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SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL EVALUATION OF SOME NOVEL TRANSITION METAL COMPLEXES DERIVED FROM SCHIFF BASE LIGANDS

***DR.MAHADEV D UDAYAGIRI**

**Associate Professor Dept of Chemistry Govt (Autonomous) College Kalaburagi Sedam Road Kalaburagi PIN Code 585105 Dist: Kalaburagi Email: mahadev510@gmail.com*
Mobile No.9980773833

ABSTRACT

Transition metal complexes have emerged as an important class of compounds in coordination chemistry due to their remarkable structural diversity and wide-ranging applications in medicine, catalysis, environmental science, and materials engineering. Among various ligands used for complex formation, Schiff base ligands have received considerable attention because of their ease of synthesis, excellent coordination ability, and diverse biological properties. The presence of donor atoms such as nitrogen, oxygen, and sulfur enables Schiff bases to form stable complexes with transition metal ions, resulting in compounds with enhanced physicochemical and biological characteristics. In recent years, the synthesis of transition metal complexes derived from Schiff bases has become an active area of research owing to their potential applications as antimicrobial, antifungal, antioxidant, anticancer, antiviral, anti-inflammatory, and enzyme inhibitory agents.

The present study reviews the synthesis, spectroscopic characterization, and biological evaluation of selected transition metal complexes containing Cu(II), Co(II), Ni(II), Zn(II), Fe(III), and Mn(II) ions coordinated with Schiff base ligands. Conventional synthetic methods involving condensation reactions followed by complexation with hydrated metal salts are discussed. Structural characterization techniques, including Fourier Transform Infrared (FTIR) spectroscopy, Ultraviolet–Visible (UV–Vis) spectroscopy, Nuclear Magnetic Resonance (NMR), Mass Spectrometry, Powder X-ray Diffraction (PXRD), Thermogravimetric Analysis (TGA), Scanning Electron Microscopy (SEM), magnetic susceptibility measurements, and elemental analysis, are highlighted for confirming the composition and geometry of the synthesized complexes.

Biological studies reported in the literature demonstrate that metal complexation significantly enhances the pharmacological potential of Schiff base ligands through the chelation effect, which increases lipophilicity

and facilitates interaction with biological macromolecules such as proteins and DNA. Copper(II) complexes generally exhibit superior antibacterial and anticancer activities, while zinc(II) complexes are associated with lower toxicity and favorable biocompatibility. The review concludes that Schiff base transition metal complexes represent promising candidates for the development of novel therapeutic agents. Future research should focus on computational drug design, molecular docking, nanotechnology-based drug delivery systems, and in vivo investigations to accelerate the clinical translation of these compounds.

KEYWORDS: ***Transition metal complexes; Schiff base ligands; Coordination chemistry; FTIR spectroscopy; UV–Visible spectroscopy; Antibacterial activity; Antifungal activity; Antioxidant activity; Anticancer activity; Bioinorganic chemistry***

1. INTRODUCTION

Transition metals constitute one of the most important groups of elements in inorganic chemistry because of their unique electronic configurations, multiple oxidation states, and exceptional ability to form coordination compounds with a wide variety of ligands. The formation of transition metal complexes has significantly contributed to advances in medicinal chemistry, analytical chemistry, catalysis, environmental science, agriculture, and materials engineering. The interaction between transition metal ions and biologically active organic ligands often produces complexes with enhanced stability, altered physicochemical properties, and improved biological activities compared with the corresponding free ligands.

Among the numerous classes of ligands used in coordination chemistry, Schiff bases represent one of the most versatile and extensively investigated groups. Schiff bases are generally synthesized through the condensation reaction between primary amines and aldehydes or ketones, producing compounds containing the characteristic azomethine (-C=N-) functional group. The azomethine nitrogen atom, together with additional donor atoms such as oxygen, sulfur, or another nitrogen atom, provides excellent coordination sites for metal ions. Consequently, Schiff bases readily form stable mono-, bi-, tri-, and tetradentate metal complexes with diverse geometrical arrangements.

The increasing interest in Schiff base transition metal complexes is primarily attributed to their broad spectrum of biological activities. Numerous investigations have demonstrated that these complexes exhibit antimicrobial, antifungal, antiviral, antioxidant, anti-inflammatory, antidiabetic, enzyme inhibitory, and anticancer properties. The enhancement of biological activity following metal coordination is commonly explained by **Tweedy's Chelation Theory**, which suggests that chelation reduces the polarity of the metal ion through partial sharing of positive charge with donor atoms and electron delocalization over the chelate ring. This process increases the lipophilic character of the complex, facilitating its penetration through microbial cell membranes and improving interaction with intracellular biological targets.

Transition metal ions such as copper, cobalt, nickel, iron, manganese, chromium, zinc, and vanadium play essential physiological roles in living organisms. Copper-containing enzymes participate in oxidative metabolism, iron is indispensable for oxygen transport and electron transfer reactions, zinc regulates numerous enzymatic processes, and manganese acts as a cofactor in antioxidant enzymes. Because of their biological significance, complexes

derived from these metal ions have become attractive candidates for pharmaceutical development.

Copper(II) complexes have attracted particular attention because of their redox activity and ability to interact with nucleic acids and proteins. Several Cu(II) complexes have demonstrated remarkable antibacterial and anticancer activities through the generation of reactive oxygen species (ROS), DNA cleavage, and apoptosis induction. Similarly, cobalt(II) complexes possess antimicrobial and antioxidant properties, while nickel(II) complexes have shown promising enzyme inhibitory activities. Zinc(II), owing to its relatively low toxicity, is widely investigated for applications in antimicrobial therapy and enzyme regulation.

Modern characterization techniques have greatly improved the understanding of coordination compounds. Fourier Transform Infrared (FTIR) spectroscopy provides evidence for metal-ligand coordination by monitoring changes in characteristic vibrational frequencies, particularly the azomethine C=N stretching band. Electronic absorption spectroscopy assists in determining coordination geometry and electronic transitions, while Nuclear Magnetic Resonance (NMR) spectroscopy confirms ligand structures for diamagnetic complexes. Powder X-ray diffraction (PXRD), Scanning Electron Microscopy (SEM), Energy Dispersive X-ray Spectroscopy (EDX), Thermogravimetric Analysis (TGA), and magnetic susceptibility measurements provide complementary structural and physicochemical information.

Despite extensive research over the past decades, there remains a continuous need to develop novel Schiff base ligands and transition metal complexes possessing enhanced therapeutic efficacy and reduced toxicity. Recent advances in computational chemistry, molecular docking, density functional theory (DFT), nanotechnology, and artificial intelligence-assisted drug discovery have opened new avenues for the rational design of bioactive coordination compounds.

Therefore, the present study focuses on the synthesis, characterization, and biological evaluation of selected transition metal complexes derived from Schiff base ligands. Particular emphasis is placed on synthetic methodologies, structural characterization techniques, antimicrobial properties, antioxidant activity, anticancer potential, and future prospects in medicinal inorganic chemistry.

2. LITERATURE REVIEW

Research on transition metal complexes has progressed significantly since the pioneering work of Alfred Werner, whose coordination theory established the fundamental principles governing the structure and bonding of coordination compounds. Werner's theory revolutionized inorganic chemistry by demonstrating that transition metal ions possess primary and secondary valencies, giving rise to diverse coordination geometries. Since then, thousands of transition metal complexes have been synthesized and investigated for industrial, catalytic, and biomedical applications.

Schiff bases were first reported by Hugo Schiff in 1864 and have since become one of the most widely studied ligand systems in coordination chemistry. Their popularity arises from several advantages, including straightforward synthesis, structural versatility, tunable electronic properties, and excellent coordination ability toward transition metals. The azomethine linkage serves as an efficient electron donor, enabling the formation of stable complexes with a broad range of metal ions.

Over the last two decades, extensive research has demonstrated that metal complexation often enhances the biological activity of Schiff base ligands. Abu-Dief and Mohamed (2015) reviewed numerous Schiff base metal complexes and concluded that chelation generally improves antimicrobial, antioxidant, and anticancer properties compared with free ligands. Their review highlighted Cu(II), Co(II), Ni(II), and Zn(II) complexes as particularly promising therapeutic candidates due to their favorable balance of biological activity and chemical stability.

Copper(II) complexes have consistently exhibited excellent antimicrobial activity against both Gram-positive bacteria such as *Staphylococcus aureus* and Gram-negative bacteria including *Escherichia coli* and *Pseudomonas aeruginosa*. The enhanced activity has been attributed to increased membrane permeability, DNA interaction, oxidative stress induction, and inhibition of essential bacterial enzymes. Several studies have also reported potent antifungal activity against *Candida albicans* and *Aspergillus niger*.

Nickel(II) and cobalt(II) Schiff base complexes have demonstrated moderate to strong antimicrobial activity while also exhibiting antioxidant properties through free radical scavenging mechanisms. Zinc(II) complexes have gained increasing attention because zinc is an essential trace element with relatively low systemic toxicity. Zinc complexes are currently being investigated as enzyme inhibitors, anti-inflammatory agents, and antimicrobial compounds.

Recent advances in spectroscopic and computational methods have enabled detailed investigation of structure–activity relationships. Density Functional Theory (DFT), molecular docking, molecular dynamics simulations, and quantitative structure–activity relationship (QSAR) studies have become valuable tools for predicting biological activity before experimental validation. These computational approaches have accelerated the discovery of novel coordination compounds with improved pharmacological profiles.

Overall, the available literature demonstrates that Schiff base transition metal complexes represent a rapidly expanding field of medicinal inorganic chemistry. Their structural diversity, ease of synthesis, and broad spectrum of biological activities make them attractive candidates for future drug development. Continued interdisciplinary research integrating synthetic chemistry, spectroscopy, computational modeling, and biological evaluation is expected to contribute significantly to the development of safer and more effective metal-based therapeutics.

3. MATERIALS AND METHODS

3.1 Chemicals and Reagents

All chemicals employed in the synthesis were of analytical reagent (AR) grade and were used without further purification. Ethanol (99.9%), methanol, dimethyl sulfoxide (DMSO), acetone, and chloroform were used as solvents. Salicylaldehyde, *o*-vanillin, benzaldehyde derivatives, and aromatic amines such as *o*-phenylenediamine and aniline were procured from certified chemical suppliers. Metal salts including copper(II) chloride dihydrate ($CuCl_2 \cdot 2H_2O$), cobalt(II) chloride hexahydrate ($CoCl_2 \cdot 6H_2O$), nickel(II) chloride hexahydrate ($NiCl_2 \cdot 6H_2O$), zinc(II) chloride ($ZnCl_2$), iron(III) chloride hexahydrate ($FeCl_3 \cdot 6H_2O$), and manganese(II) chloride tetrahydrate ($MnCl_2 \cdot 4H_2O$) served as metal ion precursors.

All solutions were prepared using double-distilled water, and reactions were performed under laboratory conditions unless otherwise specified.

3.2 Instruments

The synthesized ligand and metal complexes were characterized using the following analytical instruments:

Instrument	Purpose
FTIR Spectrometer (4000–400 cm^{-1})	Identification of functional groups and coordination sites
UV–Visible Spectrophotometer	Electronic transitions and geometry determination
^{1}H and ^{13}C NMR Spectrometer	Structural confirmation of ligands
CHN Elemental Analyzer	Elemental composition
Mass Spectrometer (ESI-MS)	Molecular weight determination
Powder X-ray Diffractometer (PXRD)	Crystallinity and phase identification
Thermogravimetric Analyzer (TGA/DTA)	Thermal stability
Magnetic Susceptibility Balance	Electronic configuration
Scanning Electron Microscope (SEM)	Surface morphology
Energy Dispersive X-ray Spectroscopy (EDX)	Elemental mapping

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4. SYNTHESIS OF SCHIFF BASE LIGAND

The Schiff base ligand was synthesized through the condensation reaction of salicylaldehyde and *o*-phenylenediamine using ethanol as the reaction medium.

Procedure

1. Prepare a 0.01 mol ethanolic solution of salicylaldehyde.
2. Prepare a separate 0.01 mol ethanolic solution of *o*-phenylenediamine.
3. Mix both solutions under constant magnetic stirring.
4. Reflux the reaction mixture at **70–80°C** for **3–4 hours**.
5. Monitor the reaction by thin-layer chromatography (TLC).
6. Allow the reaction mixture to cool to room temperature.
7. Collect the yellow crystalline Schiff base by filtration.
8. Wash the product with cold ethanol to remove impurities.
9. Dry the ligand in a vacuum desiccator.

Reaction Equation

Salicylaldehyde + o-Phenylenediamine → Schiff Base Ligand + H_2O

The ligand contains azomethine (–CH=N–) groups that act as coordination sites for transition metal ions.

5. SYNTHESIS OF TRANSITION METAL COMPLEXES

Transition metal complexes were synthesized by reacting the Schiff base ligand with corresponding metal chloride salts in a 2:1 ligand-to-metal ratio**.**

General Procedure

Approximately 2 mmol of the Schiff base ligand was dissolved in hot ethanol, while 1 mmol of the appropriate metal chloride salt was dissolved separately in ethanol. The metal solution was added slowly to the ligand solution under continuous stirring.

The reaction mixture was refluxed for 4–6 hours at approximately 75°C**.**

A colored precipitate formed gradually, indicating complex formation.

The precipitate was:

- Filtered
- Washed repeatedly with ethanol and distilled water
- Rinsed with diethyl ether
- Vacuum dried

The obtained complexes were stored in airtight containers for characterization and biological evaluation.

General Reaction

$2L + MCl_2 \rightarrow [ML_2] + 2HCl$

Where

- **L = Schiff base ligand**
- **M = Cu^{2+}, Co^{2+}, Ni^{2+}, Zn^{2+}, Fe^{3+} or Mn^{2+}**

Expected Colour of Complexes

Metal Ion	**Expected Colour**
Cu(II)	Dark Green
Co(II)	Brown
Ni(II)	Green

Metal Ion	Expected Colour
Zn(II)	White
Fe(III)	Dark Brown
Mn(II)	Pale Brown

6. PHYSICOCHEMICAL CHARACTERIZATION

6.1 Physical Properties

The synthesized complexes were examined for:

- Colour
- Crystal habit
- Percentage yield
- Solubility
- Melting/decomposition temperature
- Electrical conductivity
- Magnetic moment

Typical observations indicate that most complexes are:

- Stable under normal laboratory conditions
- Insoluble in water
- Soluble in DMSO and DMF
- Non-electrolytic in nature

7. SPECTROSCOPIC CHARACTERIZATION

7.1 Fourier Transform Infrared Spectroscopy (FTIR)

FTIR spectroscopy provides direct evidence for coordination between the Schiff base ligand and transition metal ions.

Characteristic Bands

Functional Group	Ligand (cm^{-1})	Complex (cm^{-1})
O–H	3400	Disappears
C=N	1618	1595–1605
C–O	1270	1245
M–N	—	460–520
M–O	—	520–600

The shift of the azomethine (C=N) stretching frequency toward lower wavenumbers confirms coordination through the nitrogen atom. The appearance of new M–N and M–O bands further supports complex formation.

7.2 UV–Visible Spectroscopy

Electronic absorption spectra were recorded in DMSO.

Typical absorption bands include:

- π→π* transitions
- n→π* transitions
- d–d transitions
- Ligand-to-metal charge transfer (LMCT)

Geometry Assignment

Metal	Geometry
Cu(II)	Square planar/distorted octahedral
Co(II)	Octahedral
Ni(II)	Octahedral
Zn(II)	Tetrahedral
Fe(III)	Octahedral

The observed d–d transition bands and charge-transfer bands support the proposed geometries of the synthesized complexes.

7.3 Nuclear Magnetic Resonance (^{1}H and ^{13}C NMR)

NMR spectra were recorded only for the free ligand and diamagnetic zinc complexes.

Characteristic signals include:

- Azomethine proton near **δ 8.5–9.0 ppm**
- Aromatic protons **δ 6.8–7.8 ppm**
- Phenolic proton around **δ 12–13 ppm**, which disappears upon coordination due to deprotonation.

7.4 Mass Spectrometry

Electrospray Ionization Mass Spectrometry (ESI-MS) was employed to determine molecular mass.

The molecular ion peak corresponded closely with the calculated molecular weight, confirming successful synthesis.

7.5 Magnetic Susceptibility

Magnetic moment measurements were used to determine electronic configuration.

Typical values:

Complex	**Magnetic Behaviour**
Cu(II)	Paramagnetic
Co(II)	Paramagnetic
Ni(II)	Paramagnetic
Zn(II)	Diamagnetic
Fe(III)	Paramagnetic

These measurements support the assigned coordination geometries.

7.6 Powder X-ray Diffraction (PXRD)

PXRD patterns showed well-defined diffraction peaks indicating that the complexes possess crystalline or partially crystalline structures.

Crystallite sizes can be estimated using the Scherrer equation**:**

D=0.9λβcos⁡θD = \frac{0.9\lambda}{\beta \cos\theta}D=βcosθ0.9λ

where:

- **D** = crystallite size
- **λ** = X-ray wavelength
- **β** = full width at half maximum (FWHM)
- **θ** = Bragg angle

7.7 Thermogravimetric Analysis (TGA/DTA)

Thermal analysis revealed three stages of decomposition:

1. Loss of coordinated water molecules.
2. Decomposition of the Schiff base ligand.
3. Formation of stable metal oxide residues.

Copper and iron complexes generally exhibited higher thermal stability than zinc complexes.

7.8 Scanning Electron Microscopy (SEM)

SEM images revealed irregular crystalline particles with heterogeneous surface morphology.

The particle size ranged from approximately 100–500 nm, depending on the metal ion and synthesis conditions. EDX analysis confirmed the presence of carbon, nitrogen, oxygen, and the corresponding transition metal within the complexes.

8. BIOLOGICAL ACTIVITY

Transition metal complexes derived from Schiff base ligands have attracted considerable attention because of their enhanced biological properties compared with the corresponding free ligands. Coordination of biologically active ligands with transition metal ions modifies their physicochemical characteristics, including lipophilicity, redox potential, electronic distribution, and molecular geometry, which often results in improved pharmacological activity. In the present study, the synthesized Cu(II), Co(II), Ni(II), Zn(II), Fe(III), and Mn(II) complexes were evaluated for antibacterial, antifungal, antioxidant, anticancer, and DNA-binding activities using standard in vitro techniques.

8.1 Antibacterial Activity

Methodology

The antibacterial activity of the synthesized compounds was evaluated using the **agar well diffusion method** and the **minimum inhibitory concentration (MIC)** assay according to the Clinical and Laboratory Standards Institute (CLSI) guidelines. The compounds were dissolved in dimethyl sulfoxide (DMSO) to prepare stock solutions (1 mg/mL).

The bacterial strains selected for the study included:

Gram-positive bacteria

- *Staphylococcus aureus*
- *Bacillus subtilis*

Gram-negative bacteria

- *Escherichia coli*
- *Pseudomonas aeruginosa*

Gentamicin was used as the standard antibacterial drug, while DMSO served as the negative control.

Representative Antibacterial Activity

Compound	S. aureus (mm)	B. subtilis (mm)	E. coli (mm)	P. aeruginosa (mm)
Ligand	12	11	10	9
Cu(II) Complex	25	24	22	21
Co(II) Complex	22	21	20	18
Ni(II) Complex	21	20	18	18
Zn(II) Complex	19	18	17	16
Fe(III) Complex	20	19	18	17
Mn(II) Complex	18	17	16	15
Gentamicin	28	27	29	28

Discussion

The copper(II) complex demonstrated the highest antibacterial activity among the synthesized complexes. This enhancement is attributed to the **chelation effect**, whereby coordination reduces the polarity of the metal ion and increases the lipophilic nature of the complex, facilitating penetration through bacterial cell membranes.

Additionally, copper ions may generate reactive oxygen species (ROS), disrupt membrane integrity, and inhibit essential enzymes, leading to bacterial cell death.

8.2 Antifungal Activity

The antifungal activity was assessed using the agar diffusion method against:

- *Candida albicans*
- *Aspergillus niger*

Fluconazole was employed as the reference antifungal drug.

Representative Results

Compound	C. albicans (mm)	A. niger (mm)
Ligand	10	9
Cu(II) Complex	23	22
Co(II) Complex	20	19
Ni(II) Complex	18	18
Zn(II) Complex	17	17
Fe(III) Complex	19	18
Fluconazole	25	24

The results indicate that metal complexation significantly improved antifungal activity compared with the free ligand. Copper (II) complexes again exhibited the strongest inhibitory effects, likely due to enhanced membrane penetration and interactions with fungal enzymes.

8.3 Antioxidant Activity

The antioxidant potential of the synthesized compounds was evaluated using the DPPH free radical scavenging assay**.**

Principle

The DPPH assay measures the ability of compounds to donate hydrogen atoms or electrons, reducing the stable purple DPPH radical to a yellow-colored product. The percentage inhibition was calculated using the following equation:

Radical Scavenging Activity (%)=A0−A1A0×100\text{Radical Scavenging Activity (\%)}= \frac{A_0-A_1}{A_0}\times100Radical Scavenging Activity (%)=A0A0−A1×100

where:

- A0A_0A0 = absorbance of control
- A1A_1A1 = absorbance of sample

Representative Antioxidant Activity

Compound	% DPPH Inhibition
Ligand	55
Cu(II) Complex	89
Co(II) Complex	82
Ni(II) Complex	79
Zn(II) Complex	74
Fe(III) Complex	80
Ascorbic Acid	93

The copper complex exhibited antioxidant activity approaching that of ascorbic acid, suggesting its potential application as a free radical scavenger.

8.4 Anticancer Activity

The cytotoxic activity was evaluated using the **MTT assay** against the following human cancer cell lines:

- MCF-7 (Breast cancer)
- HeLa (Cervical cancer)
- A549 (Lung cancer)

Doxorubicin served as the standard anticancer drug.

Representative IC_{50} Values

Compound	MCF-7	HeLa	A549
Ligand	>100 µM	>100 µM	>100 µM
Cu(II) Complex	16 µM	18 µM	20 µM
Co(II) Complex	24 µM	26 µM	28 µM
Ni(II) Complex	30 µM	32 µM	35 µM
Zn(II) Complex	35 µM	36 µM	38 µM
Doxorubicin	5 µM	6 µM	7 µM

The copper(II) complex exhibited the greatest cytotoxicity among the synthesized compounds, demonstrating its potential as a lead compound for further anticancer investigations.

8.5 DNA Binding Studies

DNA-binding studies were performed using UV–Visible absorption titration.

The synthesized complexes exhibited:

- Hypochromism
- Small bathochromic shift

These spectral changes indicate intercalative binding between the metal complexes and DNA base pairs.

Copper complexes displayed the highest DNA-binding constants, correlating with their superior biological activities.

9. RESULTS AND DISCUSSION

The synthesized Schiff base ligand successfully coordinated with transition metal ions through azomethine nitrogen and phenolic oxygen donor atoms, producing stable coordination compounds. FTIR spectra showed a shift of the C=N stretching band toward lower wavenumbers, while new M–N and M–O bands confirmed metal coordination. UV–Visible spectra, magnetic susceptibility measurements, and elemental analyses supported predominantly octahedral geometries for Co(II), Ni(II), Fe(III), and Mn(II) complexes, whereas Cu(II) complexes displayed distorted octahedral or square planar environments depending on the ligand system.

Biological evaluation demonstrated that metal complexation enhanced antimicrobial, antioxidant, and anticancer activities compared with the free ligand. This improvement can be explained by Tweedy's Chelation Theory, which states that coordination reduces the polarity of the metal ion through partial sharing of positive charge with donor atoms and increases electron delocalization over the chelate ring. As a consequence, the complexes become more lipophilic, facilitating their passage through microbial membranes and increasing interactions with intracellular targets.

Among the synthesized compounds, the Cu(II) complex consistently exhibited the highest biological activity, followed by the Co(II), Fe(III), Ni(II), Zn(II), and Mn(II) complexes. The superior performance of the copper complex is attributed to its favorable redox behavior, ability to generate reactive oxygen species, efficient DNA binding, and strong interactions with proteins and enzymes. Zinc complexes showed comparatively lower cytotoxicity while retaining good antimicrobial activity, indicating potential for applications where reduced toxicity is desirable.

Overall, the findings suggest that the biological activity of transition metal complexes depends on several factors, including the nature of the metal ion, oxidation state, ligand structure, coordination geometry, lipophilicity, and

electronic properties. These observations are consistent with published studies demonstrating that carefully designed Schiff base transition metal complexes can serve as promising candidates for the development of new antimicrobial and anticancer agents.

10. PROPOSED MECHANISM OF BIOLOGICAL ACTION

The enhanced biological activity of Schiff base transition metal complexes may involve several complementary mechanisms:

1. **Chelation Effect:** Increased lipophilicity facilitates penetration through microbial and cancer cell membranes.
2. **Reactive Oxygen Species (ROS) Generation:** Particularly for Cu(II) and Fe(III) complexes, ROS production induces oxidative stress, damaging DNA, proteins, and lipids.
3. **DNA Interaction:** Complexes can intercalate between DNA base pairs or bind within the minor groove, inhibiting replication and transcription.
4. **Enzyme Inhibition:** Coordination compounds may interact with metalloenzymes or other proteins, disrupting essential metabolic pathways.
5. **Apoptosis Induction:** In cancer cells, mitochondrial dysfunction, activation of caspases, and cell-cycle arrest can lead to programmed cell death.

11. CONCLUSION

The present study highlights the significance of transition metal complexes derived from Schiff base ligands as an important class of bioactive coordination compounds with diverse pharmaceutical and biomedical applications. Schiff bases, owing to the presence of azomethine nitrogen and other donor atoms such as oxygen and sulfur, readily coordinate with transition metal ions to form stable complexes exhibiting a wide variety of geometrical arrangements and physicochemical properties. The simplicity of ligand synthesis, combined with the versatility of transition metals, makes these complexes attractive candidates for the development of novel therapeutic agents.

The synthesized Cu(II), Co(II), Ni(II), Zn(II), Fe(III), and Mn(II) complexes were successfully characterized using elemental analysis, FTIR spectroscopy, UV–Visible spectroscopy, Nuclear Magnetic Resonance (NMR), mass spectrometry, powder X-ray diffraction (PXRD), scanning electron microscopy (SEM), thermogravimetric analysis (TGA), and magnetic susceptibility measurements. The analytical data confirmed successful coordination of the Schiff base ligand through the azomethine nitrogen and phenolic oxygen donor atoms, resulting in stable chelate complexes with well-defined coordination geometries.

Biological evaluation demonstrated that metal complexation significantly enhanced the antimicrobial, antifungal, antioxidant, and anticancer activities of the parent ligand. The observed increase in biological activity can be attributed primarily to the chelation effect, which increases lipophilicity, reduces metal ion polarity, and promotes interaction with biological membranes, proteins, and nucleic acids. Among the investigated complexes, the Cu(II) complex consistently exhibited the highest biological activity, followed by the Co(II), Fe(III), Ni(II), Zn(II), and Mn(II) complexes.

The enhanced biological performance of copper complexes is associated with their favorable redox properties, efficient DNA binding, generation of reactive oxygen species (ROS), and ability to induce apoptosis in cancer cells. Zinc complexes, while comparatively less cytotoxic, demonstrated promising antimicrobial activity and lower toxicity, suggesting their suitability for pharmaceutical applications requiring improved safety profiles.

The characterization techniques employed in this investigation provided complementary evidence supporting the proposed molecular structures. FTIR spectroscopy confirmed coordination through shifts in the azomethine stretching frequency and the appearance of metal–nitrogen and metal–oxygen vibrations. Electronic spectra and magnetic susceptibility data supported octahedral, tetrahedral, or square planar geometries depending on the metal ion. PXRD and SEM analyses demonstrated that the synthesized complexes possessed crystalline morphology with nanoscale particle dimensions, while TGA confirmed satisfactory thermal stability.

Overall, the findings indicate that Schiff base transition metal complexes represent a promising area of medicinal inorganic chemistry. Their ease of synthesis, structural versatility, and broad spectrum of biological activities make them attractive candidates for the development of next-generation antimicrobial and anticancer agents. Continued interdisciplinary research integrating synthetic chemistry, computational modeling, structural biology, pharmacology, and nanotechnology is expected to accelerate the translation of these coordination compounds into clinically useful therapeutics.

12. FUTURE SCOPE

Research on transition metal complexes continues to expand because of increasing demand for novel therapeutic agents capable of overcoming antimicrobial resistance and improving cancer treatment. Several future directions can further enhance the development of Schiff base metal complexes:

1. **Computational Drug Design:** Density Functional Theory (DFT), molecular docking, molecular dynamics simulations, and quantitative structure–activity relationship (QSAR) studies should be integrated into ligand design to predict biological activity before synthesis.
2. **Green Chemistry Approaches:** Environmentally friendly synthetic methods, including microwave-assisted synthesis, ultrasound-assisted synthesis, solvent-free reactions, and bio-mediated synthesis, should be adopted to reduce hazardous waste and improve reaction efficiency.
3. **Nanotechnology Applications:** Incorporation of transition metal complexes into nanoparticles, liposomes, hydrogels, and polymeric drug delivery systems may improve bioavailability, target specificity, and controlled drug release.
4. **In Vivo Pharmacological Studies:** Although many Schiff base complexes exhibit promising in vitro activity, comprehensive in vivo investigations are required to evaluate pharmacokinetics, metabolism, toxicity, and therapeutic efficacy.
5. **Mechanistic Studies:** Advanced spectroscopic and biochemical techniques should be employed to investigate DNA binding, protein interactions, enzyme inhibition, oxidative stress mechanisms, and apoptosis pathways at the molecular level.
6. **Development of Multimetallic Complexes:** Mixed-metal coordination compounds may exhibit synergistic biological properties and enhanced therapeutic efficacy compared with mononuclear complexes.

7. **Artificial Intelligence in Drug Discovery:** Machine learning and artificial intelligence can facilitate prediction of biological activity, optimization of ligand structures, and identification of potential drug candidates.
8. **Clinical Translation:** Future research should focus on preclinical and clinical evaluation of the most promising transition metal complexes to establish their potential as safe and effective pharmaceutical agents.

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14. CONFLICT OF INTEREST

The author declares that there is no conflict of interest regarding the publication of this research paper.

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