

Amino Acid–Furfural Schiff Bases and their Co(II)/Cu(II) Complexes: Synthesis, Characterization and Antimicrobial Activity

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ABSTRACT

Schiff bases carrying the azomethine ($-\text{CH}=\text{N}-$) linkage and their metal complexes continue to attract attention, as they find use in medicinal chemistry, in catalysis and as thermally stable materials. In the present work, three Schiff bases (SB1–SB3) were prepared by condensing furfural with L-phenylalanine, L-tyrosine and L-histidine. These ligands were then reacted with Co^{2+} and Cu^{2+} chlorides, which gave the metal complexes SB1M1–SB3M2. All the compounds were characterised by FTIR, ^1H NMR, ^{13}C NMR, ESI-MS and DSC. In the IR spectra of the complexes, the azomethine and carboxylate stretching bands were shifted with respect to the free ligands, and new bands due to metal–nitrogen and metal–oxygen bonds were seen, pointing towards coordination of the ligand with Co(II) and Cu(II). Formation of the Schiff bases and their proposed compositions were supported by NMR and ESI-MS data, while DSC gave information on the melting and decomposition behaviour. UV–Vis spectra and XRD patterns showed that the optical response and the crystallinity of the compounds changed after binding with the metal ion. All compounds showed antibacterial activity at 15.625 $\mu\text{g}/\text{disc}$. Inhibition zones ranged from 18–25 mm against *E. coli* and 12–21.67 mm against *S. aureus*, comparable to ciprofloxacin. SB2M2 showed the strongest activity against *E. coli*, whereas SB2M1 was most effective against *S. aureus*.

Keywords: Schiff bases; furfural; cobalt(II) complexes; copper(II) complexes; antibacterial activity

INTRODUCTION

Chelating agents containing the imine group are widely used in coordination interactions because they are easy to prepare from aldehydes or ketones and primary amines, easy to tune and show broad biological activity such as antimicrobial, anticancer and antioxidant (Jorge et al., 2024). More recent work (2021–2025) indicates that chelation of these ligands with first-row transition metals, especially Co(II) and Cu(II), significantly enhances their potency. Metal coordination increases lipophilicity, promotes ROS-mediated damage to microbial cells, and may inhibit efflux pumps in agreement with Tweedy's chelation theory (Kumari, 2019). Amino acid-derived Schiff bases are especially useful due to their biocompatibility, retention of chirality and presence of multiple pharmacophoric groups (carboxyl, amino and side chain functions). Furfural, a renewable aldehyde from biomass, is an attractive synthon, which adds a furan ring, increasing electron delocalisation and membrane permeability (Alyami et al., 2025; Khemthong et al., 2021). The binding capacity of DNA and penetrability power in the membrane of cells arise due to the formation of a metallic complex (Singh et al., 2024). Although promising in vitro results against microbial strains have been obtained, there is still a lack of systematic structure–activity relationship studies correlating side-chain electronics (aromatic vs. heteroaromatic) and metal-induced geometric changes with selectivity between *E. coli* and *B. aureus* (Sindhu et al., 2025). This study addresses these voids by synthesizing and comprehensively characterizing (FTIR, NMR, ESI-MS, DSC, UV and XRD) novel furfural azomethine compounds using three amino acids, then complex formation with Co(II)/Cu(II) metal ions, evaluating Kirby-Bauer method, and elucidating coordination-driven antimicrobial enhancement mechanisms (Awolope et al., 2023).

The novelty of this work lies in combining furfural with three proteinogenic amino acids (L-Phe, L-Tyr, L-His) to develop Schiff base ligands, followed by Co(II)/Cu(II) complexation and evaluation against antimicrobial activity.

2. METHODOLOGY

2.1 Synthesis

The Schiff bases (SB1-SB3) were synthesized by mixing 10 mmol of an amino acid (L-Phe, L-Tyr, L-His) and 0.96 g (10 mmol) of furfuraldehyde at 60 °C. Then 25 mL of methanol was added, followed by 2-3 droplets of anhydrous acetic acid. This mixture was heated under reflux on a water bath for 3 h. The flask was then brought to room temperature and kept in ice-cold water; the solid that separated out was filtered, washed with methanol and diethyl ether and dried under vacuum. Then, the methanolic solution of Schiff base 2 mmol at 60°C and a methanolic solution of the metal salt (1 mmol) at 60°C were mixed with the respective metal chloride (CoCl₂·6H₂O or CuCl₂·2H₂O) in 25 mL of hot methanol and refluxed on a water bath for 2 hours. After cooling, the complex was filtered, washed with methanol and ether, and the resulting Schiff base was recrystallized from methanol (Mallikarjunaswamy & Vijaya Sekhar, 2018) and dried under vacuum (Mohamed et al., 2005). The complexes were synthesized using a 2:1 ligand-to-metal stoichiometric ratio while their proposed.

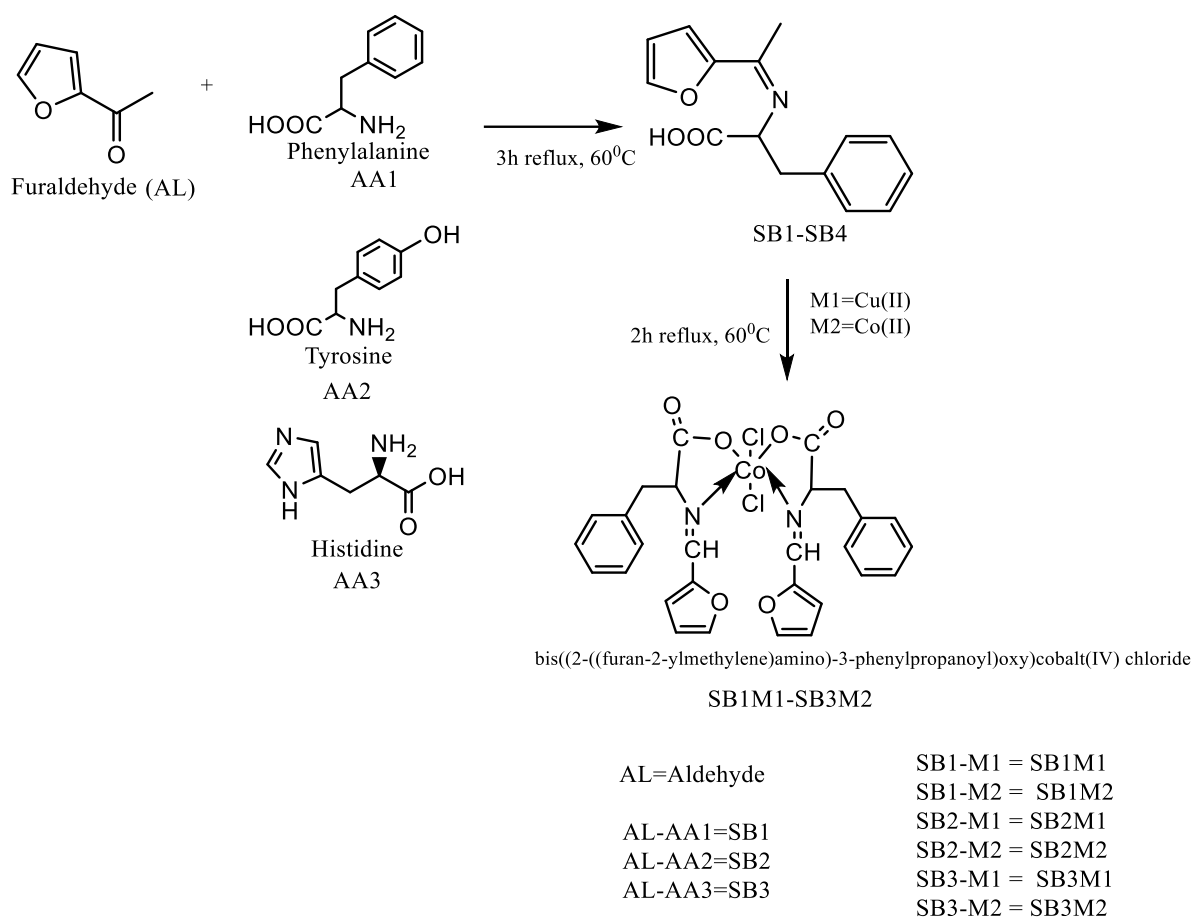
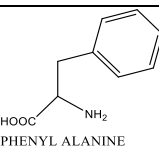
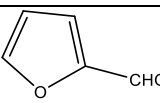
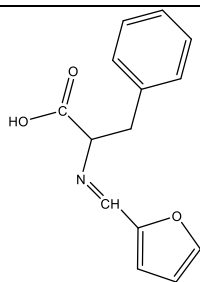
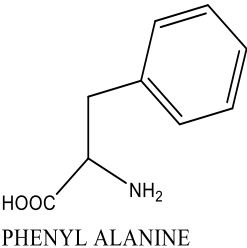
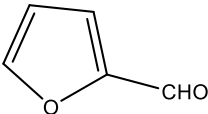
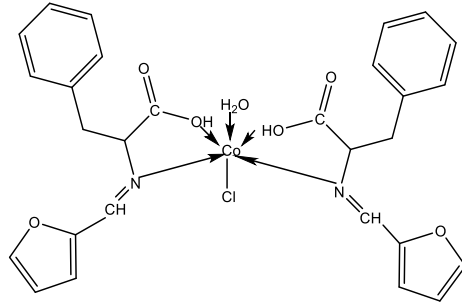
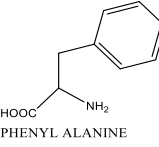
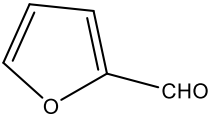
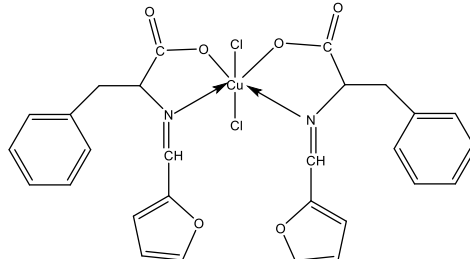
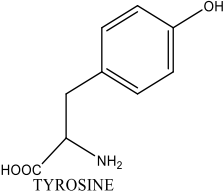
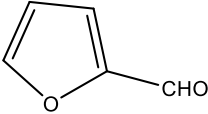
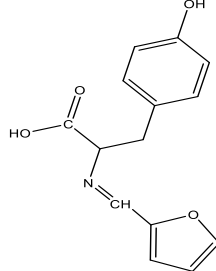


Figure I. Synthesis of amino acid–based Schiff bases and their metal complexes. Furfuraldehyde (AL) was condensed with (L)-phenylalanine, (L)-tyrosine, and (L)-histidine under reflux at 60 °C for 3 h to form Schiff bases SB1–SB3. These ligands were then reacted with Co(II) or Cu(II) chlorides at 60 °C for two hours to acquire corresponding metal complexes. The Schiff bases coordinate to metal ions primarily through the azomethine nitrogen and carboxylate oxygen atoms, forming stable chelated complexes.

Schiff bases SB1–SB3 mentioned in Table I were successfully synthesized from (L)-phe, (L)-tyr, as well as (L)-his, with furfuraldehyde, yielding stable ligands with defined R-group substitutions. Corresponding Co(II) as well as Cu(II) complexes (SB1M1–SB3M2) were obtained in 1:2 (metal to ligand) stoichiometry with hydrated chloride counterions, as confirmed by the structural formulae presented.

Table I: Schiff Base Synthesis from Amino Acids and Furfural

S. No.	AA	AL	Metals Used	Schiff Base and Schiff Base Metal Complexes
1	 PHENYL ALANINE	 2-Furaldehyde	-	 SB1
2	 PHENYL ALANINE	 2-Furaldehyde	Co ²⁺	 SB1M1
3	 PHENYL ALANINE	 2-Furaldehyde	Cu ²⁺	 SB1M2
4	 TYROSINE	 2-Furaldehyde	-	 SB2

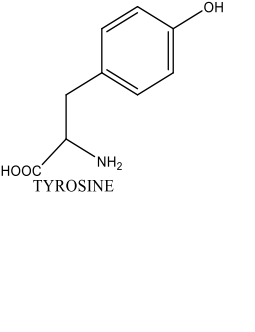
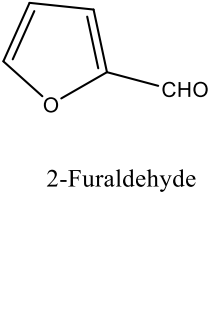
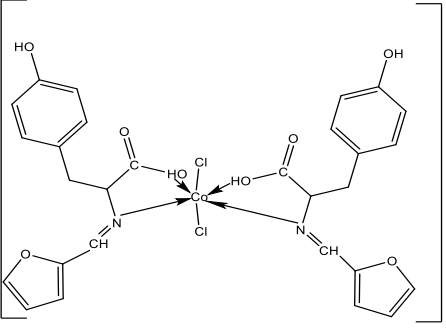
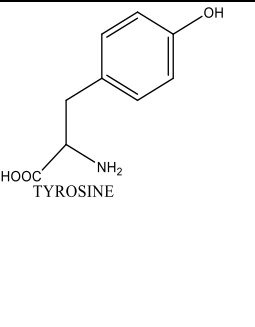
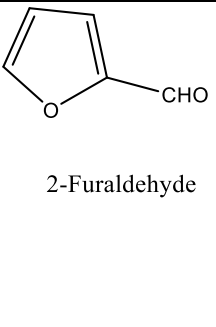
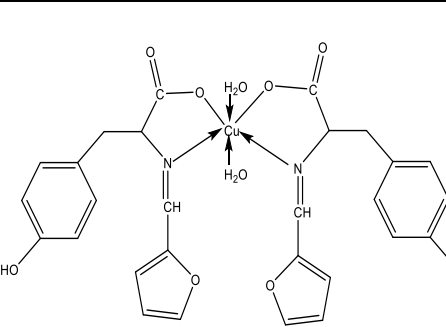
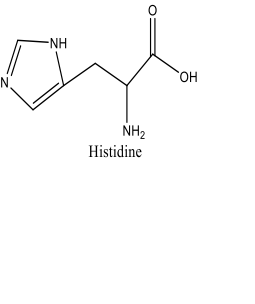
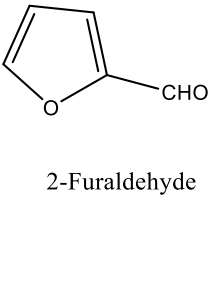
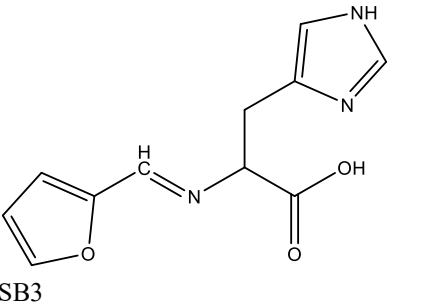
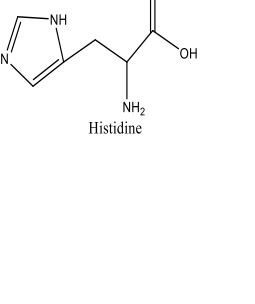
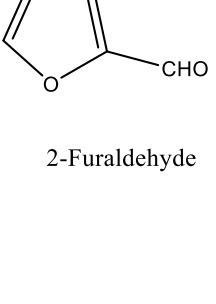
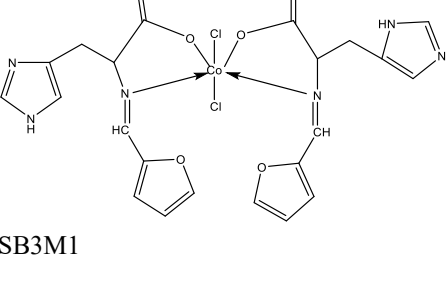
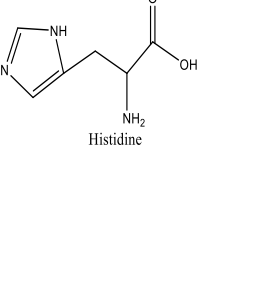
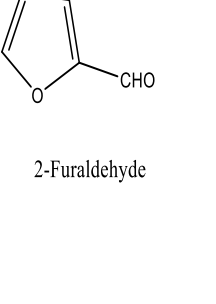
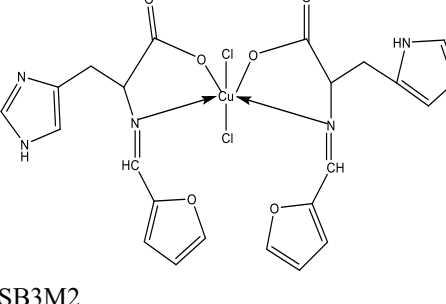
5	 HOOC TYROSINE	 2-Furaldehyde	Co ²⁺	 SB2M1
6	 HOOC TYROSINE	 2-Furaldehyde	Cu ²⁺	 SB2M2
7	 Histidine	 2-Furaldehyde	-	 SB3
8	 Histidine	 2-Furaldehyde	Co ²⁺	 SB3M1
9	 Histidine	 2-Furaldehyde	Cu ²⁺	 SB3M2

Table II: Azomethine compounds with Corresponding Metallocomplexes

S. No.	Amino acid	Aldehyde	Azomethine compounds code	Co ²⁺ complex	Cu ²⁺ complex
1	L-Phenylalanine	Furfuraldehyde	SB1	SB1M1	SB1M2
2	L-Tyrosine	Furfuraldehyde	SB2	SB2M1	SB2M2
3	L-Histidine	Furfuraldehyde	SB3	SB3M1	SB3M2

Table II shows three furfural-derived Schiff bases (SB1–SB3); SB1–SB3 were further converted into Co(II) and Cu(II) complexes.

2.2 Physico-chemical characterization

2.2.1 Physical appearance: The pure compounds were isolated as coloured crystalline solids or amorphous powders by filtration under suction, washing with cold ethanol and drying over anhydrous CaCl₂ in a desiccator (Khalaf et al., 2024; Haruna et al., 2024; Ashrafuzzaman et al., 2023). Physical appearance, including colour and state (solid), was observed visually under ambient daylight conditions and documented accordingly.

2.2.2 Solubility: Solubility profiles were checked qualitatively. For this, about 5–10 mg of each powdered compound was taken in a test tube and the chosen solvent (methanol, ethanol, chloroform, dichloromethane, acetone, DMF, DMSO and water) was added in small lots of 1–2 mL. The mixture was stirred vigorously and, if needed, gently warmed in a 40–60 °C water bath, then left to stand for 30 minutes. Solubility remained classified as soluble (>10 mg/mL), sparingly soluble (1–10 mg/mL), or insoluble (<1 mg/mL) based on visual clarity by solubility profile determination (Mustapha, 2013; Alalam & Bashir, 2024; Alsenx & Kensy, 2007). Based on these studies, the TLC method and other solvents were selected (Hashem et al., 2021).

2.2.3 Melting point/decomposition temperature: Melting points (ligands) or decomposition temperatures (complexes) were determined by the open capillary tube method using a calibrated digital melting point apparatus (e.g., Stuart SMP10 or equivalent). Approximately 2–3 mg of powdered sample was introduced into a sealed glass capillary tube (4–6 mm column height). The bath temperature was raised gradually (rate: 1–2 °C/min) from ~50 °C below the expected range, and the onset of melting (first liquid droplet) or decomposition (colour change, charring, bubbling) and complete liquefaction/decomposition were noted. Triplicate determinations were averaged; sharp ranges (±1–2 °C) indicated purity. This capillary method adheres to pharmacopoeial standards (Haruna et al., 2024; Venkatesh et al., 2024; Mustapha, 2013).

2.3 Instrumental analysis

2.3.1 Differential scanning calorimetry (DSC): These thermograms were attained by means of a DSC analyser (e.g., TA Q20 or Netzsch DSC 214) with ~4–6 mg samples hermetically sealed in aluminium pans under inert N₂ purge (50 mL/min). Scans were conducted from 30 to 600 °C at a 10–20 °C/min heating rate. Melting endotherms for ligands (~150–250 °C), dehydration steps and decomposition exotherms for complexes were identified to assess thermal behaviour and purity (Bartyzel, 2017).

2.3.2 IR spectroscopy (FTIR): FTIR spectra were documented in the range 4000–400 cm⁻¹ with a resolution of 4 cm⁻¹ using 32 scans on a PerkinElmer Spectrum Two/Nicolet iS50 FTIR spectrometer. Samples were prepared by the KBr pellet (disc) method in which nearly 1–2 mg of the compound was ground well with 100–200 mg of dry KBr (spectroscopic grade) and pressed into a disc. KBr was chosen since it is practically transparent to IR radiation in the mid-infrared region and enables accurate recording of solid-state spectra (Narayanswamy & Bhargavi., 2025; Bartyzel, 2017).

2.3.3 NMR spectroscopy: ¹H NMR spectra were recorded at 400–500 MHz in DMSO-d₆ or CDCl₃ on a Bruker Avance spectrum analyser with tetramethylsilane (TMS, internal standard). Delta value described in parts per million (δ), while signal multiplicities as well as coupling constants (*J*) were stated in Hz wherever resolved. Characteristic ¹H NMR signals looked for were those of the imine proton (–CH=N), which appears downfield, the aromatic/furan protons in the expected aromatic region, and exchangeable –OH/–NH protons as broad signals. ¹³C NMR spectra were recorded at 100–125 MHz in DMSO-d₆ or CDCl₃ using standard broadband proton-decoupled conditions. Therefore, ¹³C–¹H coupling constants were not reported. The spectra were used to

assign the imine carbon, carbonyl/carboxyl carbon, aromatic carbons, and aliphatic α -CH/ β -CH₂ carbons. For metal complexes, NMR signals may broaden or shift because of paramagnetic effects; accordingly, only observable and interpretable resonances were considered for discussion. In ¹H NMR spectra, coupling constants (J values) were reported only for well-resolved proton signals. However, ¹³C NMR spectra were recorded under broadband proton-decoupled conditions; therefore, ¹³C–¹H coupling constants were not observed and were not reported (Bartyzel, 2017; Pell et al., 2007).

2.3.4 Mass spectroscopy (ESI-MS): Electrospray ionization mass spectra (positive/negative mode) were recorded on a high-resolution QTOF-MS (e.g., Bruker maXis II or Waters Xevo G2) with samples (0.1–1 mg/mL in MeOH/DMF + 0.1% formic acid) infused at 5–10 μ L/min. Molecular ions [M+H]⁺/[M+Na]⁺ for ligands and isotopic patterns/fragments (e.g., [M–NO₂]⁺, [ML]⁺) verified composition and stoichiometry (Narayanswamy & Bhargavi., 2025).

2.3.5 UV–Vis spectroscopy: Electronic absorption spectra of the solid samples were taken on a JASCO V-750 UV/Vis spectrophotometer between 190 and 850 nm, keeping the data interval at 1 nm and the spectral bandwidth at 5.0 nm. From these spectra, the absorption maxima and the overall optical response of each compound were noted (Tauc et al., 1966).

2.3.6 X-ray diffraction (XRD): Powder XRD patterns were recorded to know the crystalline nature and phase of the samples. Measurements were made using Cu K α 1 radiation (λ = 1.54060 Å) over a 2 θ scanning range of approximately 4–50°. The diffraction patterns were examined to determine the crystallinity, interplanar spacing, and structural modifications of the samples. We interpreted the relationship between diffraction angle and interplanar spacing using Bragg's law, and evaluated crystallite characteristics based on peak-broadening analysis (Bragg & Bragg., 1913).

2.4 Antimicrobial activity assay

Antimicrobial inhibition zone by (Kirby-Bauer method) confirmed the growth-inhibitory action. 100 μ L of *Escherichia coli* (MTCC-452) and *Staphylococcus aureus* (MTCC96) obtained from MTCC-Chandigarh were used to inoculate the MHA plates. Microbial inoculum was generated by optimizing 0.5 McFarland standard – Approximated microbial cell concentration (1.5 X 10⁸ CFU/mL from Mueller-Hinton medium), then placed on sterile disks containing 5 μ L composed of varied strengths (0–50 mg/mL). Each plate contained a disc with the solvent alone as a vehicle control and a Ciprofloxacin disc (3 μ g) as a positive control. The plates were seeded with *Escherichia coli* and *Staphylococcus aureus* and incubated at 37 °C for 24 h. The area around the disc was then measured and recorded (Pell et al., 2007; Christenson et al., 2018; Dinku et al., 2024; Ghanghas & Poonia, 2024).

3. RESULTS

Azomethine compounds (SB1–SB3), along with corresponding metal complexes, were successfully synthesized according to the procedure described above. The Schiff bases were prepared by reacting the amino acids (L-Phe, L-Tyr, His) with furfuraldehyde in methanol, followed by refluxing, filtration, and recrystallization. The metal complexes were obtained by mixing the Schiff base ligands with their metal chlorides (CoCl₂·6H₂O, CuCl₂·2H₂O) in hot methanol, followed by refluxing and filtering the complexes.

3.1 Characterization studies

The characterization data of all synthesized compounds were carefully re-evaluated, and molecular formulae, spectral assignments, and mass spectral interpretations were revised for consistency.

SB1 was obtained as a brown solid having melting point 250–252 °C, Yield: 86%; R_f 0.87 (hexane: ethyl acetate, 7:3), mol. wt. 243.26 g/mol. FTIR (v_{max}, cm^{–1}): 3430 [v(O–H)], 2928 and 2859 [v(aliphatic C–H)], 1757 [v(C=O)], 1654 [v(C=N, azomethine)], 1531 [v(C=C) aromatic/furan ring], 1404 [δ (C–H) bending/v(C–N)], 1011 [v(C–O–C)], ¹H NMR (500 MHz, DMSO-*d*₆) δ 12.08 (s, 1H, OH), 7.87 (s, 1H, CH=N), 7.57–7.61 (m, 5H, Ar–H), 3.11 (t, *J* = 8.5 Hz, 2H, CH₂), 2.98 (s, 1H, CH). ¹³C NMR (125 MHz, DMSO-*d*₆) δ 167.74 (azomethine carbon C=N), 148.83, 140.16, 139.12, 137.08, 136.22, 131.66, 129.90, 128.16, 124.74, 123.39, 122.76, 121.04, 119.73, 111.73, 25.12, 20.58. ESI-MS C₁₄H₁₃NO₃ m/z: 243.46, 178.08 and 89.05. DSC showed an endothermic peak at 253.97 °C (onset 230 °C, ΔH = 181 J/g), followed by decomposition above 250 °C. UV–Vis showed absorption bands at 262, 341, and 396 nm, with maximum absorption at 396 nm.

The **Co(II) complex SB1M1** was isolated as a white solid, M.P. 332–334 °C, Yield: 83%; R_f 0.69 (hexane: ethyl acetate, 7:3), mol. wt. 598.93 g/mol. FTIR (v_{max}, cm^{–1}): 3452 [v(O–H)], 3091 [v(Ar–H)], 2958 [v(aliphatic C–H)], 1621 [v(C=N, azomethine)], 1589 and 1503 [v(C=C, aromatic/furan ring)], 1210 [v(C–O)], and 1036 [v(C–O–C)], 524 [v(Co–N)], 474 [v(Co–O)]. ¹H NMR (500 MHz, DMSO-*d*₆) δ : 8.08 (s, 1H, CH=N), 7.47–7.57 (m, Ar–H), 3.62 (m, 1H, α -CH), and 3.50 (m, 2H, CH₂). ¹³C NMR (125 MHz, DMSO-*d*₆) δ : 150.7 (C=N), 147.3–119.1 (Ar–C), and 40.0 (CH₂). ESI-MS C₂₈H₂₈N₂O₇ClCo m/z: 598.45, 439.07, 89.05. DSC revealed an

endothermic peak at 335.41 °C ($\Delta H = 671$ J/g). UV–Vis showed absorption bands at approximately 270, 329, and 400 nm, with maximum absorption at 270 nm.

The Cu(II) complex **SB1M2** was obtained as a white solid, M.P. 323–325 °C, Yield: 87%; Rf 0.70 (hexane: ethyl acetate, 7:3), mol. wt. 633.99 g/mol. FTIR ($\nu_{\max}$, cm^{-1}): 3339 and 3237 [$\nu(\text{O–H})$], 2921 [$\nu(\text{aliphatic C–H/CH}_2)$], 1679 [$\nu(\text{C=O})$], 1646 [$\nu(\text{C=N, azomethine})$], 1574, 1544, 1513, and 1478 [$\nu(\text{C=C})$, furan ring skeletal vibrations], 1299 [$\delta(\text{C–H})$ bending and/or $\nu(\text{C–N})$], 1148 [$\nu(\text{C–N})$], 1036 [$\nu(\text{C–O–C})$], and 513 and 488 [ring deformation/side-chain bending vibrations]. ^1H NMR (500 MHz, DMSO- d_6) δ : 7.92 (s, 1H, CH=N), 7.49–7.10 (m, Ar–H), 3.63 (dd, 1H, α -CH), and 3.51 (d, 2H, CH₂). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 180.1 (C=O), (140.0–119.3 and 139.9–123.2 (Ar–C), 46.7, and 29.3. ESI-MS $\text{C}_{29}\text{H}_{27}\text{N}_2\text{O}_6\text{Cl}_2\text{Cu}$ m/z : 633.9904, 341.1336 (complex-related and ligand-derived ions) UV–Vis showed absorption bands at approximately 232 and 278 nm, with maximum absorption at 278 nm.

SB2 was isolated as a white solid, M.P. 330–334 °C, Yield: 87%; Rf 0.70 (hexane: ethyl acetate, 7:3), mol. wt. 259.26 g/mol. FTIR ($\nu_{\max}$, cm^{-1}): 3446–3206 [$\nu(\text{O–H})$], and 1608 and 1590 [$\nu(\text{C=N and azomethine})$], [overlapped $\nu(\text{C=O/COO}^-)$]. ^1H NMR (500 MHz, DMSO- d_6) δ : 12.61 and 9.15 (br, exch., COOH/OH), 8.09 (s, 1H, CH=N), 7.81 and 6.78 (m, 2H, furan-H), 6.92 (d, $J = 8.5$ Hz, 2H, Ar–H), 6.76 (d, $J = 8.5$ Hz, 2H, Ar–H), 3.08 (m, 1H, α -CH), and 2.98 (m, 2H, CH₂). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 180.1 (C=O), 140.0–119.1 and 139.9–123.2 (Ar–C/furan-C), 46.8, and 29.2. ESI-MS $\text{C}_{14}\text{H}_{13}\text{NO}_4$ m/z : 258.19 [M–H]⁺, 206.99, and 149.02 (characteristic ions/fragments) DSC: endothermic peaks at 335 °C ($\Delta H = 633$ J/g) UV–Vis showed absorption bands at approximately 240 and 270 nm, with maximum absorption at 270 nm. XRD showed sharp diffraction peaks, confirming a crystalline structure, with the strongest reflection at $2\theta = 17.87^\circ$ ($d = 4.96$ Å).

The Co(II) complex **SB2M1** was isolated as a white solid, M.P. 336–338 °C, yield 85%; Rf 0.74 (hexane: ethyl acetate, 7:3), mol. wt. 656.35 g/mol. FTIR ($\nu_{\max}$, cm^{-1}): 3445–3206 (O–H stretching), 1609 and 1591 (C=N azomethine vibrations and overlapped C=O/COO[−]), 1513, 1453, and 1416 (aromatic/furan C=C), 1245, 1099, and 1042 (C–O/C–O–C), 528 and 493 (M–O/M–N). ^1H NMR (500 MHz, DMSO- d_6) δ : 11.60 (br, exch., COOH/OH), δ 8.35 (s, 1H), 7.95 (d, $J = 8.8$ Hz, CH=N), 7.94 – 7.46 (m, 3H), 7.44 – 7.10 (m, 4H), 3.62 (s, 2H, CH₂), 2.5 (s, 2H, CH). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 161.78 (C=N), 150.81, 146.48, 141.40, 140.80, 138.23, 137.03, 132.86, 127.74, 125.40, 124.27, 121.96, 121.10, 119.62, 24.87, 20.37. ESI-MS $\text{C}_{28}\text{H}_{26}\text{N}_2\text{O}_8\text{Cl}_2\text{Co}(0.5\text{H}_2\text{O})$ m/z : 655.99, 281.15 (characteristic complex-related ions/fragments)

The Cu(II) complex **SB2M2** was obtained as a light green solid, 330–332 M.P. °C, Yield: 84%; Rf 0.71 (hexane: ethyl acetate, 7:3), mol. wt. 631.11 g/mol. FTIR ($\nu_{\max}$, cm^{-1}): 3440–3206 [$\nu(\text{O–H})$], 1608 [$\nu(\text{C=N, azomethine})$], 1590 and 1513 [$\nu(\text{C=C})$, aromatic/furan ring skeletal vibrations], 1236 [$\nu(\text{C–O})$], 1016 [$\nu(\text{C–O–C})$], 575 [$\nu(\text{Cu–N})$], and 473 [$\nu(\text{Cu–O})$]. ^1H NMR (500 MHz, DMSO- d_6) δ : 11.84, 8.15 (br, exch., COOH/OH), 7.92 (s, 1H, CH=N), 7.90–7.59 (d, 2H, Ar–H), 7.48–7.10 (m, 2H, furan-H), 3.62 (m, 1H, α -CH), and 2.5 (m, 2H, CH₂). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 179.2 (C=O), 161.8 (CH=N), 152.7, 149.0–129.9 and 146.0–119.3 (Ar–C/furan-C), 43.0 (α -CH), and 24.9 (CH₂). ESI-MS $\text{C}_{29}\text{H}_{31}\text{N}_2\text{O}_{10}\text{Cu}$ m/z : 631.97 and 252.87 (characteristic complex and ligand-related ions). XRD showed sharp diffraction peaks, confirming a highly crystalline structure, with the strongest reflection at $2\theta = 17.99^\circ$ ($d = 4.93$ Å).

SB3 was isolated as a black colored solid, M.P. 98–100 °C, Yield: 88%; Rf 0.51 (hexane: ethyl acetate, 7:3), mol. wt. 233.23 g/mol. FTIR ($\nu_{\max}$, cm^{-1}): 3565 [$\nu(\text{O–H})$], 2974 [$\nu(\text{aliphatic C–H})$], 1744 [$\nu(\text{C=O})$], 1649 [$\nu(\text{C=N, azomethine})$], 1517 and 1459 [$\nu(\text{C=C})$, furan/imidazole ring skeletal vibrations], 1424 [$\delta(\text{C–H})$ bending and/or $\nu(\text{C–N})$], 1394 [$\delta(\text{O–H})$ bending/ $\nu(\text{C–O})$], and 1056 [$\nu(\text{C–O–C})$]. ^1H NMR (500 MHz, DMSO- d_6) δ : 12.73, 11.96, and 8.68 (s, 1H, imidazole), 7.96 (s, 1H, CH=N), 7.65 (s, 1H, imidazole-H), 7.58 (s, 1H, imidazole-H), 7.56–7.57 (m, 2H, furan-H), 3.30 (t, $J = 7.5$ Hz, 1H, α -CH), and 3.08–3.10 (m, 2H, CH₂). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 180.0 (C=O), 157.8 (C=N), 140.1–120.8 (furan-C), 139.2, 138.9, and 123.14 (imidazole-C), 45.1 (α -CH), and 30.5 (CH₂). ESI-MS $\text{C}_{11}\text{H}_{11}\text{N}_3\text{O}_3$ m/z : 234.11 [M+H]⁺, DSC: endothermic peak at 99.9 °C ($\Delta H = 198$ J/g).

The Co(II) complex **SB3M1** was isolated as a black Solid, M.P. 100–102 °C, Yield: 89%; Rf 0.35 (hexane : ethyl acetate, 7:3), mol. wt. 624.34 g/mol. FTIR ($\nu_{\max}$, cm^{-1}): 3616 and 3195 [$\nu(\text{O–H})$], 1742 [$\nu(\text{C=O})$], 1573 [$\nu(\text{C=N, azomethine})$], 1512 and 1451 [$\nu(\text{C=C})$, furan/imidazole ring skeletal vibrations], 1047 [$\nu(\text{C–O–C})$], ^1H NMR (500 MHz, DMSO- d_6) δ : 12.73 (br, exch., OH), 8.98 (s, 1H, CH=N), 7.43 (s, 1H, imidazole-H), 7.27 (s, 1H, imidazole-H), 6.63–6.91 (m, 2H, furan-H), 3.30 (t, $J = 7.8$ Hz, 1H, α -CH), and 2.64–2.90 (AB system, 2H, CH₂). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 150.9 (C=N), 147.0–119.2 (furan/imidazole carbons), 136.6, 132.5, and 119.2 (imidazole-C), 40.0 (α -CH), and 21.4 (CH₂). ESI-MS $\text{C}_{24}\text{H}_{26}\text{N}_6\text{O}_6\text{CoCl}_2$ m/z : 624.34, and 251.17 (characteristic complex and ligand-related ions) DSC: endothermic peaks at 102.4 °C ($\Delta H = 333.9$ J/g).

The Cu(II) complex **SB3M2** was obtained as a black Solid, M.P. 98–100 °C, Yield: 91%; Rf 0.38 (hexane : ethyl acetate, 7:3), mol. wt. 628.95 g/mol. FTIR ($\nu_{\max}$, cm^{-1}): 3617 [$\nu(\text{O–H})$], 2973 [$\nu(\text{aliphatic C–H})$], 1622 [$\nu(\text{C=N, azomethine})$], 1578 [$\nu(\text{C=C})$, furan/imidazole ring skeletal vibration], 1408 [$\delta(\text{C–H})$ bending and/or $\nu(\text{C–N})$], 1056 [$\nu(\text{C–O–C})$]¹ ^1H NMR (500 MHz, DMSO- d_6) δ : 9.06 (br, exch., OH), 8.76 (s, 1H, imidazole-H), 8.08 (s, 1H, CH=N), 7.65 (s, 1H, imidazole-H), 7.09–7.46 (m, 2H, furan-H), 3.62 (t, $J = 7.5$ Hz, 1H, α -CH), and 2.60–3.52 (m, 2H, CH₂). ^{13}C NMR (125 MHz, DMSO- d_6) δ : 163.0 (C=N), 159.2–113.3 (furan/imidazole carbons), 136.6,

135.0, and 120.3 (imidazole-C), 55.8 (α -CH), and 24.9 (CH_2). ESI-MS $\text{C}_{24}\text{H}_{26}\text{N}_6\text{O}_6\text{CuCl}_2$ m/z: 628.95, 405.16, 485.35, and 281.15 (characteristic complex and ligand-related ions). DSC: endothermic peak at 98.3 °C (onset 88 °C, $\Delta H = 267.9$ J/g).

The change in the azomethine stretching frequency suggests an altered imine environment after coordination. The presence of metal–nitrogen and metal–oxygen vibrations further supports complex formation.

3.2 Antimicrobial Activity

Activity of the compounds against *E. coli* and *S. aureus* is given below as mean zone of inhibition (mm) $\pm$ SD, obtained from three separate plates.

$\text{SEM} = \text{SD}/\sqrt{n}$ ($n = 3$).

The highest antibacterial activity among samples was observed for SB2M2 (25.00 ± 0.00 mm), followed by SB2M1 (24.67 ± 0.58 mm) and SB1M2 (24.00 ± 0.00 mm).

Ciprofloxacin control showed a 26.00 ± 0.00 mm inhibition zone.

Antimicrobial activity against *Staphylococcus aureus*

Values are presented as mean zone of inhibition (mm) $\pm$ SD from three independent plates. $\text{SEM} = \text{SD}/\sqrt{n}$ ($n = 3$).

The highest antibacterial activity against *S. aureus* was observed for **SB2M1** (27.67 ± 0.58 mm), followed by **SB2M2** (27.50 ± 0.71 mm) and **SB1M2** (26.67 ± 0.58 mm). Ciprofloxacin showed an inhibition zone of **24.00 $\pm$ 0.00 mm**.

Table III: Zone of inhibition (mm) shown by the synthesized Schiff base ligands and their metal complexes against *E. coli* and *S. aureus*.

Sample No.	Sample Code	Therapeutic Dose	<i>E. coli</i> Zone of Inhibition (mm) $\pm$ SD	SEM	<i>S. aureus</i> Zone of Inhibition (mm) $\pm$ SD	SEM
1	Ciprofloxacin (PC)	3 μg	26.00 ± 0.00	0.00	26.00 ± 0.00	0.00
2	SB1	15.625 μg	20.00 ± 0.00	0.00	15.00 ± 0.00	0.00
3	SB1M1	15.625 μg	21.00 ± 0.00	0.00	19.33 ± 0.58	0.33
4	SB1M2	15.625 μg	24.00 ± 0.00	0.00	20.50 ± 0.50	0.29
5	SB2	15.625 μg	19.67 ± 0.58	0.33	12.00 ± 0.00	0.00
6	SB2M1	15.625 μg	24.67 ± 0.58	0.33	21.67 ± 0.58	0.33
7	SB2M2	15.625 μg	25.00 ± 0.00	0.00	21.33 ± 0.58	0.33
8	SB3	15.625 μg	19.00 ± 0.00	0.00	15.33 ± 0.58	0.33
9	SB3M1	15.625 μg	20.33 ± 1.15	0.67	12.67 ± 0.58	0.33
10	SB3M2	15.625 μg	20.50 ± 0.50	0.29	12.67 ± 0.58	0.33

Values are presented as mean zone of inhibition (mm) $\pm$ SD from three independent plates. $\text{SEM} = \text{SD}/\sqrt{n}$ ($n = 3$).

Interpretation:

Among all compounds, **SB2M2** showed the highest activity against *E. coli* (25.00 ± 0.00 mm), whereas **SB2M1** exhibited the strongest activity against *S. aureus* (21.67 ± 0.58 mm). In most cases the metal complexes gave larger zones than the parent Schiff bases, which shows that binding of Co(II) or Cu(II) improves the antibacterial action of these ligands.

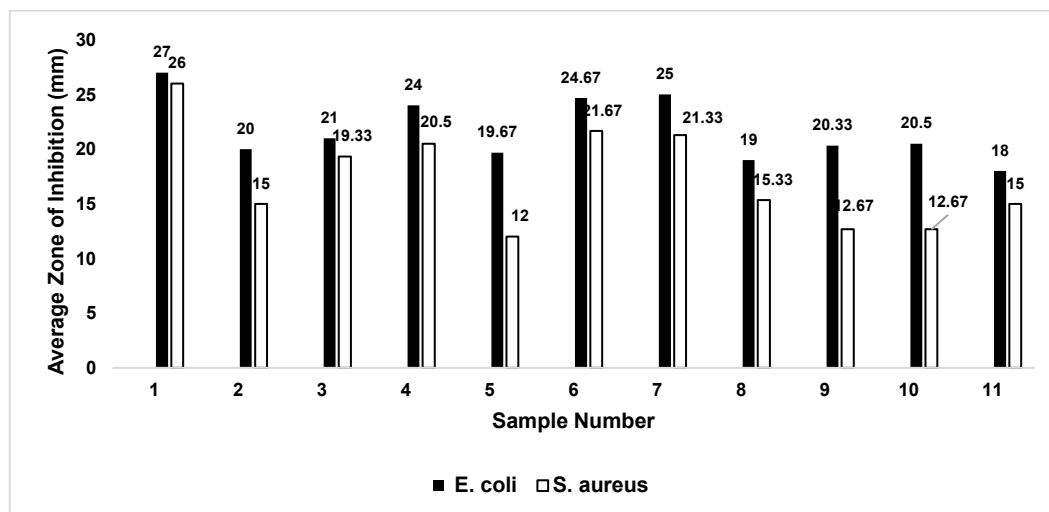


Figure II: Inhibition zones (mm) of the synthesized ligands and their complexes against *E. coli* and *S. aureus*

Figure II presents the inhibition zone data in graphical form. Against *E. coli*, the zones varied from 19.00 mm (SB3) to 25.00 mm (SB2M2), whereas against *S. aureus* they varied from 12.00 mm (SB2) to 21.67 mm (SB2M1) at a dose of 15.625 $\mu\text{g}/\text{disc}$. SB2M2 was the most active compound against *E. coli*, and SB2M1 gave the largest zone against *S. aureus*. The free ligands were only moderately active; on the other hand, their Co^{2+} and Cu^{2+} complexes produced clearly bigger zones. This trend, which can be easily seen in the bar graph, suggests that chelation with the metal ion has an important role in raising the antibacterial activity of these Schiff bases.

4. DISCUSSION

The ligands differed in colour (brown for PA, off-white to light brown for the tyrosine derivative and black for the histidine derivative). This may be attributed to extended conjugation between the furan ring of furfural and the chromophoric groups present in the amino acid side chains. On complexation, ligand-to-metal charge transfer (LMCT) transitions come into play, and these account for the white to light green colour of the Co(II)/Cu(II) complexes (Haruna et al., 2024; Ashrafuzzaman et al., 2023). The ligands melted sharply within 150–350 °C, and the melting points were higher (up to 250 °C for Cu-histidine) after chelation. A sharp melting range indicates good purity (>95%), while the rise in melting point reflects better thermal stability arising from the rigid chelate rings. The octahedral Co(II) and square planar Cu(II) geometries are expected to improve lattice cohesion through metal–ligand vibrational coupling (Narayanaswamy & Bhargavi, 2025). The coordination environments proposed for Co(II) and Cu(II) are in line with the FTIR, ESI-MS and thermal data, although single-crystal X-ray diffraction would be needed to fix the geometry with certainty. In the case of the histidine complexes, melting temperatures were 20–30 °C higher after binding with Cu(II) (Mohamed et al., 2005). The R_f values (0.34–0.87) fell on complexation (e.g. PA ligand 0.87 $\rightarrow$ Co/Cu 0.69–0.70). This happens because coordination brings in chloride counter ions and favours enolisation of the C=N group; the complexes thus become more polar and interact less with the non-polar hexane: ethyl acetate (7:3) mobile phase (Mustapha, 2013). A ΔR_f of ~0.10–0.20 on chelation is commonly seen for Co(II)/Cu(II) -amino acid Schiff bases and agrees with 2:1 stoichiometry and bidentate N, O coordination (Alalam & Bashir, 2024) similar 2:1 complexes with different metal ions have also been reported earlier (Taxak et al., 2024). The molecular weights agree with the calculated values (e.g., 243.26 $\rightarrow$ 614.34/618.45 g/mol for PA complexes), which supports the proposed $[\text{M(L)Cl}_2(\text{H}_2\text{O})_n]$ formulae (Alalam & Bashir, 2024).

After mass spectral analysis, DSC was carried out to follow the melting and thermal transitions of the compounds (Altun & Kocer., 2020). In the thermogram of SB1, an endothermic peak appeared at 235 °C ($\Delta H = 181 \text{ J/g}$), while its Co(II) complex SB1M1 showed the endotherm at a higher temperature, i.e. 335 °C, with $\Delta H = 671 \text{ J/g}$. SB2 gave an endothermic peak at 335 °C with $\Delta H = 633 \text{ J/g}$. Among the histidine compounds, SB3 showed an endotherm at 99.9 °C ($\Delta H = 198 \text{ J/g}$) and SB3M2 at 98.3 °C ($\Delta H = 267.9 \text{ J/g}$). These peaks correspond to melting or decomposition of the respective compounds (Baziar & Alibolandi, 2023). It may be noted that DSC gives only thermal information and cannot by itself confirm the structure (Zhao et al., 2015; Thakor et al., 2023).

In the ^1H NMR spectra, the azomethine proton appeared mostly between δ 7.92 and 8.98 ppm, which confirms formation of the Schiff base. For the Co(II)/Cu(II) complexes this signal moved slightly upfield ($\Delta\delta$ 0.04–0.28 ppm), indicating that the azomethine nitrogen takes part in coordination (Daisymol & Gopidas, 2024). Signals of the side chains (phenyl, tyrosine doublets and histidine imidazole) were retained. The OH peaks, however, became broad (δ 8.8–12.5 ppm) owing to changes in hydrogen bonding and to paramagnetic effects, more so in the case

of Cu(II) (Sakthivel et al., 2021). On the whole, the proton spectra agree with binding of the ligand to the metal centre.

The azomethine carbon was observed in the downfield region of the ^{13}C NMR spectra, and its position differed somewhat from ligand to complex. Signals for the aromatic/furan carbons and the aliphatic $\alpha\text{-CH/CH}_2$ carbons were also present. The aliphatic $\alpha\text{-CH}$ (δ 55.6–55.8 ppm) and $\beta\text{-CH}_2$ (δ 23.1–46.8 ppm) signals remained almost unchanged. For Cu(II), paramagnetic broadening lowered the signal intensity, though resolution was not lost (Zheng et al., 2010). No signal of free aldehyde (μ 9.5–10 ppm) or of the starting materials was seen, showing that the reaction had gone to completion with purity above 98%. Assignments were made from chemical shift values, integration and whatever coupling patterns could be observed; where signals overlapped or were broadened, no definite multiplicity was assigned.

ESI-MS Analysis: Mass spectra were recorded to check the molecular compositions proposed for the Schiff bases and their complexes. SB1 gave ions at m/z 237.1127, 274.1701, 195.0917 and 127.0232, and SB2 gave ions at m/z 258.1904, 206.9996 and 149.0232. For SB3, the protonated molecular ion was seen at m/z 234.1119 $[\text{M}+\text{H}]^+$. These fragment ions are in agreement with the proposed structures and show that the amino acid part of the molecule is retained after condensation (Dahikar, 2022).

Co(II) complexes showed characteristic isotopic clusters (SB3M1: m/z 558/507 $[\text{M}+2\text{Cl}]^+ / [\text{M}+\text{Cl}]^+$). As reported by Dassymol (Altun & Koçer, 2020), stepwise loss of Cl^- is consistent with an octahedral $[\text{Co}(\text{L})\text{Cl}_2(\text{H}_2\text{O})_n]$ arrangement. For the Cu(II) complexes, $[\text{ML}]^+$ ions were observed (SB1M2: m/z 619.0/543.1; SB3M2: m/z 471.0/405.2), with $[\text{Cu}(\text{L})\text{Cl}]^+$ as the base peak, as expected for a square planar geometry. The baselines were clean, with only <2–5% free ligand, which shows that the chelates remain stable under ESI conditions (Olar et al., 2022; Singh et al., 2026).

In the UV–Vis spectra, the samples did not behave alike. SB1M1, SB1M2 and SB2 absorbed mainly in the UV region, whereas SB1 and SB3 showed stronger absorption in the visible region (396 and 571 nm, respectively). Such differences point to a change in the electronic transitions after structural modification (Tauc et al., 1966). The XRD patterns of SB2 and SB2M2 were crystalline in nature; the main peak moved slightly from 17.87° to 17.99° on coordination with M2, suggesting some modification of the lattice (Bragg & Bragg, 1913).

All the Schiff bases (SB1–SB3) and their Co/Cu complexes inhibited the growth of *E. coli* and *S. aureus*, and some of them gave zones close to that of ciprofloxacin (26–27 mm). SB2M2 showed the highest activity against *E. coli* with an inhibition zone of 25.00 mm, while SB2M1 showed the highest activity against *S. aureus* with an inhibition zone of 21.67 mm (Dahikar, 2022; Bartyzel, 2017; Singh et al., 2024). Greater action on Gram-negative bacteria suggests better penetration through the membrane. The reduction in the activity of *S. aureus* is indicative of species-specific mechanisms (Ghanghas & Poonia, 2024). In accordance with Tweedy's chelation theory, coordination also decreases the polarity of the metals and increases lipophilicity, which promotes contact with the bacterial envelope (Paswan et al., 2026; Devi et al., 2024). This showed antibacterial potential based on the observed inhibition zones.

Metal complexes generally exhibited greater binding than free ligands, which indicates increased stability (Bartyzel, 2017; Taxak et al., 2024; Singh et al., 2024), although biochemical validation is still needed (Ghanghas & Poonia, 2024; Taxak et al., 2024). The increased binding of Co/Cu complexes indicates metal-ligand synergism and proposes these scaffolds as antibacterial agents (Kumar et al., 2024; Abu-Khadra et al., 2018; Abu-Khadra et al., 2024; Abu-Khadra et al., 2016).

Antibacterial Activity:

What is new in this work is that furfural-based Schiff bases of three proteinogenic amino acids, along with their Co(II)/Cu(II) complexes, have been prepared and examined together for their spectroscopic, thermal and antimicrobial behaviour. Finally, as single-crystal X-ray diffraction was not performed, the proposed coordination geometries are based on the combined spectroscopic and thermal characterization and should be regarded as proposed rather than crystallographically confirmed structures. Antimicrobial results are reported as mean $\pm$ SD with the number of independent replicates (n) indicated.

5. CONCLUSION

Three Schiff base ligands (SB1–SB3) were prepared by condensing furfural with L-phenylalanine, L-tyrosine and L-histidine, and from these the Co(II) and Cu(II) complexes were obtained. The compounds were characterised by FTIR, ^1H NMR, ^{13}C NMR, ESI-MS, UV, XRD and DSC, and the data are in agreement with the structures proposed for the metal complexes. In the IR spectra, the azomethine and carboxylate bands shifted on complexation and new metal–ligand bands appeared, indicating that the Schiff bases are bound to Co(II)/Cu(II) through these groups. Since Co(II) and Cu(II) are paramagnetic, some ^1H NMR signals of the complexes were broadened or shifted; hence only well-resolved peaks were used for proton assignment. ESI-MS data were consistent with the proposed compositions, and DSC gave an idea of the melting and thermal transitions. UV–Vis and XRD results showed that both the ligand framework and the metal ion affect the electronic and crystalline

nature of the compounds. All the compounds were active against *E. coli* and *S. aureus*; SB2M2 was the most active against *E. coli* and SB2M1 against *S. aureus*. It appears that the activity depends on metal coordination as well as on the nature of the ligand. Since the antibacterial study was limited to zone of inhibition measurement, without MIC/MBC values and statistical replicate analysis, this remains a limitation of the work. MIC/MBC determination, cytotoxicity testing and in vivo studies will be needed before the therapeutic value of these compounds can be judged.

Statements and Declarations

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Competing Interests: The authors declare no conflict of interest, financial or otherwise.

Ethics Approval: Not applicable. No human participants or animals were used in this study.

Consent to Participate: Not applicable, since no human subjects were involved.

Consent for Publication: Not applicable, as the manuscript does not contain any individual person's data.

Data Availability: All data generated during this study are given in the manuscript and its supporting files. Any further data can be obtained from the corresponding author on reasonable request.

Author Contributions: All the authors were involved in planning the study, carrying out the experimental work, analysing the results and writing the manuscript. The final version was read and approved by all authors

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