious diseases in an era of escalating resistance.

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