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SYNTHESIS, SPECTRAL CHARACTERIZATION AND BIOLOGICAL STUDIES OF Co(II) COMPLEXES WITH SCHIFF BASES DERIVED FROM SULPHA DRUGS

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ABSTRACT. This study reports the synthesis, spectral characterization, and antimicrobial evaluation of a cobalt(II) complex, $[Co(L)_2Cl_2]$, derived from 4-amino-N-(5-methyl-1,2-oxazol-3-yl)benzenesulfonamide and 2-hydroxybenzaldehyde. The complex was synthesized via refluxing the Schiff base ligand with Co(II) chloride in ethanol. Spectroscopic and analytical techniques (molar conductance, elemental analysis, IR, UV-Vis, ^1H and ^{13}C NMR, and mass spectrometry) confirmed complex formation and bidentate coordination through azomethine nitrogen (-CH=N) and phenolic oxygen (-OH). Electronic spectra and magnetic moment data suggested an octahedral geometry. The electrochemical behavior of the complex was analyzed using cyclic voltammetry, revealing quasi-reversible Co(II)/Co(I) redox behavior. Antimicrobial activity was evaluated using the disc diffusion method against *Staphylococcus aureus*, *Proteus vulgaris*, and *Candida albicans*. The Co(II) complex exhibited enhanced antibacterial and antifungal activity compared to the free Schiff base, attributed to increased lipophilicity and better microbial membrane interaction. Minimum inhibitory concentration (MIC) studies further confirmed its effectiveness. These findings highlight the potential of Schiff base Co(II) complexes as promising antimicrobial agents, supporting further exploration for biomedical applications.

KEY WORDS: Schiff base, Co(II) complex, Elemental analysis, Spectral characterization, Redox behavior, Fluorescence, Antibacterial assay, Antifungal activity and MIC studies.

INTRODUCTION

Schiff bases, named after the eminent chemist Hugo Schiff, are formed when primary amines react with aldehydes or ketones, resulting in compounds known as imines or azomethines. In these compounds, the carbonyl group (C=O) is substituted by an imine group [1]. The synthesis of novel compounds aimed at treating infections with reduced secondary effects presents a significant biomedical challenge [2, 3]. Recent research has increasingly focused on the development of transition metal complexes with Schiff-type ligands due to their promising biological properties. Numerous compounds derived from Schiff bases have been reported to exhibit antibacterial [4], antifungal [5], antitumor [6], and anti-HIV [7] activities. An interesting application of Schiff bases, is their use as an effective corrosion inhibitor [8].Among transition metals, cobalt(II) complexes have attracted interest due to their diverse biological and catalytic properties. Cobalt plays a vital role in enzymatic reactions and vitamin B_{12} analogs, contributing to biochemical and pharmacological advancements [9]. The chelation of Schiff bases with Co(II) significantly alters their physicochemical properties, often leading to increased bioavailability, enhanced lipophilicity, and superior antimicrobial activity. Chelation enhances the permeability of these metal complexes across microbial cell membranes, disrupting vital enzymatic functions and metabolic pathways, making them promising candidates for drug development [9, 10]. It can also be key points in the development of inorganic biochemistry, catalysis and optical materials [11].

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Their structural flexibility allows for tunable properties, making them valuable in various scientific and technological domains [12].

This study aims to enhance the understanding of Schiff bases by focusing on the synthesis and characterization of a Co(II) complex derived from 4-amino-N-(5-methyl-1,2-oxazol-3-yl)benzenesulfonamide and 2-hydroxybenzaldehyde. A comprehensive investigation of the ligand and its metal complex will be conducted using various analytical techniques, including molar conductance, elemental analysis, infrared spectroscopy, electronic spectra, proton and ^{13}C NMR and mass spectrometry. Antibacterial assays will be performed against gram-positive bacteria and fungi to evaluate the biological activity of the synthesized complex. This research will provide insight into the potential applications of the Co(II) complex in biomedical fields [13].

EXPERIMENTAL

All chemicals and reagents used in this study were of analytical grade. Conductance measurements were performed using an Elico Conductivity Bridge equipped with a dip conductivity cell. Solvents were purified and dried according to standard procedures. Elemental analysis of the ligand and complexes was conducted using an Elementar Vario EL CHN rapid analyzer. Infrared (IR) spectra of the ligand and complex were recorded as KBr pellets on a SHIMADZU 8000 FT-IR spectrophotometer. The ^{1}H and ^{13}C NMR spectra of the ligand were obtained with a Bruker Avance DPX-400 spectrometer, utilizing TMS as the internal standard and DMSO-d6 as the solvent. Melting points were determined using an open capillary method with a silicon bath electric melting point apparatus and were uncorrected. Electronic spectra were recorded using a UV-Vis spectrophotometer, and fluorescence spectra were detected using a Perkin Elmer LS 45 Spectrofluorometer. The antibacterial activity of the complexes was evaluated using the disc diffusion method against gram-positive *Staphylococcus aureus* and gram-negative *Proteus vulgaris*, along with the fungal species *Candida albicans*, with the results compared to standard drugs. Statistical analysis was performed to determine the minimum inhibitory concentration (MIC) values for the most active compound.

Synthesis of Schiff base ligand

An ethanolic solution of 4-amino-N-(5-methyl-1,2-oxazol-3-yl)benzenesulfonamide (0.01 mol) was stirred and heated, followed by the addition of an ethanolic solution of 2-hydroxy-benzaldehyde (0.01 mol) [14].The mixture was refluxed for 4 hours. Upon cooling, an orange-colored solid formed, which was filtered, washed, and dried over anhydrous $CaCl_2$ in a desiccator. The purity of the ligands was confirmed using TLC and spectral data analysis.

Synthesis of complex

An ethanolic solution of Schiff base (0.718 g, 0.002 mol) in a minimal amount of dimethyl formamide was heated and stirred magnetically. To this, an ethanolic solution of the respective Co(II) chloride (0.001 mol) was added. The mixture was then refluxed on a water bath for 8 hours. The resulting colored precipitate were cooled in an ice bath, collected by suction filtration, thoroughly washed with ethanol and ether, and finally dried.

Preparation of disc for antimicrobial studies

Sterile Whatman No. 1 filter paper discs (6 mm in diameter) were used for antimicrobial testing. The discs were impregnated with a specific concentration (25, 50, 75, and 100 mg/L) of the cobalt(II) complex dissolved in DMSO by soaking them in the solution for a few minutes. After impregnation, the discs were air-dried under aseptic conditions in a laminar airflow chamber to remove excess solvent. For comparison, standard antibiotic discs (ciprofloxacin for bacteria and nystatin for fungi) were used as positive controls, while a DMSO-impregnated disc was used as a negative control to confirm that the solvent had no inhibitory effect. The prepared discs were then stored in sterile Petri dishes at 4 °C until use in the disc diffusion assay.

RESULTS AND DISCUSSION

The reaction between 4-((2-hydroxybenzylidene)-amino)-N-(5-methyl-1,2-oxazole-3-yl)-benzenesulfonamide (L) and metal chlorides in equimolar amounts forms the complexes, as represented by the following equations.

$$\mathrm{MCl_2\,.nH_2O + 2L \xrightarrow[\text{reflux}]{\text{ethanol\textbackslash DMF}} [M(L)_2(Cl)_2] + nH_2O}$$

where M = Co(II). The microanalytical data (Table 1) confirmed the composition of the ligand and its complexes. Conductance measurements indicate the non-electrolytic [15] nature of the metal complexes, suggesting that no anions exist outside the coordination sphere.

Table 1. Physical characteristics and analytical data of Schiff base and its complex.

S. No.	Schiff base and Complex	Molecular formula	Colour	Yield %	M.Pt °C	Λ_m ohm^{-1} cm^2mol^{-1}	Elemental analysis % found (calcd.)				
							C	H	N	S	Metal
1	L	$C_{18}H_{16}N_3O_4S$	Yellow	80	170	----	57.79 (58.37)	4.21 (4.32)	10.92 (11.31)	8.52 (8.64)	---
2	$[Co(L)_2Cl_2]$	$C_{36}H_{28}N_6O_6S_2CoCl_2$	Pale yellow	70	232	12.08	51.81 (51.86)	3.19 (3.36)	9.86 (10.08)	7.53 (7.68)	6.89 (7.07)

FT–IR spectra

The IR spectra of the complexes (Figures 1 and 1a) were analyzed in comparison with the Schiff base (L) to identify the coordination sites involved in metal binding. The Schiff base ligand contains five potential donor sites: i) phenolic oxygen, ii) azomethine nitrogen, iii) sulfonamide nitrogen, iv) sulfonamide oxygen, and v) ring nitrogen. Schiff base (L) IR (solid state, cm^{-1}): ν(>C=N) 616; ν(O-H)3471; $[Co(L)_2Cl_2]$ (solid state, cm^{-1}): ν(>C=N) 1617; ν(O-H) 3407; ν(M-O) 569; ν(M-N) 466; $\nu_{as}(SO_2)$ 2853; ν(C–O) 1209.

The IR spectrum of the Schiff base (Figure 1) displays a strong band at 1616 cm^{-1}, attributed to the azomethine ν(-CH=N) group. A broad band around 3471 cm^{-1} corresponds to the phenolic ν(O-H) stretching, indicating hydrogen bonding. Upon complexation with Co(II), the azomethine ν(-CH=N) shift from 1616 cm^{-1} to 1617 cm^{-1} confirms the coordination of the nitrogen atom. The phenolic ν(O-H) remains unchanged, suggesting oxygen coordination without deprotonation. Bands at 569 cm^{-1} and 466 cm^{-1} correspond to ν(M-O) and ν(M-N), indicating metal-ligand bonding. No significant changes in the sulfonamide oxygen, amido nitrogen, or S-N and C-S vibrations indicate their non-involvement in coordination. A shift in phenolic ν(C-O) from 1225 cm^{-1} in the Schiff base to 1209-1213 cm^{-1} in the complexes confirms coordination through oxygen[16]. Overall, the IR data (Figure 1) suggest that the Schiff base acts as a bidentate ligand, coordinating via azomethine nitrogen and phenolic oxygen.

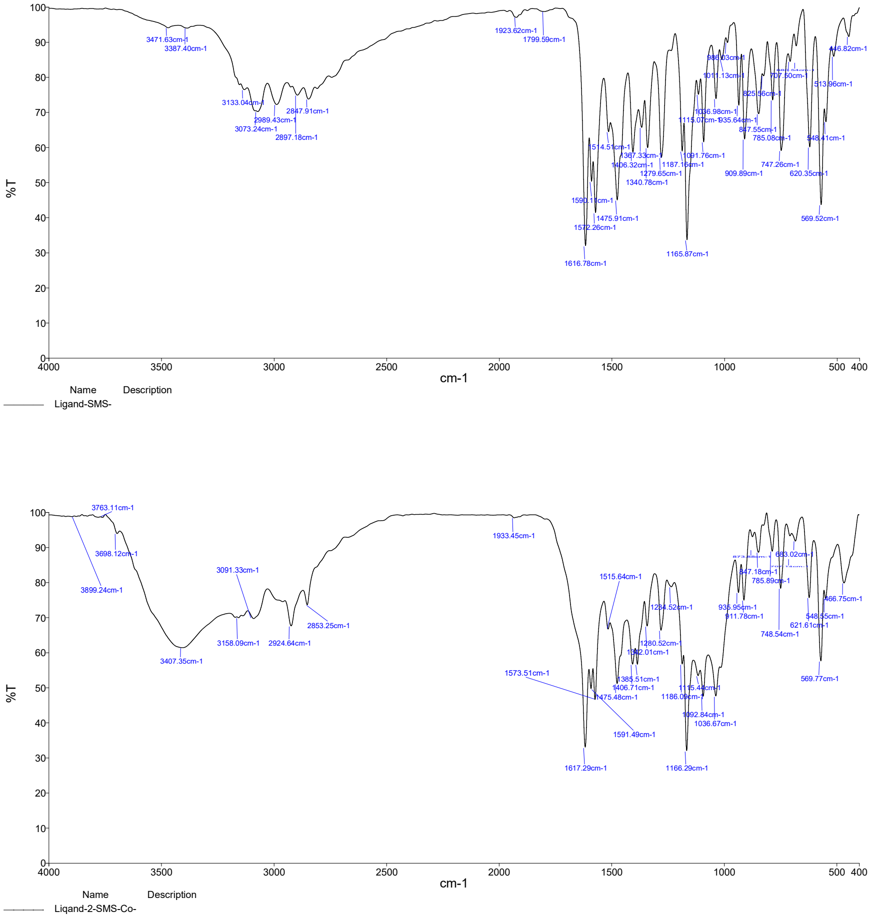


Figure 1. IR spectrum of the ligand and Co(II) complex.

Electronic spectra and magnetic susceptibility measurements

The electronic spectra and magnetic susceptibility measurements have been used to determine the ligand field environment around the metal ion and the geometry of the complex. Ligand (L) (λ_{max}nm (cm^{-1})): 277 (36101) π-π*; 344 (29096) n-π* -ILCT. [Co(L)$_2$Cl$_2$] (λ_{max}nm (cm^{-1})): i) 262 (38168) - M→L, ii) 303 (33003) – M→L, and iii) 473 (21142) - ^{4}T1g→^{4}T$_{2g}$ [4.81 BM].

The electronic spectrum of the ligand displays two absorption maxima. The band at 277 nm (36101 cm^{-1}) is attributed to the π-π* transition in the aromatic portion of the ligand, while the band at 344 nm (29069 cm^{-1}) is assigned to the n-π* transition [17] associated with the azomethine linkage.

The nature of the ligand field around the cobalt ion and the geometry of the complex have been determined from electronic spectral and magnetic susceptibility measurements. In the UV-Vis spectra (Figure 2), the bands in the 350-400 nm region are attributed to charge transfer bands in the cobalt complex, which are absent in the free Schiff base. The broad band observed in the 400-600 nm range corresponds to the various d-d transitions of the metal ion. Specifically, the

Co(II) complex exhibits bands at 262 nm (38167 cm^{-1}) and 303 nm (33003 cm^{-1}) due to metal-to-ligand charge transfer transitions. The band at 473 nm (21142 cm^{-1}) is assigned to the $^4T_1g \rightarrow {}^4T_2g$ transition, indicating an octahedral geometry [18] for the complex. The magnetic moment of the Co(II) complex is 4.81 B.M., consistent with a six-coordinate geometry.

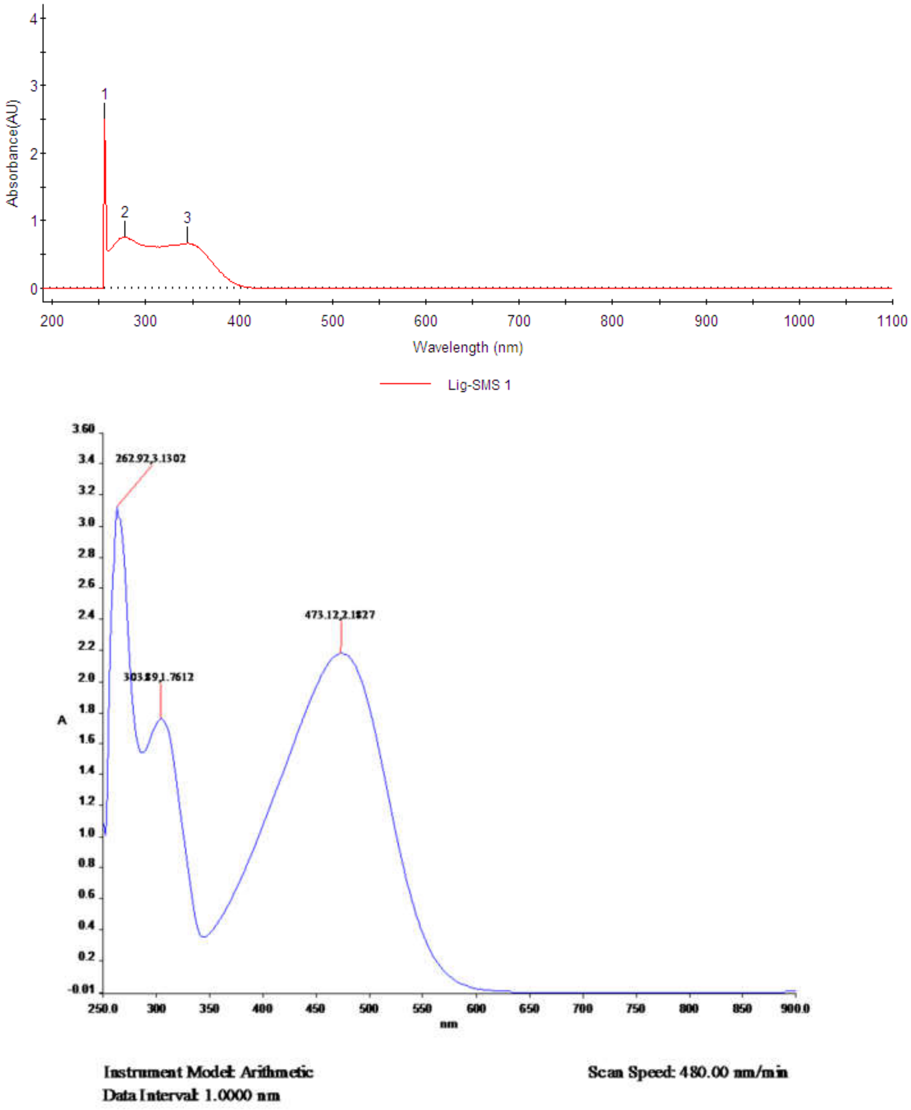


Figure 2. UV spectrum of ligand and Co(II) complex.

^{1}H-NMR spectra

Schiff base (L) (DMSO-d$_6$, δ, ppm): 7.440-7.573(m, aromatic), 7.911(s,-C=N-). The ^{1}H NMR spectrum of Ligand L (Figure 3) exhibits peak at δ 8.94 ppm (s,1H) suggesting the appearance of –CH=N proton. The peak at δ 12.47 ppm (s, 1H) and peak in the range 6.57-7.91 ppm indicate hydroxyl and aromatic protons [19].

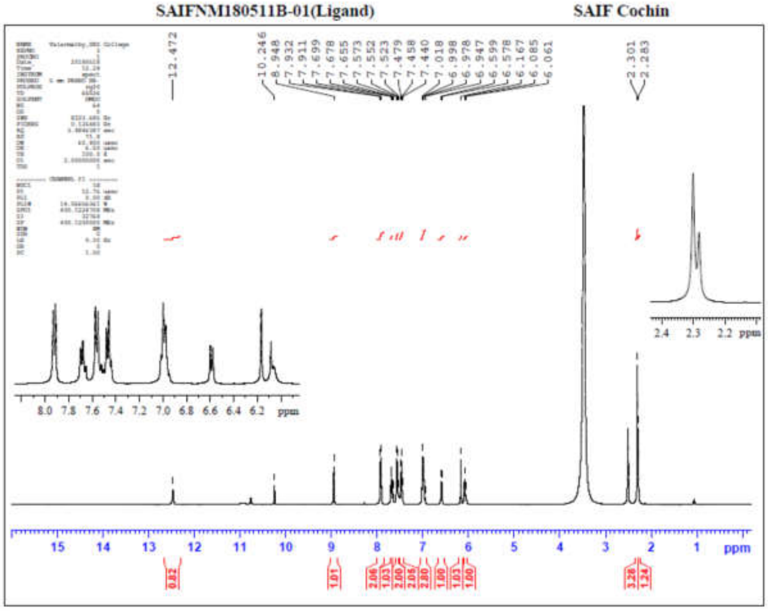


Figure 3. ^{1}H NMR spectrum of [4-amino-N-(5-methyl-1,2-oxazol-3-yl)benzenesulfonamide (L).

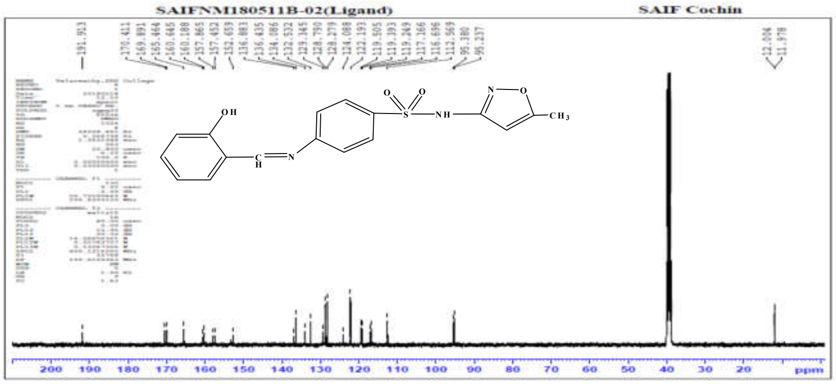


Figure 4. ^{13}C NMR spectrum of [4-amino-N-(5-methyl-1,2-oxazol-3-yl)benzenesulfonamide (L).

^{13}C-NMR spectra

The^{13}C-NMR spectrum of the Schiff base was taken in DMSO-d$_6$ solvent. The ^{13}C-NMR spectrum of the ligand L exhibits peak at downfield shifting of the –CH=N- signal from the 165.4 ppm in the ligand (Figure 4). Schiff base (L1) (DMSO-d_6, δ, ppm): 165.4(–CH=N-), 160.6 (phenolic C-OH)

EI-mass spectra

The EI-Mass spectra of the ligand shows a molecular ion peak at m/z 370.54 and 366.74 which corresponds to calculated value. The mass spectra of $C_{36}H_{28}N_6O_6S_2CoCl_2$ show peaks at m/z = 752.54 and corresponds to [M+2] peak. These peaks support the expected molecular masses of the complexes and confirm the formulae of metal chelates as $[Co(L)_2Cl_2]$ type. The spectra of the Schiff base and its complexes show characteristic molecular ion peaks at their expected m/z values confirming their stoichiometry as suggested (Figure 5).

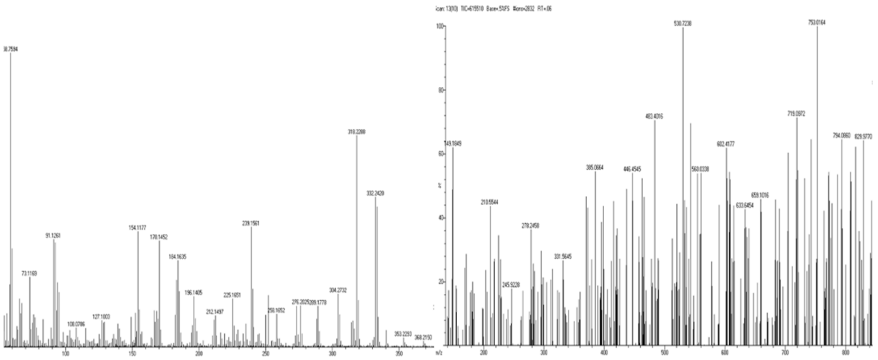


Figure 5. Mass spectra of the ligand and Co(II) complex.

Electrochemical behavior

Measurements were carried out over a potential range of -2.5 V to +2.5 V for the Co(II) complex at a scan rate of 0.1 V/s. Since no redox waves were detected for the Schiff base in this range, the observed reductive responses (Figure 6) were attributed solely to the Co(II) metal center. The separation in peak potential (ΔEp) and an i_{pa}/i_{pc} ratio less than one suggest that the one-electron transfer reaction of the Co(II)/Co(I) couple exhibits quasi-reversible behavior [20].

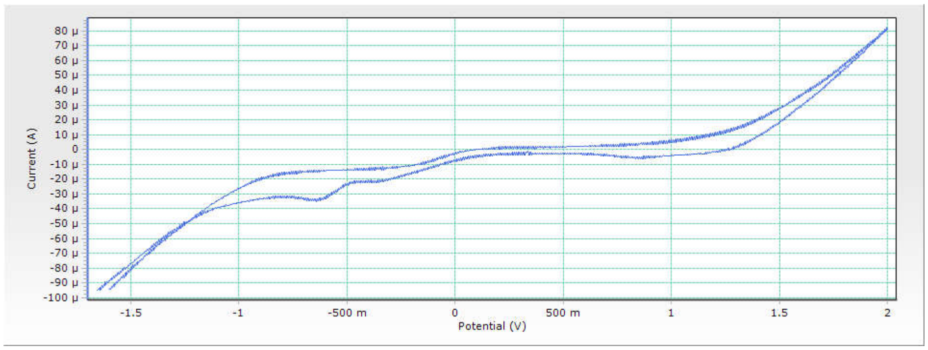
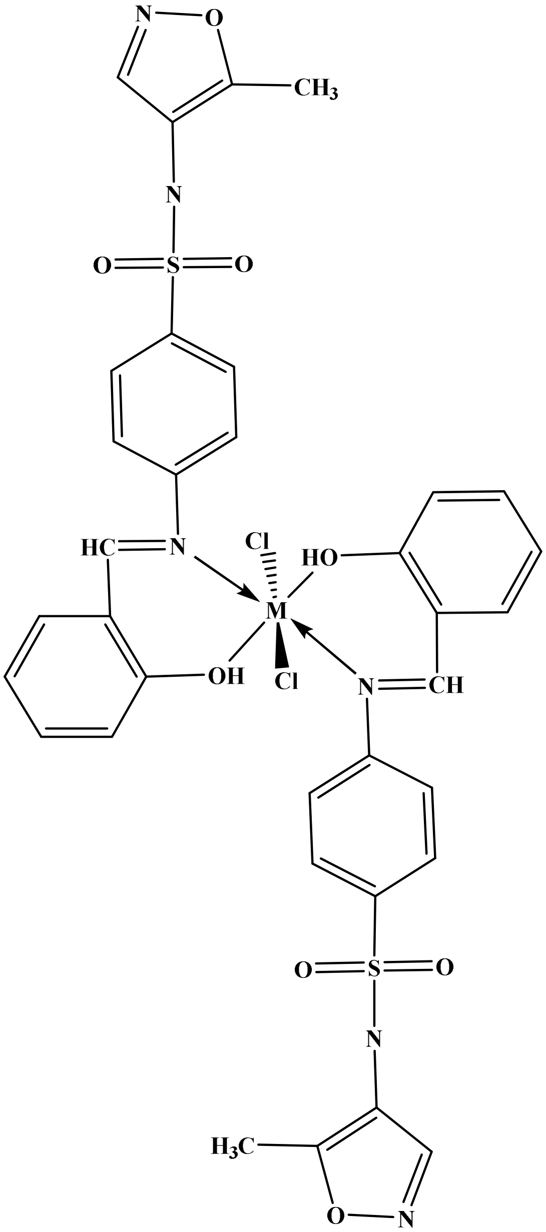


Figure 6. Cyclic voltammogram of $[CoL_2Cl_2]$.

Based on the above evidence the proposed structure for the complex is given below.



Structure of the complex M = Co(II)

Fluorescence spectra

The Schiff base ligand exhibits fluorescence excitation at 478 nm, while the Co(II) complex shows an excitation at 479 nm. The noticeable variations in the emission maxima between the Schiff base and its complexes (Figure 7) indicate successful coordination of the metal ion to the ligand. Metal ions may either increase or suppress the fluorescence emission intensity of the Schiff base. For the Co(II) complex, there is a slight enhancement in fluorescence emission compared to the free ligand. The overall fluorescence emission intensities follow the trend: Co(II) > L.

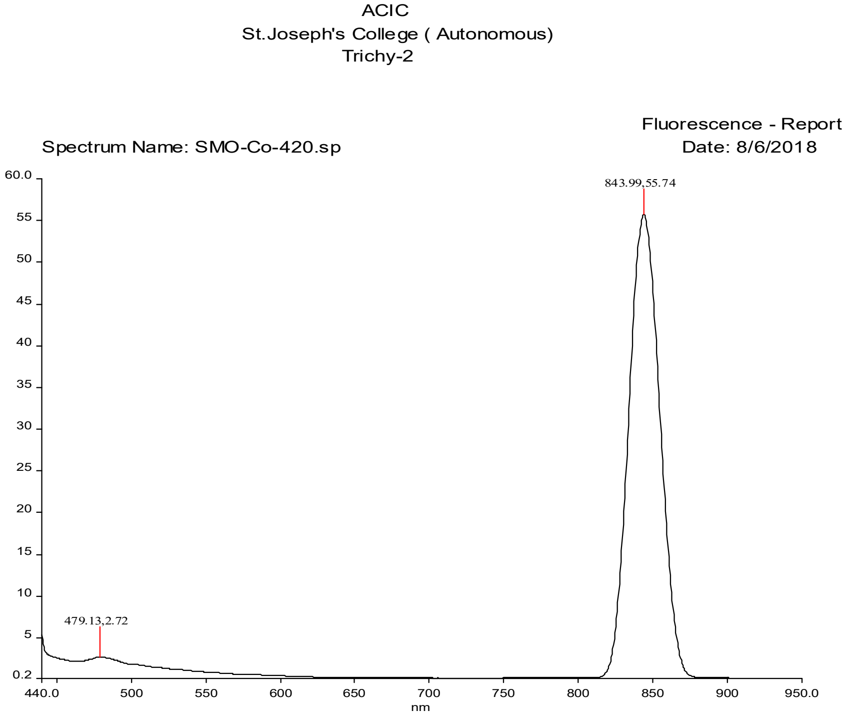


Figure 7. Fluorescence spectrum of [CoL_2Cl_2].

In-vitro antimicrobial bioassay for [CoL_2Cl_2]

The biocidal properties of the Schiff base and its cobalt complex were assessed through antibacterial screening (Table 2, Figure 8). The antibacterial activity of the Schiff base and the Co(II) complex was tested against gram-positive bacteria *Staphylococcus aureus*, gram-negative bacteria *Proteus vulgaris*, and fungal species *Candida albicans* using the disc diffusion method. The tests were performed in DMSO solution at a concentration of 100 mg/L, and the results were compared with standard drugs Ciprofloxacin (for bacteria) and Nystatin (for fungi) at the same concentration. All complexes displayed varying inhibition zone diameters against the tested microorganisms. While the Schiff base exhibited moderate biological activity, the Co(II) complex demonstrated significantly enhanced activity compared to the Schiff base, especially against *Staphylococcus aureus* and *Candida albicans*. The increased antimicrobial efficiency followed the trend Co(II) > L. The Co(II) complex showed strong activity against *Staphylococcus aureus* and *Candida albicans*. This heightened inhibition activity can be explained by Tweedy's chelation theory, which suggests that increased lipophilicity enhances the ability of the Co(II) complex to penetrate lipid membranes and block metal-binding sites in enzymes [21]. Furthermore, the Co(II) complex disrupts the respiration process of microbial cells, inhibiting protein synthesis and, consequently, halting further growth of the organisms.

Minimum inhibitory concentration (MIC)

Compounds displaying significant antimicrobial activity were selected for minimum inhibitory concentration (MIC) studies (Table 2). Based on preliminary screening, the following complex was found to be most active against specific species: The $[Co(L)_2Cl_2]$ complex of 4-[(2-hydroxybenzylidene)amino-N-(5-methyl-1,2-oxazol-3-yl)benzenesulfonamide showed potent activity against *Staphylococcus aureus* at a concentration of 100 mg/L. At a concentration of 75 mg/L, the $[Co(L)_2Cl_2]$ complex exhibited moderate activity against *Candida albicans* and was highly active at 100 mg/L (Figure 8).

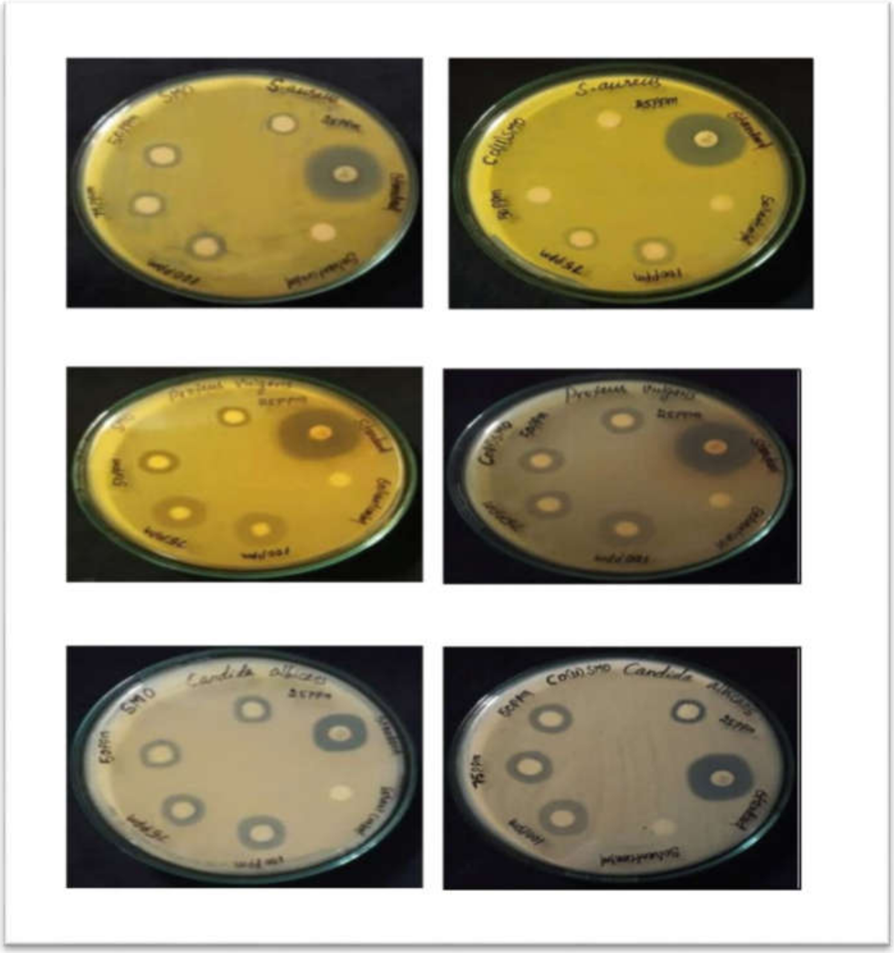


Figure 8. *In vitro* antibacterial and antifungal screening of Schiff base and its metal complex.

Table 2. Antimicrobial activity for [CoL_2Cl_2].

S. No.	Name of the microorganisms	Zone of inhibition in mm							
		Ligand-SMO				Complex-Co(II)SMO			
		25 mg/L	50 mg/L	75 mg/L	100 mg/L	25 mg/L	50 mg/L	75 mg/L	100 mg/L
1	*Staphylococcus aureus* (NCIM 2079)	Nil	Nil	8	10	10	12	15	16
2	*Proteus vulgaris* (NCIM 2027)	10	10	11	11	Nil	Nil	8	8
3	*Candida albicans* (NCIM 3102)	12	15	16	18	12	15	16	20

CONCLUSION

The synthesized Co(II) complex from 4-amino-N-(5-methyl-1,2-oxazol-3-yl)benzenesulfonamide and 2-hydroxybenzaldehyde demonstrates significant biological potential, particularly against *Staphylococcus aureus* and *Candida albicans.* Characterization techniques, including IR, UV-Vis, NMR, EI mass spectrometry, and cyclic voltammetry, confirmed the successful coordination of the metal with the ligand, highlighting its bidentate nature. The electrochemical studies revealed quasi-reversible behavior, suggesting favorable electron transfer properties. Overall, this research underscores the promising applications of Co(II) complex in medicinal chemistry, particularly in the development of effective antimicrobial agents with reduced side effects. Further studies are warranted to explore the mechanisms underlying the observed biological activities and to assess the complex potential in broader biomedical applications.

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