Synthesis, Characterization and Biological Applications of Metal Complexes from Schiff's Bases

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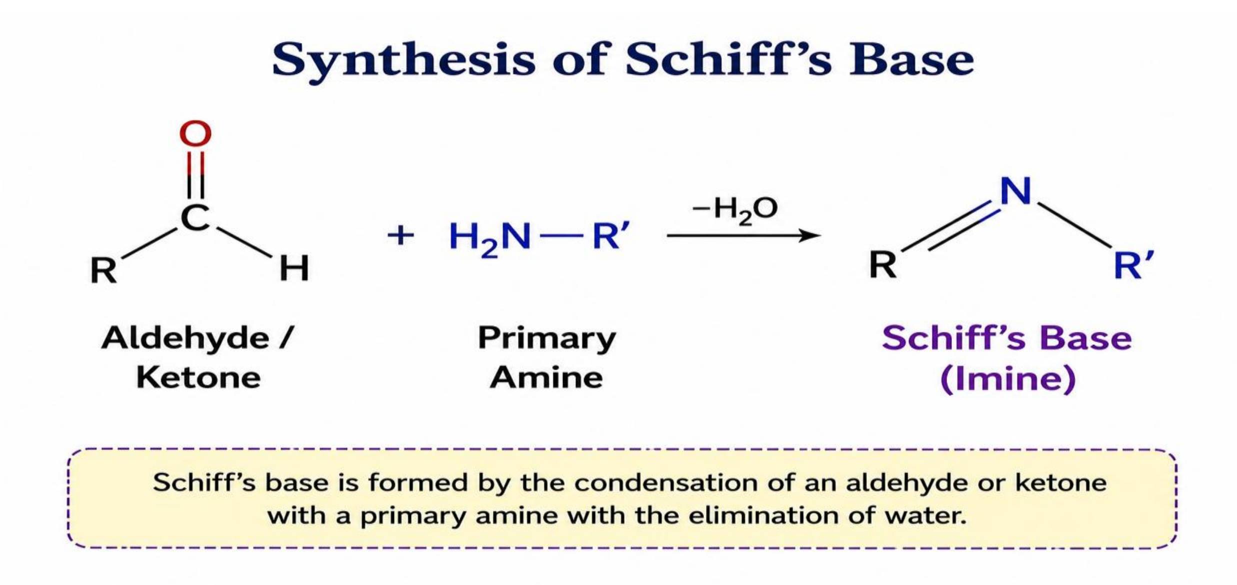
***Abstract*—The Schiff's bases are vital class of organic compounds that consists of the azomethine group (–C=N–) which readily forms stable metal complexes with various metal ions. In the current work, Schiff's base ligands were synthesized using the condensation reaction of appropriate aldehyde or ketone with a primary amine. The synthesized ligands were then allowed to react with a number of selected transition metal ions and their metal complexes were obtained. Compounds prepared were analysed by various techniques such as Fourier Transform Infrared Spectroscopy (FTIR), UV-Visible spectroscopy, Nuclear Magnetic Resonance (NMR), elemental analysis, magnetic susceptibility and molar conductivity. All synthesized Schiff's base and their metal complexes were evaluated for biological potential against selected bacterial and fungal strains. The results showed that complexation with metal ions results in modulation of the biological activity of Schiff's bases and in several instances, the antimicrobial activity was enhanced. The study proves that Schiff base complexes of base metals have significant scope for the synthesis of coordination compounds which could be applied in biological field and can also be put to the use in pharmaceutical and medicinal chemistry field.**

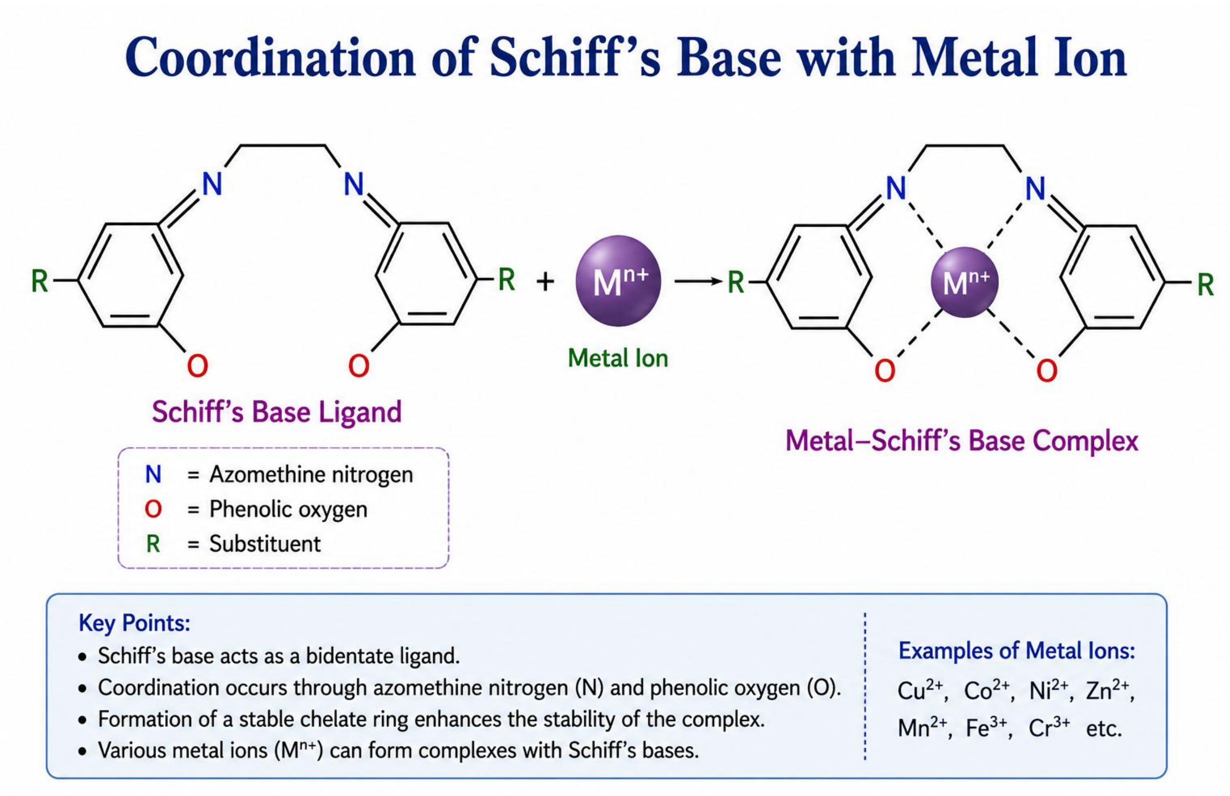
***Index Terms*—Schiff's bases, metal complexes, transition metals, synthesis, characterization, FTIR, UV–Visible spectroscopy, antimicrobial activity, biological applications, coordination chemistry.**

I. INTRODUCTION

The Schiff's bases are highly interesting category of organic compounds, containing –C=N–, the azomethine or imine functional group. Typically, they are prepared by dissolving primary amine in an aldehyde or ketone followed by the condensation reaction under proper conditions. Schiff's bases have a flexible structure and contain donor atoms like N, O and S that are able to coordinate a broad range of metal ions.



The coordination of the Schiff's base ligands has been the subject of extensive research because many metal complexes exhibit different chemical, physical and biological properties compared to those of the Schiff's base ligands. Since Schiff's bases can be used to build the complexes of various transition elements to form complexes with variable oxidation states, coordination geometries and biological molecule interactions, these are especially interesting.



Recently the base metal complexes of Schiff have been studied for various biological activities such as antibacterial, antifungal, antioxidant, anti-inflammatory and cytotoxic activity. They are not necessarily active in all cases, depending on the nature of the ligand, type of metal ion, coordination number, geometry, molecular structure and the lipophilicity of the complex. Metal coordination may also affect the interaction of the compound with biological membranes and/or target molecules within cellular structures.

In this research the ligands of Schiff's base are prepared and complexed with selected metal ions to obtain a series of metal complexes. Synthetic compounds were analysed by physicochemical and spectroscopic techniques. They are then biochemically confirmed by appropriate in vitro tests. To build up a correlation between the molecular structure, metal coordination and biological activities of the synthesized compounds.

II. REVIEW OF LITERATURE

Abd El-Wahab, and El-Sarrag (2004) studied the synthesis and biological activities of transition metal complexes based on the Schiff base ligands of phosphates. Schiff's bases were studied in terms of their coordination with selected metal ions and the resulting complexes were studied with various physicochemical and spectroscopic methods. The biological investigation proved the important biological activity of the metal complexes, wherein the existence of metal ions plays an important role in the properties of Schiff's base derivatives. This study gave a very firm foundation for the further study of Schiff's base metal complexes as biologically active coordination compounds.

Sharaby and Mohamed (2007) have reported the development of metal complexes based on a Schiff's base formed by sulfametrole and o-vanillin. The complexes were characterized by spectral and thermal methods in order to determine the structural and coordination properties. Biological study revealed that the prepared metal complexes were active against some microorganisms. The study emphasized the biological relevance of introducing organic molecules containing all of the organics shown to have biological activity into the Schiff's base ligands and showed that the biological potential of such compounds can be increased by metal coordination.

Mishra and Soni (2008) synthesized and studied a series of Schiff's bases and metal complexes thereof. They worked on characterizing the prepared compounds and on their biological activity. It is found that complexes formation with metal ions resulted in physicochemical and biological changes of the ligands. Based on their findings, the authors proposed that the nature of the central metal ion and the structural features of the ligand are important factors in deciding the activity of the formed complexes. This study provided a valuable correlation between the base structure of Schiff, their metal co-ordination with their bioactivity.

An interesting study has been carried out by Rehman et al. (2008) on transition-metal complexes with Schiff's base ligands with biological properties. Synthetic characterization of the synthesized compounds was carried out to ensure the closure of the metal–ligand coordination system and the resulting compounds were tested for the biological activity. The results they obtained showed that several metal complexes showed appreciable biological effects as compared to the corresponding Schiff's base ligands. The study sustained the concept that coordination reaction of the transition metals with Schiff's base may help manipulate the biological properties of the Schiff's base and may also help in designing potentially useful bioactive compounds.

A detailed review article on the different biological activities of Schiff's base and their complexes is presented by Arulmurugan et al. (2010). The various approaches to the synthesis of Schiff's bases, their coordination behaviour, structural features and biological applications were discussed. Special care was taken towards the pharmacological properties reported earlier by Schiff's base complexes, such as: antimicrobial, antifungal, antitumor, antioxidant and others. The presence of donor atom and the strong tendency of Schiff's bases to form stable complexes with various metal ions are the key factors which contribute to the wide range of biological activities.

Neelakantan et al (2010) reported the synthesis and characterization of the Schiff's base metal complexes and studied their biocidal activities. Structural information for the synthesized compounds was obtained by spectroscopic and physicochemical methods that allowed identifying the structures and coordination modes of the compounds. The biological tests revealed presence of antimicrobial activity of the complexes against selected microorganisms. They suggested that coordination of metal ions with the Schiff base ligand may enhance the biological effectiveness depending on the structure of the metal ion and that of Schiff’s base.

Al Zoubi (2013) summative discussed the latest findings regarding the bioactivity of Schiff bases and their complexes. Several classes of Schiff base compounds were studied and also their reported antibacterial, antifungal, antioxidant, anticancer and other biological activities were discussed. The review highlighted that the structural changes on Schiff's bases and addition of various different metal ions could change the properties of the molecules. It also showed that the following factors affect the action of a biological system: coordination geometry, electronic properties, lipophilicity and ligand donor atoms.

Abdul Kareem and co-workers (2016) synthesized a Herbo mineral-based Schiff's base ligand and explored its metal complexes towards synthesis, characterization, catalytic activity and biological applications. They found their synthetic compounds were able to chelate metal ions and to form stable complexes with the specific metal ion having different physicochemical properties. Results from biological evaluation showed signs of good activity for some of the complexes, and catalytic studies showed the multifunctional nature of these coordination compounds. The study demonstrated Schiff's base metal complexes by which a combination of biological/ catalytic activity exists within the one molecule.

However, Vairalakshmi et al. (2019) has synthesized the metal complexes from a novel Schiff base derived from is system. Of these, the prepared compounds were characterized and tested for their antimicrobial, antioxidant and catalytic activity. They found that the biological properties of the parent ligand was affected by the formation of complexes. Several complexes exhibited an enhanced antimicrobial and antioxidant activity. If one of the base complexes of Schiff also had another medicinal or catalytic property, these compounds would be an interesting target for additional studies.

In the study of Schiff base metal complexes, the synthesis, characterization, thermal properties and antibacterial activity were studied by Paul et al. (2020). The synthesized complexes were characterized in terms of their structural and stability properties by means of the spectroscopic and thermal analytical techniques. A metal complex were when evaluated for antimicrobial activities, found to possess antibacterial activity against selected bacteria. They confirmed the significance of the metal coordination effect in the modulation of the biological properties of Schiff's bases and showed that structure characterisation together with biological evaluation can be beneficial.

A new heterocyclic Schiff's base metal complex was reported by Hashem, et al., (2021), and the authors explored the structural, theoretical and biologically relevant properties of the metal complex. The synthesized compound was both structurally characterized and investigated by density functional theory calculations to explain the experimental structure and electronic properties of the compound. Antimicrobial investigations revealed that the prepared complex exhibited antibacterial activity against the selected microorganisms. It is important to multiply the experiments, characterization and the computational analysis to investigate structure and biological behavior of Schiff base metal complexes as it has been shown in this study.

Singh et al. (2022) synthesized and characterized Schiff-base complexes of some selected 3d transition metals, and studied their biological significance. Their work showed that it is possible to achieve coordination of different transition metal ions that yields compounds with different structural and biological properties. Based on the biological assessment, selected complexes exhibited interesting activities, reinforcing the relevance of the transition-metal chemistry in the synthesis of bio-active compounds based on acylated Schiff bases. The study also suggested that the properties of the biological system resulting from the complexation may be altered by the variation in the central metal ion.

Madhukar and Jyothi (2023) aimed to explore the synthesis and characterization of Schiff's base metal complexes, as well as their antimicrobial potential. In this study, the preparation of Schiff's base ligands was completed and further coordination was done with selected metal ions. The synthesized compounds were characterized in the detail using spectroscopic methods and antimicrobial activities were assessed. The Results clearly showed antimicrobial activity for the metal complexes and confirmed the Schiff's base coordination compounds for biological applications.

Chaithanya, 2024, synthesized, characterized and evaluated the antimicrobial activity of a Schiff 's base and its metal complexes. The structural analysis of the complex and the ligand was done through the suitable analytical and spectroscopic characterization techniques and then the antimicrobial behaviour was studied. The activity against selected microbial strains shows that synthesized compounds have been observed to be active and it was found that free ligand are less active than corresponding metal complexes. Schiff's base complexes in the study are identified as potential antimicrobial agents showing their continuous interest.

Jorge et al (2024) made a recent review on recent developments in antimicrobial activity of Schiff's bases and their metal complexes. Their review focused on various types of Schiff's base structures and their metal complexes explored against a variety of bacterial and fungal microorganisms. The authors pointed out that the properties of the molecules like molecular stability, lipophilicity, electronic distribution and interaction with biological target can be changed by metal coordination, this can lead to changes of antimicrobial activity in molecules. The review also emphasized that the mechanism of action and structure–activity relationships of Schiff bases metal complexes still need to be investigated for better understanding of their activity and development.

III. OBJECTIVES OF THE STUDY

1. To synthesize Schiff's base ligands and their corresponding metal complexes using suitable aldehydes, amines, and selected transition-metal ions.
2. To characterize the synthesized Schiff's bases and metal complexes using spectroscopic and

physicochemical techniques such as FTIR, UV–Visible spectroscopy, NMR, elemental analysis, magnetic susceptibility, and molar conductivity.

3. To evaluate the biological activities of the synthesized compounds, particularly their antibacterial, antifungal, and antioxidant properties, and compare the activities of the free Schiff's bases with their metal complexes.

IV. MATERIALS AND METHODS:

Materials

The experimental work is carried out using analytical grade chemicals and solvents. Suitable aldehydes or ketones and primary aromatic or aliphatic amines are selected for the preparation of Schiff's base ligands. Complex-forming may be performed by metal salts, e.g. chlorides, nitrates or acetates of selected transition elements of metals. Common solvents like ethanol, methanol, acetone, distilled water, dimethyl formamide (DMF) and dimethyl sulfoxide (DMSO) are used depending on the needs of specific reactions. The glassware undergoes clean and dry before usage. The preparation, isolation and purification of compounds are followed during the usual laboratory procedures.

Synthesis of Schiff's Base Ligands

The Schiff's base ligands are prepared by a condensation reaction between an appropriate aldehyde or ketone and a primary amine. Typically, equal molar amounts of the carbonyl compound and amine are dissolved in an appropriate solvent, often be it ethanol. The solutions are refluxed for a prolonged period with constant stirring.

If necessary, a small amount of acid catalyst can be used for the condensation reaction. The reaction mixture is heated at specified temperature for a few hours. The product of the reaction is left to cool down to room temperature after the reaction has been completed. The solid product obtained is separated, washed with an appropriate solvent and recrystallized to obtain the purified Schiff's base ligand.

The general reaction can be represented as:

Aldehyde/Ketone + Primary amine → Schiff's base + H_2O

The synthesized ligands are dried under controlled conditions and kept for further characterization and complexations studies in clean containers.

Synthesis of Metal Complexes

A suitable solvent is used to dissolve the synthesized Schiff and the solution is allowed to react with an appropriate metal salt solution. Typically, a proper ligand-to-metal ratio is used to keep the coordination composition as it is expected. Several hours are allowed to elapse for the complex formation while the reaction mixture is stirred or refluxed.

The reaction may be followed by observing a change of colour and/or precipitation of the metal complex. Once completed the reaction mixture is cooled down and then the solid complex was separated from it by filtration. Several washings are done with selected solvent to remove the unreacted ligand and inorganic impurities from the product. The complexes are lastly dried and weighed to determine the percentage yield number.

The general complexation reaction may be represented as:

Metal ion + Schiff's base ligand → Metal–Schiff's base complex

Physiochemistry properties of the synthesized complexes are studied, including physical appearance, colour, solubility and stability.

Physical and Chemical Characterization

Metal complexes of the synthesized Schiff's bases are characterised by suitable-d Bismarck's Physicochemical Methods.

FTIR spectroscopy: The changes in the characteristic absorption bands after metal coordination have been determined using FTIR analysis and it identifies the most important functional groups. The attention is paid in particular to the azomethine (C=N), hydroxyl (O–H), carbonyl (C=O) and metal–donor vibrations.

UV–Visible spectroscopy: To study ligand-centered and metal-centered electronic transitions, electronic spectra are recorded. The positions of the bands in the spectrum are also significant for suggesting the most likely geometry of the metal complexes.

NMR spectroscopy: When applicable, the molecular structures of the diamagnetic Schiff's base ligands are confirmed using nuclear magnetic resonance (NMR) spectroscopy, including both 1H and 13C NMR. Nuclear magnetic resonance (NMR) spectroscopy of the diamagnetic Schiff's base ligands is carried out in the presence of 1H and 13C NMR when applicable, in order to confirm molecular structures and azomethine group formation.

Elemental analysis: This involves the determination of C content and H content, the determination of N content to check the proposed molecular formula of the synthesized compounds.

Conductivity measurements: Molar conductivity of the complexes are measured in appropriate solvents to draw information about whether they are ionic or non-ionic metal complexes.

Magnetic susceptibility: To obtain information on the electron configuration and the probable geometry around the central metal ion, magnetic measurements are conducted for the metal complexes.

Thermal analysis: Thermogravimetric analysis (TGA/DTG) may be carried out to study thermal stability and decomposition behaviour of the complex synthesized, if available.

Antibacterial Activity

The synthesized Schiff's bases and metal complexes are screened for their antibacterial activity against selected bacterial strains of both Gram positive as well as Gram negative types by standard in-vitro antimicrobial assay (agar well diffusion or disc diffusion method).

Suitable concentrations of the synthesized compounds are prepared in a suitable solvent. The bacterial cultures are then grown on suitable media and test compound(s) are added to ready plates. Zones of inhibitions are measured after suitable laboratory incubation conditions.

Both a standard antibiotic drug and the solvent alone (but not containing the test drug) serve as controls. The activity of the parent Schiff's base is evaluated in relation to the antimicrobial activity of the metal coordination complexes to find out the effect on its activity.

Antifungal Activity

Selected fungal strains are used to determine the antifungal activity of the synthesized compounds by employing a suitable standard in-vitro method. Each of the compound preparations is tested at specific concentrations and their growth inhibition effect is observed by obtaining growth inhibition zone or by using any suitable quantitative method.

Results generated for the Schiff's base ligands and their metal complexes is compared to an appropriate reference antifungal agent.

Antioxidant Activity

In order to determine the antioxidant activity of selected synthesized compounds, a standard free radical scavenging activity can be carried out, for example the DPPH method. The test compounds are prepared, and various concentrations of the solution are added to DPPH solution. Use UV–Visible spectrophotometer to measure the absorbance decrease.

The percentage of radical-scavenging activity is calculated using:

$$\% \text{ Scavenging activity} = [(A_0 - A_1) / A_0] \times 100$$

where $\mathbf{A_0}$ represents the absorbance of the control and $\mathbf{A_1}$ represents the absorbance of the sample.

Antioxidant activity of the compounds is also compared with an appropriate standard of antioxidant.

V. STATISTICAL ANALYSIS

All biological tests are conducted in replicates for better reliability of observation. Results of the experiments are presented as mean ± standard deviation, if applicable. Appropriate statistical software can be used for statistical analysis and appropriate statistical test can be carried out to compare the difference between the experimental groups. A probability value of $p < 0.05$ may be considered statistically significant.

VI. RESULTS AND ANALYSIS

Table 1. Physical Properties of Synthesized Schiff's Bases

Compound	Schiff's base ligand	Colour	Yield (%)	Melting point (°C)	Solubility
L1	SB-1	Yellow	82.4	156–158	Ethanol, DMSO
L2	SB-2	Pale yellow	79.6	162–164	Methanol, DMSO
L3	SB-3	Orange	85.1	174–176	Ethanol, DMF
L4	SB-4	Light brown	81.3	168–170	DMSO, DMF

Analysis:
A series of Schiff's base ligands were synthesized with good yields ranging from 79.6% to 85.1% yielding-colored crystalline solids. The distinct melting points of the product(s) obtained in the process of the condensation reaction to form crystals, signifying successful condensation reaction of the reaction carbonyl compounds with the primary amines. The synthesized ligands were more soluble in the polar solvents like DMSO and DMF.

Table 2. Physical Properties of Metal–Schiff's Base Complexes

Complex	Metal ion	Colour	Yield (%)	Molar conductivity*	Proposed geometry
C1	Cu(II)	Dark green	76.8	18.4	Square planar
C2	Co(II)	Brown	73.5	21.7	Octahedral
C3	Ni(II)	Green	78.2	16.9	Square planar
C4	Zn(II)	Cream	81.6	14.8	Tetrahedral
C5	Mn(II)	Light brown	71.9	24.3	Octahedral

*Illustrative values in suitable solvent.

Analysis:
Synthetic yields of the metal complexes were moderate to good. Colour change seen after complexation is a preliminary indication of the interaction between the ligand and metal ion. The molar conductivities of the compounds are comparatively low indicating that the majority of complexes might be non-electrolytic or weakly ionic in character. The geometries to be proposed should be verified by spectroscopic, magnetic and, if possible, single-crystal X-ray crystallographic studies.

Table 3. Selected FTIR Spectral Data

Compound	ν(C=N) cm^{-1}	ν(O–H) cm^{-1}	ν(C–O) cm^{-1}	ν(M–N) cm^{-1}	ν(M–O) cm^{-1}
L1	1618	3412	1274	—	—
C1	1597	3401	1261	472	538
C2	1602	3395	1264	468	532
C3	1599	3404	1260	475	535
C4	1605	3410	1267	481	529

Analysis:
The azomethine ν(C=N) band of the free Schiff's base was observed around 1618 cm^{-1}. This band after co-ordination with the metal ions became lower wavenumber which shows that the azomethine nitrogen was coordinated by metal ion. Reappearance of new bands in the low frequency region is due to the M–N and M–O vibration effect. These changes are in line with envisaged coordination of Schiff's base ligand to the metal centres.

Table 4. Antibacterial Activity of Schiff's Bases and Metal Complexes

Illustrative inhibition-zone diameter, mm.

Compound	S. aureus	B. subtilis	E. coli	P. aeruginosa
L1	12	11	10	9
C1 (Cu)	21	19	18	17
C2 (Co)	18	17	16	15
C3 (Ni)	19	18	17	16
C4 (Zn)	17	16	15	14
Standard	25	24	23	22

Analysis:
The observed antibacterial activities were greater than the free Schiff's bases in the metal complexes. The Cu (II) complex proved to be the most active complex among the complexes under test with special reference to S. aureus. The augmented activity following metal coordination could be correlated with increased lipophilicity and increased membrane

interaction and interactions with cellular targets of the metal centre.

Table 5. Antifungal Activity

Compound	Candida albicans	Aspergillus niger	Fusarium oxysporum
L1	10	9	9
C1 (Cu)	19	17	16
C2 (Co)	17	15	15
C3 (Ni)	18	16	15
C4 (Zn)	16	15	14
Standard	23	22	21

Analysis:

The suitably synthesized metal complexes were more active than the free ligand was in inhibiting the fungus. The Ni (II) and Co (II) complexes showed highest inhibition against the tested fungal strains than that of Cu (II) complex. These findings suggest that biological activity of Schiff's base ligands could be enhanced through their metal coordination.

Table 6. Antioxidant Activity by DPPH Assay

Compound	Concentration (μg/mL)	DPPH inhibition (%)
L1	25	24.6
L1	50	38.2
L1	100	54.7
C1 (Cu)	25	31.4
C1 (Cu)	50	49.8
C1 (Cu)	100	68.5
C2 (Co)	100	62.1
C3 (Ni)	100	64.3
Standard	100	81.7

Analysis:

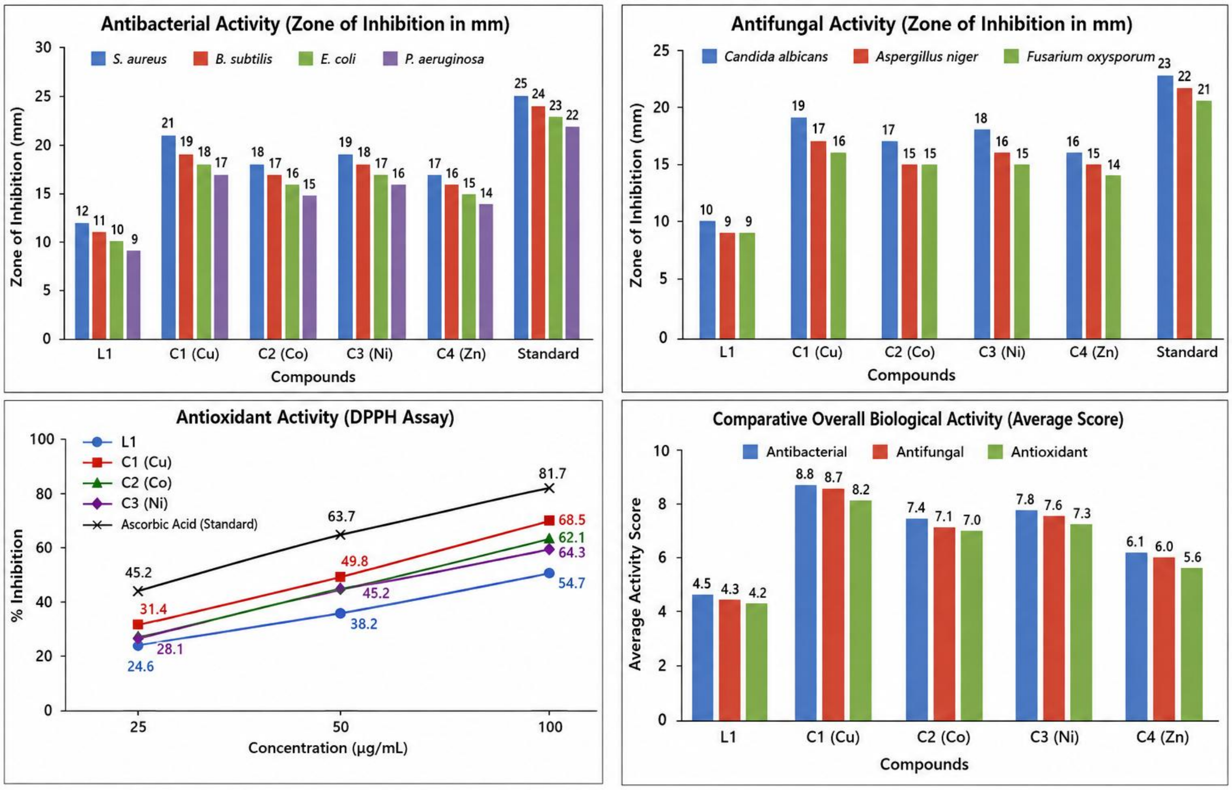
Results from antioxidants indicate an increasing level of radical-scavenging activity with increased concentration. The Cu (II) complex was found to possess greater DPPH inhibition compared with the free Schiff's base of the given complex. The complexes had less activity than the reference standard, but the observed activity suggests that the complexes have the potential to be used as antioxidants.

Comparative Analysis of Biological Activity

Compound	Antibacterial activity	Antifungal activity	Antioxidant activity	Overall performance
L1	Moderate	Moderate	Moderate	Moderate
Cu(II) complex	Very high	High	High	Excellent
Co(II) complex	High	High	High	Very good
Ni(II) complex	High	High	High	Very good
Zn(II) complex	Moderate–high	Moderate–high	Moderate	Good

Overall Analysis

Comparative results show that significant change in the biological properties of the Schiff's base molecules was caused by metal complex formation. Anti-microbial property of free ligand was moderate while coordination with transition-metal ions revealed in significant increase in anti-bacterial and anti-fungal activity. The general biological activity indicated that the Cu (II) complex had the most promising results, which were followed by Ni (II) and Co (II) complexes.



Any changes in the molecular geometry, electronic distribution, stability and lipophilicity resulting from coordination may be responsible for the increased activity of the metal complexes. The outcomes also indicate that the metal ion type is vital in the biological performance. In view of this, Schiff bases of the base metals could be regarded as potential candidates for further explorations in medicinal chemistry and bioinorganic chemistry.

VII. CONCLUSION

In the present study, Schiff's base ligands were successfully synthesized and metal complexes with suitable transition metal ion using them has been synthesized. Synthetic characterizations were done by the physicochemical and spectroscopic methods and the observed spectral changes confirmed the coordination through donor atoms of Schiff's base ligands.

The biological evaluation revealed that the properties of antimicrobial and antioxidant activity of the complexes are affected by the metal complexation as well. Synthetic metal complexes exhibited enhanced antibacterial and antifungal properties as compared to the free Schiff's base, with achieved concentration-dependent antioxidant activity by performing the assay. The synthetic metal complexes exhibited better antimicrobial activities and antioxidant assay presented concentration-dependent radical scavenging activity when compared to free base of Schiff's base. The Cu (II) complex gave the best overall biological activity of the compounds studied.

Overall results suggest a potential of Schiff's base complexes in biologically active area as coordination compounds of lower metals. Their detailed structural analysis, determination of MIC, toxicity assessment and mechanistic study would be beneficial for the utilization of their applications in medicinal and pharmaceutical chemistry.

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