Synthesis, Characterization, and Antimicrobial Activity of a Schiff Base Derived from 2-Pyridinecarboxaldehyde and 5-Amino-2-Methoxypyridine and Its Mn(II), Co(II), and Ni(II) Complexes

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Research Article

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Synthesis, Characterization, and Antimicrobial Activity of a Schiff Base Derived from 2-Pyridinecarboxaldehyde and 5-Amino-2-Methoxypyridine and Its Mn(II), Co(II), and Ni(II) Complexes

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Abstract

A new pyridyl Schiff base ligand, L ($C_{12}H_{11}N_3O$), was synthesized by condensation of 2-pyridinecarboxaldehyde with 5-amino-2-methoxypyridine, and its Mn(II), Co(II), and Ni(II) complexes of the type $[M(L)_2Cl_2].xH_2O$ were prepared. The ligand and its complexes were characterized by melting/decomposition temperature, elemental analysis, solubility, molar conductance, magnetic susceptibility, FTIR and UV-Vis spectroscopy. L is a coffee-brown solid with a melting point of 90 ˚C and forms dark brown/black non-electrolytic complexes with Mn(II), Co(II) and Ni(II) in good yields (63 - 77%), all soluble in DMSO and DMF. FTIR spectra show a ν(C=N) band at 1622 cm^{-1} in L, shifting to 1568 – 1626 cm^{-1} in the complexes, together with new bands assigned to M-N and coordinated water, consistent with coordination via the azomethine nitrogen and pyridyl nitrogen. Electronic spectra and effective magnetic moments (Mn: 5.66 BM; Co: 3.94 BM; Ni: 2.78 BM) support octahedral geometries around the metal centers. Antimicrobial activity of L and its complexes was evaluated by the agar well diffusion method against Gram-positive bacteria (*Streptococcus mutans*, and *Staphylococcus aureus*), Gram-negative bacteria (*Escherichia coli*) and fungal strains (*Candida albicans, Trichophyton rubrum, Trichophyton* sp. Associated with *Tinea pedis*). All compounds exhibited concentration-dependent activity (250 – 2000 µg/mL). Notably, the free Schiff base ligand generally displayed higher antimicrobial activity than its corresponding metal complexes, with inhibition zones reaching up to 18 mm against *Streptococcus mutans* and *Trichophyton rubrum* at 2000 µg/mL. These results demonstrate that metal coordination does not universally enhance antimicrobial efficacy and highlight the critical influence of ligand structure and metal ion identity on biological activity.

Keywords: Pyridyl Schiff base; Transition metal complexes; Spectral characterization; Octahedral geometry; Antimicrobial activity.

1. Introduction

Schiff bases and their metal complexes have attracted sustained scientific interest due to their remarkable structural versatility and wide spectrum of biological activities, including antibacterial, antimicrobial, anticancer, antioxidant, antiviral, and antifungal properties [1-6]. These compounds, first reported by Hugo Schiff in 1864, are formed through the condensation of primary amines with aldehydes or ketones, leading to the formation of an imine or azomethine (–C=N–) functional group [7]. The presence of this azomethine linkage is central to the chemical reactivity, coordination behavior, and biological efficacy of Schiff bases.

Heterocyclic Schiff bases, particularly those derived from nitrogen-containing heterocycles such as pyridine, have gained increasing attention owing to their enhanced chelating ability and biological relevance. Pyridine is a key structural motif found in vitamin B_6 coenzymes, alkaloids, and numerous therapeutic agents, and its derivatives are known to exhibit antioxidant, anti-inflammatory, and antimicrobial activities [4]. The presence of one or more ring nitrogen atoms with localized lone pairs of electrons makes pyridine-based ligands highly effective donors in coordination chemistry [4,7,8]. Upon coordination with transition metal ions, the biological activity of these ligands is often significantly enhanced due to increased lipophilicity, improved membrane permeability, and altered electronic properties [5,6].

Schiff bases containing electron-donating or electron-withdrawing substituents near the azomethine group have been reported to exhibit improved pharmacological properties. In particular, substituents such as methoxy and ethoxy groups positioned close to the azomethine moiety can influence electron density distribution, molecular stability, and metal-binding behavior, thereby enhancing biological and antitumor activity [7,8]. Aromatic aldehydes, such as pyridinecarboxaldehyde, are especially favorable for Schiff base formation due to effective conjugation within the ring system, which contributes to ligand stability compared to aliphatic analogues [9].

From a coordination chemistry perspective, Schiff bases serve as versatile ligands due to their ease of synthesis, strong donor characteristics, and ability to form stable chelate complexes with a wide range of transition metal ions. The azomethine nitrogen atom, with its sp^2-hybridized lone pair of electrons, plays a crucial role in metal coordination and chelation [9,10,15]. Transition metal complexes of Schiff bases have found extensive applications not only in medicinal chemistry but

also in catalysis, corrosion inhibition, sensing, analytical chemistry, and material science [3,10]. In particular, complexes of Mn(II), Co(II), and Ni(II) have been widely investigated for their structural diversity and biological relevance [3,8,15].

In recent years, the rapid emergence of antimicrobial resistance, including multidrug-resistant (MDR) bacterial and fungal strains, has become a major global public health challenge. The limited availability of effective antibiotics, coupled with increasing morbidity, mortality, and treatment costs, necessitates the development of novel antimicrobial agents with improved efficacy and alternative mechanisms of action [17]. Schiff bases and their metal complexes have demonstrated promising antimicrobial potential, often exhibiting enhanced activity compared to free ligands due to synergistic metal–ligand interactions [11,16].

This work reports the synthesis and comprehensive characterization of a new Schiff base ligand (L) derived from 2-pyridinecarboxaldehyde and 5-amino-2-methoxypyridine, together with its Mn(II), Co(II), and Ni(II) chloride complexes. Although the ligand design follows established strategies for the development of metal-based antimicrobial agents [11,12], the biological evaluation revealed a counter-intuitive and scientifically significant outcome: the free ligand frequently exhibited comparable or superior inhibitory activity relative to its corresponding metal complexes. This finding challenges the widely accepted assumption of a universal "chelation effect" and underscores the decisive role of ligand architecture and metal ion identity in governing antimicrobial performance [12,18]. Accordingly, this study presents a complete account of the synthesis, spectroscopic and magnetic characterization, and a comparative antimicrobial evaluation of the ligand and its metal complexes.

2. Experimental

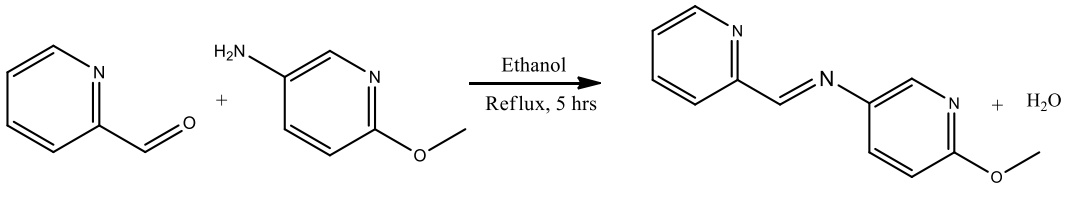
2.1. Materials and Methods

All reagents and solvents were of analytical grade and used without further purification. 2-pyridinecarboxaldehyde, 5-amino-2-methoxypyridine, and metal salts ($MnCl_2.4H_2O$, $CoCl_2.6H_2O$, $NiCl_2.6H_2O$) were purchased from Sigma-Aldrich. Melting and decomposition points were determined using Stuart melting point apparatus. Elemental analysis (C, H, N) was performed on an EMASoft Elemental Analyser, (serial no: 688596 SW Ver.: 2.0.2.0). FT-IR

spectra were recorded on a Fourier transform infrared spectrophotometer (FTIR-8400S) in the range 4000-400 cm^{-1}. Electronic spectra were measured in DMSO solution using a PerkinElmer Lambda-35 UV-Vis spectrophotometer. Molar conductivities 1 mM DMSO solutions were measured at 25 ˚C using a Jenway 4010 conductivity meter (range 20 – 200 µS). Magnetic susceptibility measurements were carried out at room temperature using a Sherwood Scientific MKI magnetic susceptibility balance.

2.2 Synthesis of Schiff base Ligand (L)

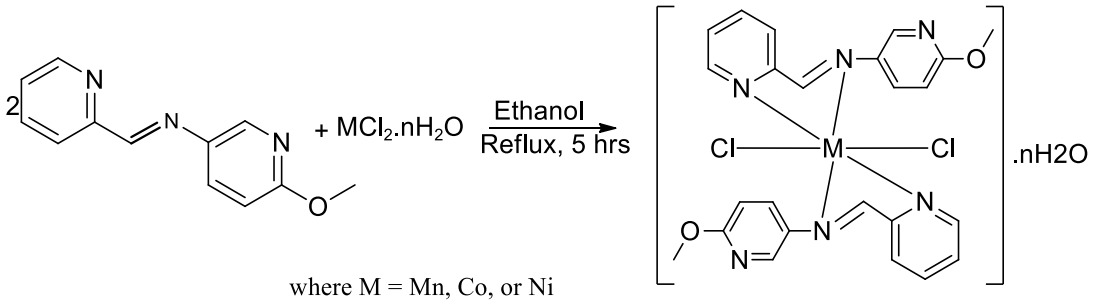
An ethanolic solution (30 mL) of 2-pyridinecarboxaldehyde (1.07 g, 10 mmol) was added dropwise to a stirred ethanolic solution (30 mL) of 5-amino-2-methoxypyridine (1.24 g, 10 mmol). Three drops of glacial acetic acid were added to the mixture. The reaction mixture was refluxed for 5 hours, then allowed to cool to room temperature. Coffee-brown crystals formed upon standing and were collected by filtration. The crystals were dried in a desiccator over phosphorus pentoxide (P_2O_5) to yield the Schiff base ligand as shown in Scheme 1.



Scheme 1: Proposed structure of the Schiff base ligand (L)

2.3 Synthesis of Metal Complexes

A hot ethanolic solution (30 mL) of the Schiff base ligand L (0.469 g, 2.2 mmol) was mixed with a hot ethanolic solution (30 mL) of the respective metal chloride (1.1 mmol) under continuous stirring. To the reaction mixture, three drops of glacial acetic acid were added to facilitate coordination. The resulting mixture was refluxed for 5 hours. Upon cooling, the precipitate was filtered, washed with ethanol, and dried over P_2O_5 to yield the desired metal complex [1].



Scheme 2: Proposed structure of the complexes

2.4 Antimicrobial Assay

Antimicrobial activity was evaluated using the well diffusion method, a standard technique for preliminary screening[3,4]. Test organisms included Gram-positive bacteria (*Streptococcus mutans, Staphylococcus aureus*), Gram-negative bacteria (*Escherichia coli*), and fungi (*Candida albicans, Trichophyton rubrum, Trichophyton* sp, from *Tinea pedis*). Compounds were dissolved in DMSO to prepare stock solutions (2000 µg/mL), and serially diluted to final concentrations of 250, 500, 1000, and 2000 µg/mL. Wells of 6 mm diameter were bored in inoculated agar plates filled with 100 µL of the test solutions. DMSO and standard antibiotics (Ciprofloxacin for bacteria, Ketoconazole for fungi) served as negative and positive controls, respectively. Plates were incubated at 37 ˚C for 24 h (bacteria) and 28 ˚C for 48 -72 h (fungi), Zones of inhibition (mm) were measured and tests were performed in triplicate.

3. Results and Discussion

3.1 Physical Properties and Elemental Analysis

The Schiff base ligand (L) was obtained as a coffee-brown crystalline solid with a sharp melting point at 90 ˚C, indicating good purity and a well-defined molecular structure. In contrast, Mn(II), Co(II), and Ni(II) complexes did not melt sharply but decomposed at higher temperatures (126 - 140 ˚C), reflecting enhanced thermal stability upon coordination (Table 1). This increase in decomposition temperature is consistent with the formation of more rigid chelate structures around the metal ions, a behavior widely reported for Schiff base metal complexes [4,7,8].

Elemental analysis data for carbon, hydrogen, and nitrogen were in good agreement with the calculated values for both the ligand and the complexes, supporting the proposed stoichiometry and molecular formulae (Table 1). Minor deviations between calculated and experimental values

are attributable to coordinated and lattice water molecules, a common feature in first-row transition metal complexes [10,15]. The slightly lower experimental carbon value for the ligand may be attributed to residual solvent or moisture content, a common occurrence in azomethine compounds. The analytical data confirm the formation of complexes of the general formula $[M(L)_2Cl_2].xH_2O$.

3.2 Solubility Behavior

Solubility data (Table 2) show that the Schiff base ligand and its metal complexes are insoluble or sparingly soluble in non-polar solvents such as benzene and diethyl ether, but readily soluble in polar aprotic solvents like DMSO and DMF. This solubility pattern reflects the polar nature of the azomethine group and the heterocyclic nitrogen atoms, which enhance dipole-dipole interactions with polar solvents [2,15]. The good solubility in DMSO justified its use as the solvent for conductivity, spectroscopic, and antimicrobial studies.

3.3 Infrared and Electronic Spectral Studies

The FT-IR spectrum of the free ligand exhibits a strong band at 1622 cm^{-1}, characteristic of the azomethine ν(C=N) stretching vibration. Upon coordination, this band shifts to lower frequencies (1568-1626 cm^{-1}) in the metal complexes (Table 3), indicating the involvement of the azomethine nitrogen in coordination to the metal ions [1,7]. The downward shift is attributed to a reduction in the C=N bond order due to electron donation to the metal center.

Broad absorption bands observed in the region 3275-3387 cm^{-1} in the complexes are assigned to O-H stretching vibrations of coordinated or lattice water molecules, consistent with elemental analysis and thermal behavior. The absence of these bands in the ligand spectrum further supports complex formation [4,8].

The electronic spectra of the ligand show absorption bands at 267.94 nm and 330.04 nm, corresponding to $\pi \rightarrow \pi^*$ and $n \rightarrow \pi^*$ transitions of the azomethine chromophore. These bands undergo slight bathochromic shift in the metal complexes (Table 3), reflecting increased conjugation and ligand-to-metal charge transfer interactions upon coordination [4,7,8]. Such spectral changes are typical of octahedral Schiff base complexes of Mn(II), Co(II), and Ni(II).

3.4 Molar Conductance Studies

The molar conductance values of the metal complexes in DMSO fall within the range 16.26-23.41 $\Omega^{-1}cm^2mol^{-1}$ (Table 4), indicating non-electrolytic behavior in solution. This confirms that chloride ions are coordinated to the metal centers rather than existing as free counter ions [15]. The non-electrolytic nature further supports the proposed neutral formulation $[M(L)_2Cl_2].xH_2O$.

3.5 Magnetic Susceptibility and Geometry

Magnetic susceptibility measurements shows effective magnetic moments of 5.66 BM for Mn(II), 3.94 BM for Co(II), and 2.78 BM for Ni(II) complexes (Table 5). These values correspond well with high-spin octahedral configurations for d^5 Mn(II), d^7 Co(II), and d^8 Ni(II) ions, respectively [4,16]. The magnetic data, together with spectroscopic evidence, strongly support an octahedral geometry around each metal center, where the Schiff base ligand coordinates through azomethine and pyridyl nitrogen atoms.

3.6 Antimicrobial Activity

The antimicrobial screening results (Table 6) reveal that all compounds exhibit concentration-dependent activity against the tested bacterial and fungal strains. Notably, the free Schiff base ligand generally showed higher or comparable zones of inhibition than its corresponding metal complexes, particularly against *Streptococcus mutans* and *Trichophyton rubrum*, where inhibition zones reached up to 18 mm at 2000 µg/mL.

This observation deviates from the widely cited "chelation theory" proposed by Tweedy (18), which suggests that metal coordination enhances biological activity by increasing lipophilicity and membrane permeability. Similar counter-intuitive trends have been reported in recent studies, where specific ligand architecture, hydrogen-bonding ability, and electronic distribution play a more dominant role than metal coordination alone.

The reduced activity of some metal complexes may be attributed to steric hindrance, reduced diffusion through microbial cell membranes, or partial masking of pharmacophoric sites upon coordination [14,19,20]. Nonetheless, certain complexes, particularly the Co(II) and Ni(II)

derivatives, retained or improved activity against selected strains such as *Escherichia coli* and *Candida albicans*, indicating strain-dependent metal-ligand synergy [16,20].

Compared with standard drugs (ciprofloxacin and ketoconazole), the synthesized compounds exhibit moderate antimicrobial activity, however, their broad-spectrum behavior and tunable structure make them promising scaffolds for further structural optimization [20].

Table 1: Physical Properties and Elemental Analysis of Schiff base ligand (L) and its Metal Complexes

Compound	Colour	MP/Decomp. Temp. (˚C)	% Yield	Formula	Elemental Analysis Calculated (Found)		
					%C	%H	%N
Schiff base Ligand (L)	Coffee brown	90	66.13	$C_{12}H_{11}N_3O$	67.59 (62.33)	5.20 (4.60)	19.71 (18.23)
$[Mn(L)_2Cl_2].4H_2O$	Dark brown	140	63.13	$C_{24}H_{32}Cl_2MnN_6O_6$	46.16 (46.98)	4.84 (4.47)	13.46 (14.09)
$[Co(L)_2Cl_2].4H_2O$	Black	126	73.13	$C_{24}H_{32}Cl_2CoN_6O_6$	45.87 (45.63)	4.81 (3.65)	13.37 (12.45)
$[Ni(L)_2Cl_2].6H_2O$	Black	130	77.23	$C_{24}H_{36}Cl_2N_6NiO_6$	43.40 (43.62)	5.16 (3.96)	12.65 (12.61)

Table 2: Solubility of the Schiff base Ligand (L) and its Metal Complexes in Common Solvents

Compound	**Water**	**Ethanol**	**Methanol**	**Diethyl ether**	**Acetone**	**Benzene**	**DMSO**	**DMF**
L	IS	S	S	IS	S	SS	S	S
$[Mn(L)_2Cl_2].4H_2O$	S	S	S	IS	S	IS	S	S
$[Co(L)_2Cl_2].4H_2O$	S	S	S	SS	S	SS	S	S
$[Ni(L)_2Cl_2].6H_2O$	S	S	S	SS	SS	SS	S	S

Key: L = $C_{12}H_{11}N_3O$, S = soluble, SS = slightly soluble, IS = insoluble, DMSO = Dimethylsulfoxide, DMF = Dimethylformamide

Table 3: Spectroscopic Data (FT-IR and UV-Vis) of the Schiff base Ligand (L) and its Metal Complexes

Compound	ν(C=N) (cm^{-1})	ν(M-N) (cm^{-1})	ν(H_2O) (cm^{-1})	$\pi \longrightarrow \pi^*$ (nm)	$n \longrightarrow \pi^*$ (nm)
Schiff base (L)	1622	-	-	267.94	330.04
$[Mn(L)_2Cl_2].4H_2O$	1626	641	3275	273.54	330.23
$[Co(L)_2Cl_2].4H_2O$	1568	589	3387	279.05	337.06
$[Ni(L)_2Cl_2].6H_2O$	1626	604		268.14	333.88

L= $C_{12}H_{11}N_3O$, ν = stretching vibration, $\pi \longrightarrow \pi^*$ and $n \longrightarrow \pi^*$ = electronic transitions

Table 4: Molar Conductance of Schiff base Metal Complexes in DMSO

Complex	**Specific Conductance × 10^{-6} (Ω^{-1} cm^{-1})**	**Molar Conductance (Ω^{-1} cm^2 mol^{-1})**	**Electrolytic nature**
$[Mn(L)_2Cl_2].4H_2O$	19.05	19.05	Non-electrolyte
$[Co(L)_2Cl_2].4H_2O$	16.26	16.26	Non-electrolyte
$[Ni(L)_2Cl_2].6H_2O$	23.41	23.41	Non-electrolyte

Measurements were carried out in 1 × 10^{-3} mol/L DMSO solutions at 25 °C. L = $C_{12}H_{11}N_3O$.

Table 5: Magnetic Susceptibility data and proposed geometries of the Schiff base metal complexes

Complex	**Xg(erg.$G^{-2}g^{-1}$)**	**Xm(erg.$G^{-2}mol^{-1}$)**	**μ_{eff} (BM)**	**Unpaired electrons (n)**	**Magnetic behavior**	**Proposed geometry**
$[Mn(L)_2Cl_2].4H_2O$	5.6 × 10^{-6}	1.342× 10^{-2}	5.66	5	Paramagnetic	Octahedral
$[Co(L)_2Cl_2].4H_2O$	1.0 × 10^{-5}	6.517 × 10^{-3}	3.94	3	Paramagnetic	Octahedral
$[Ni(L)_2Cl_2].6H_2O$	4.9 × 10^{-6}	3.235 × 10^{-3}	2.78	2	Paramagnetic	Octahedral

Xg(erg.$G^{-2}g^{-1}$) = gram magnetic susceptibility; Xm = molar magnetic susceptibility; μ_{eff} = effective magnetic moment; L = $C_{12}H_{11}N_3O$

Table 6: Antimicrobial Activity (Zone of Inhibition, mm) of the Schiff base Ligand (L) and its Mn(II), Co(II), and Ni(II) Complexes

i) Antibacterial Activity

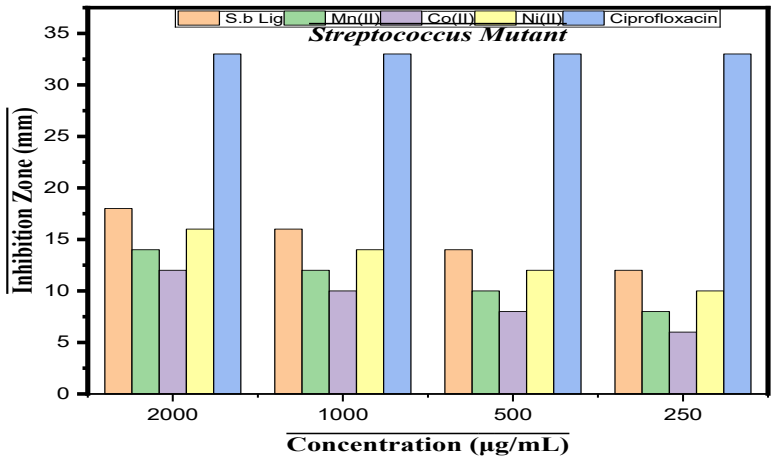
Compound	Concentration (µg/mL)	Gram-positive Bacteria (mm)		Gram-negative Bacteria (mm)
		Streptococcus mutans	*Staphylococcus aureus*	*Escherichia coli*
Schiff base Ligand	2000	18	15	14
	1000	16	14	12
	500	14	11	10
	250	12	9	8
$[Mn(L)_2Cl_2].4H_2O$	2000	14	14	13
	1000	12	12	11
	500	10	10	9
	250	8	8	6
$[Co(L)_2Cl_2].4H_2O$	2000	12	16	17
	1000	10	14	15
	500	8	12	10
	250	6	10	11
$[Ni(L)_2Cl_2].6H_2O$	2000	16	14	16
	1000	14	12	14
	500	12	10	13
	250	10	8	11
Ciprofloxacin		33	30	27

L = $C_{12}H_{11}N_3O$

ii) Anti-Fungal Activity

Compound	Concentration (µg/mL)	Fungi		
		Candida albicans	*Trichophyton rubrum*	*Trichophyton* sp (*Tinea pedis)*
Schiff base	2000	16	18	14
Ligand	1000	14	15	11
	500	12	13	9
	250	10	11	6
$[Mn(L)_2Cl_2].4H_2O$	2000	14	15	13
	1000	12	13	11
	500	10	11	9
	250	8	10	7
$[Co(L)_2Cl_2].4H_2O$	2000	13	15	18
	1000	12	13	16
	500	10	11	14
	250	7	9	12
$[Ni(L)_2Cl_2].6H_2O$	2000	13	15	12
	1000	11	13	10
	500	8	10	8
	250	6	8	6
Ketoconazole		31	29	24

$L = C_{12}H_{11}N_3O$


S.b Lig
Mn(II)
Co(II)
Ni(II)
Ciprofloxacin
Streptococcus Mutant
Inhibition Zone (mm)
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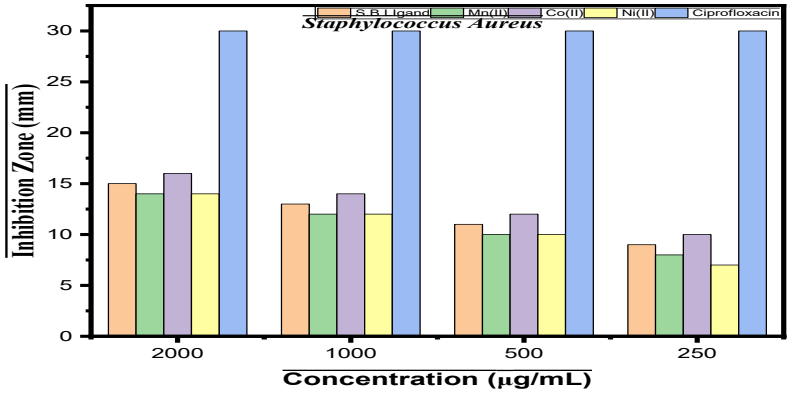
Concentration (µg/mL)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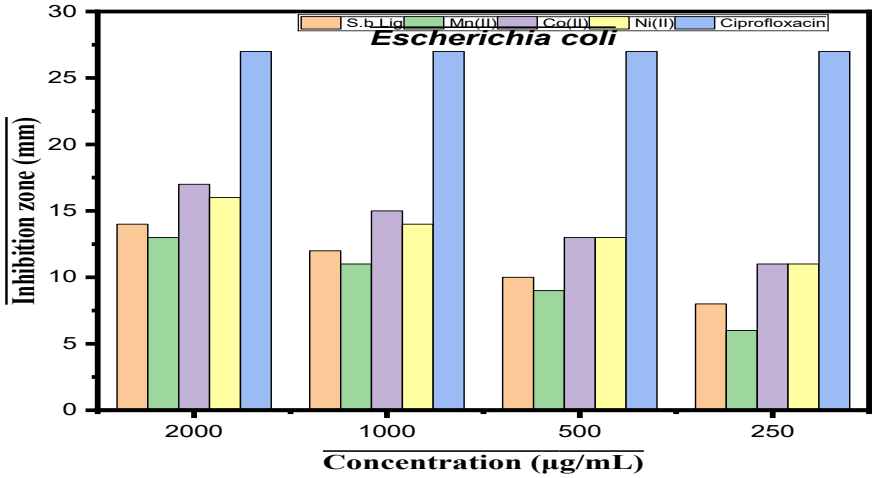
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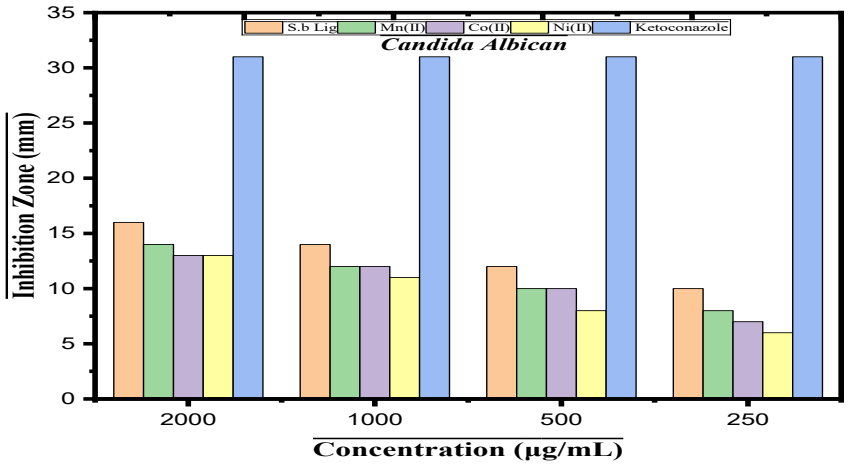
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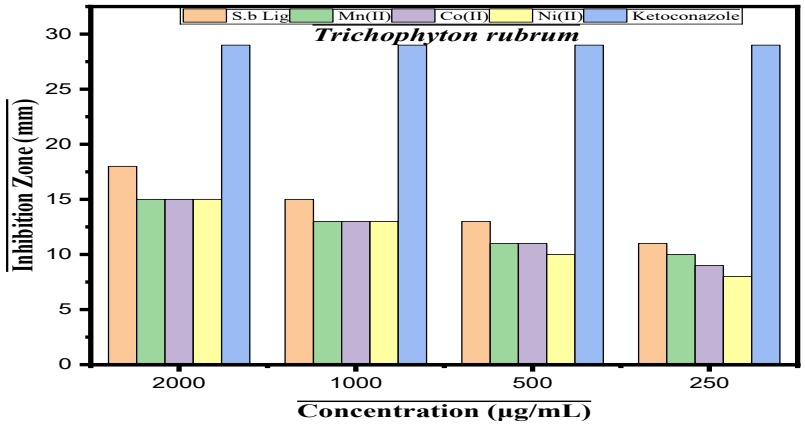
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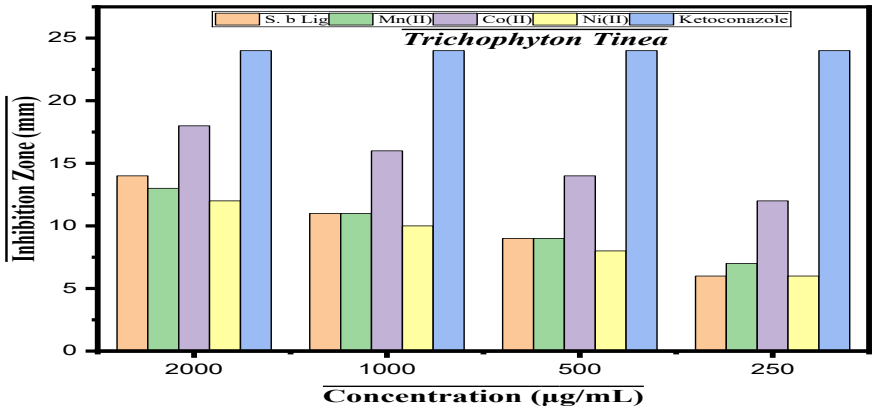
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Inhibition Zone (mm)
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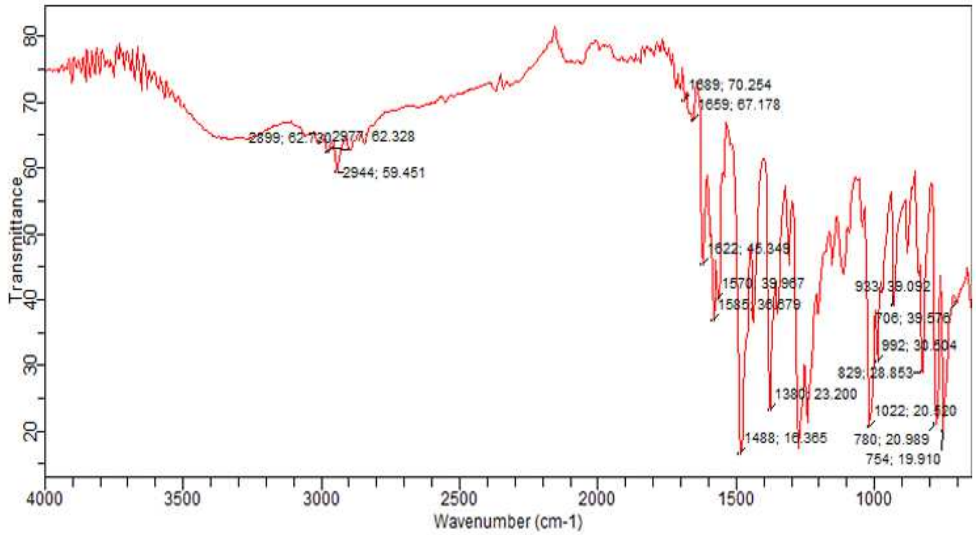
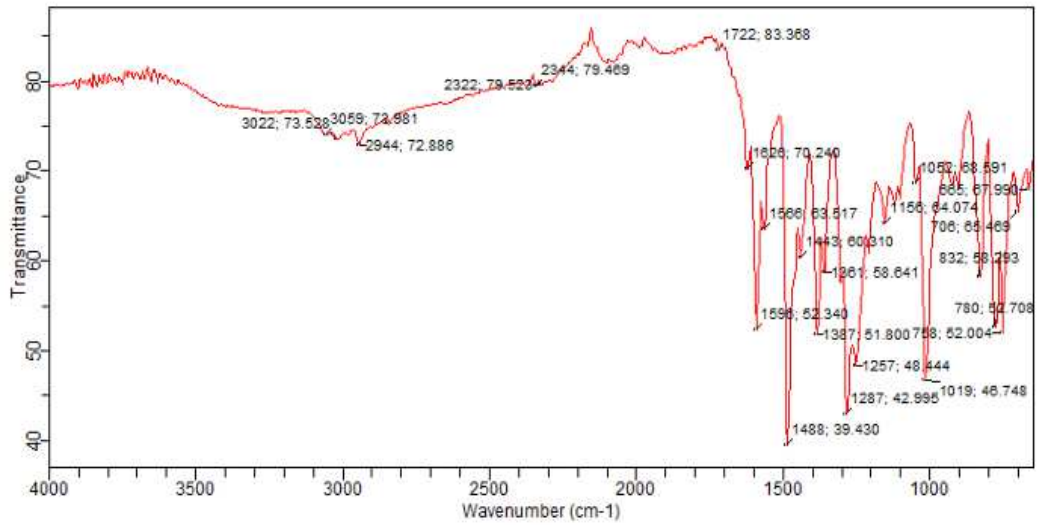
Concentration (µg/mL)

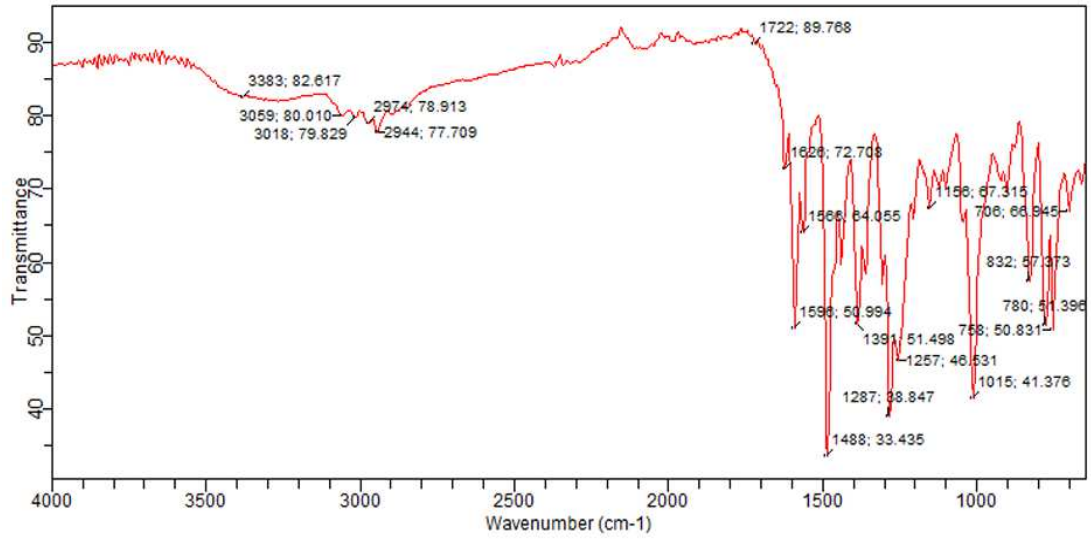
Schiff base Ligand



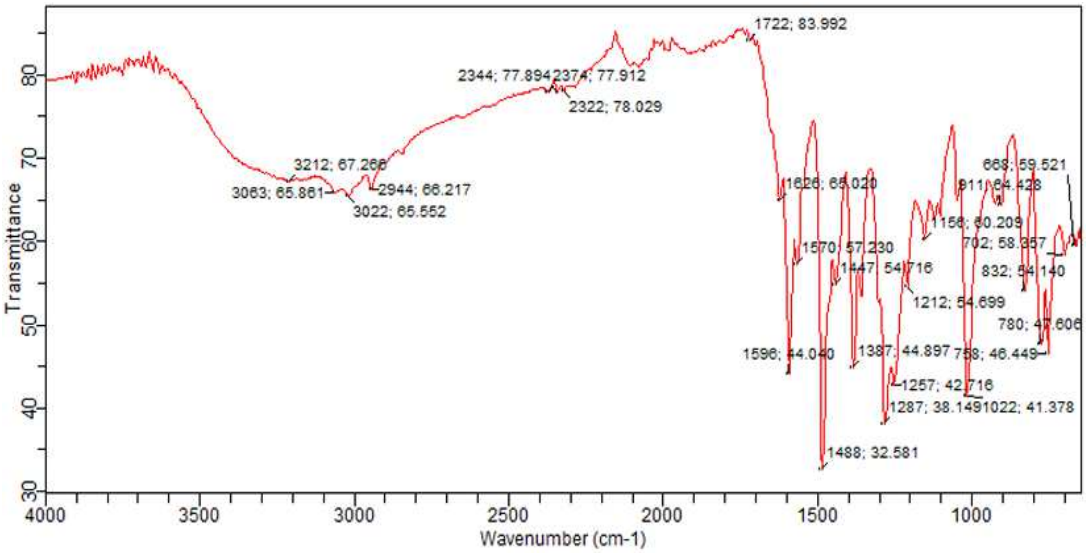
Co(II) complex



Mn(II) Complex



Ni(II)Complex



Conclusion

A new pyridyl Schiff base ligand and its Mn(II), Co(II) and Ni(II) complexes were synthesized and characterized. Spectroscopic, conductivity and magnetic data support octahedral geometries for the metal complexes. Antimicrobial screening revealed that the free ligand frequently matched or exceeded complex activity, demonstrating that coordination does not always enhance

antimicrobial efficacy. The ligand framework therefore represents a promising scaffold for further optimization and structure–activity studies.

Author Contribution

Samira S.M,: synthesis, characterization, manuscript preparation;

J.N: spectral interpretation and data analysis;

S.J.: antimicrobial analysis;

Idris I.U.: sample preparation.

All authors have read and approved the final manuscript.

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Ethics, Consent to Participate, and Consent to Publish

Ethics approval, consent to participate, and consent to publish are not applicable to this study.

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