



Therapeutic And Anticorrosive Prospects Of Schiff Base Metal Complexes: A Comprehensive Review

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Abstract: Schiff base metal complexes have gained increasing attention due to their broad functional diversity and straightforward synthesis. Their capacity to coordinate with various transition metals imparts distinct biological and physicochemical characteristics. Within biomedical research, these complexes exhibit a spectrum of therapeutic activities such as antimicrobial, anticancer, antioxidant, anti-inflammatory, and antiviral properties indicating significant potential in medicinal chemistry and drug discovery. In industrial applications, Schiff base metal complexes act as efficient corrosion inhibitors for metals and alloys exposed to aggressive media. Their performance in this role is attributed to adsorption on the metal surface, protective-film formation, and strong electronic interactions between donor atoms and the metal substrate. This comprehensive review highlights the dual potential of Schiff base metal complexes in therapeutic applications and corrosion inhibition, emphasizing structure activity relationships, mechanistic insights, and recent advancements. Furthermore, challenges and future research directions are discussed to provide a foundation for the design of novel Schiff base complexes with enhanced biomedical efficacy and industrial utility.

Keywords:- Schiff base, Metal complexes, Therapeutic applications, Anticorrosive agents, Corrosion inhibition, Biomedical activity, Medicinal chemistry

1. Introduction

Schiff bases are condensation products of primary amines with carbonyl compounds, generally characterized by the azomethine ($-\text{CH}=\text{N}-$) group, which plays a crucial role in biological recognition processes [1-3]. Their coordination with transition metals enhances chemical stability and modulates biological and electrochemical behaviour [4]. Schiff bases serve as models for biological systems due to their resemblance to natural imine linkages [5-6].

Metal complexes derived from these ligands have found applications in medicinal chemistry, catalysis, polymer science, and corrosion inhibition [7-9]. Schiff base-metal complexes display excellent antibacterial, antifungal, and anticancer activity due to improved redox potential and electronic transfer properties [10, 11].

2. Biological Activities

2.1 Antibacterial Activities

Schiff base metal complexes have been widely explored for their potent antibacterial activity, mainly due to their ability to coordinate through azomethine nitrogen and phenolic oxygen atoms, enhancing lipophilicity and membrane permeability. Upon complexation, the polarity of the metal ion is reduced via partial sharing of its positive charge with donor atoms, leading to improved penetration through microbial cell membranes [12].

Raman *et al.*, have reported Cu(II), Ni(II), and Zn(II) complexes derived from 2-aminopyridine–salicylaldehyde systems that exhibited strong bactericidal effects against *Pseudomonas aeruginosa* and *Bacillus subtilis*. The Cu(II) complex showed the highest activity, attributed to its square-planar geometry promoting better DNA interaction [13]. Chaudhary *et al.*, synthesized the halogenated salicylaldehyde Schiff bases of Cd(II) and Zn(II) complexes that inhibited both Gram-positive and Gram-negative strains, possibly due to chelation-induced activation of the ligand [14]. Bhowmik *et al.*, synthesized mixed-ligand Schiff base complexes with Ni(II) and Cu(II), showing enhanced antibacterial properties through coordination-induced rigidity, which stabilizes the imine framework [15]. Nair & Thankachan *et al.*, have reported that vanadium Schiff base complexes derived from 3-aminopyridine possessed superior antibacterial activity against *Staphylococcus aureus* and *Klebsiella pneumoniae*, possibly through reactive oxygen species generation [16]. Kumar *et al.*, investigated that Ru(III) Schiff base complexes containing bidentate O,N-donors exhibited strong inhibition of bacterial growth by interfering with bacterial DNA replication and metabolic enzymes [17]. Gupta *et al.*, have reported that the antibacterial performance of Cu(II) and Ni(II) Schiff base complexes is governed by ligand planarity, conjugation and delocalization of π -electrons, enhancing their interaction with microbial membranes [18]. Ahamed *et al.*, evaluated Schiff base complexes of Zn(II) with heterocyclic ligands, noting that zinc enhances oxidative stress-based antibacterial pathways [19]. Al-Farhan *et al.*, demonstrated the synergistic effects of Schiff base ligands bearing pyridine or quinoline rings in Cu(II) and Ru(III) complexes against *E. coli*, suggesting that heteroaromatic moieties improve coordination strength and bioresponse [20]. Bharathi *et al.*, have prepared Co(II) and Ni(II) complexes from substituted salicylaldehydes and reported that Schiff base coordination modifies electronic density around the metal center, improving interaction with bacterial enzymes [21]. Jadhav & Mane *et al.*, synthesized 5-bromosalicylaldehyde-based Schiff base complexes with Cu(II), Ni(II), and Zn(II), exhibiting 80–90% inhibition against *Streptococcus* species [22]. Malik *et al.*, have reported that mixed Schiff base complexes containing 2-aminopyridine and 3-aminopyridine ligands show remarkable antibacterial activity due to their multiple coordination sites and high degree of conjugation [23]. Raza *et al.*, worked on molecular docking that Cu(II) complexes interact with bacterial DNA gyrase and DHFR enzymes [24].

2.2 Antifungal Activities

Schiff base ligands and their metal complexes have shown remarkable antifungal potential, often outperforming their parent ligands due to enhanced coordination-induced rigidity, and improved interaction with fungal cell membranes. Metal complexation increases electron delocalization and stabilizes the imine framework, which improves binding to microbial enzymes and DNA [25, 26].

Dharmaraj *et al.*, synthesized Ru(II) triphenylphosphine Schiff base complexes derived from salicylaldehyde and aniline derivatives, which exhibited significant antifungal activity against *Aspergillus flavus*. The activity was higher for ortho- and para-substituted ligands due to electronic effects on the azomethine group [27]. Gudasi *et al.*, have reported that N-(2-hydroxy-1-naphthylidene)-phenylglycine and its Cu(II), Ni(II) and Co(II) complexes showed superior antifungal activity compared to free ligands. The Cu(II) complex exhibited the highest activity against *Aspergillus niger* and *Fusarium oxysporum*, highlighting the role of the metal center in enhancing bioactivity [28]. Chandra *et al.*, have prepared Schiff base Cu(II) complexes of 3,3'-thiodipropionic acid bis(4-amino-5-ethylimino-2,3-dimethyl-1-phenyl-3-pyrazoline), demonstrating increased antifungal efficacy against *A. brassicae*, *A. niger*, and *F. oxysporum*, suggesting that π -electron delocalization in the ligand framework enhances cell penetration [29]. Zahid *et al.*, worked on Cu(II) complexes of Schiff bases derived from 2-aminobenzthiazole and 4-aminosalicylic

acid, and reported that benzthiazole derivatives were more effective against *Aspergillus niger* and *Candida corda*, emphasizing the importance of heterocyclic rings for antifungal activity [30]. Sherif *et al.*, have synthesized Cu(II) Schiff base complexes from 1,4-phenylenediamine derivatives and tested them against *Candida albicans* and *Stachybotrys chartarum*. The Cu(II) complexes showed stronger antifungal activity than the corresponding Co(II) and Ni(II) analogues [31]. Raman *et al.*, have reported Ni(II), Cu(II) and Zn(II) Schiff base complexes derived from 2-aminopyridine-salicylaldehyde, showing strong antifungal activity against *Candida albicans*, *Aspergillus fumigatus*, and *Fusarium solani*, with Cu(II) complexes being the most active [32]. Chaudhary *et al.*, worked on Cd(II) and Zn(II) Schiff base complexes with halogenated salicylaldehyde ligands that inhibited *Candida albicans* and *Aspergillus niger*, with higher efficacy than free ligands due to the formation of a stable chelate ring [33]. Kumar *et al.*, have prepared Ru(III) Schiff base complexes containing O,N-donor ligands that exhibited broad-spectrum antifungal activity, potentially due to interference with ergosterol biosynthesis and cell membrane disruption [34]. Bharathi *et al.*, showed that Co(II) and Ni(II) Schiff base complexes of substituted salicylaldehydes inhibited *Aspergillus niger* and *Candida albicans*, suggesting that metal coordination improves cell membrane interaction and intracellular target binding [35]. Raza *et al.*, have reported the Cu(II) Schiff base complexes bind to fungal enzymes, inhibiting growth, while the planar geometry of the complexes allows enhanced insertion into fungal DNA grooves, similar to antifungal drug mechanisms [36].

2.3 Anticancer Activities

The anticancer potential of Schiff base metal complexes arises from their DNA-binding, ROS-generation, and enzyme inhibition capabilities [37]. Gupta *et al.*, have reported the Cu(II) and Ni(II) complexes of salicylaldehyde-pyridine Schiff bases showed significant cytotoxicity against HeLa and MCF-7 cell lines [38]. Reddy *et al.*, synthesized Ru(III) and V(V) Schiff base complexes with remarkable selectivity toward tumor cells, attributed to ligand-assisted redox cycling [39]. Malik *et al.*, reviewed that halogen substitution (such as 5-Br in salicylaldehyde) enhances the lipophilic character and promotes better cell permeability, improving anticancer efficiency [40]. Basu *et al.*, have reported the Cd(II) complexes bind selectively to DNA minor grooves and suppress topoisomerase II activity, leading to apoptosis [41]. Raman *et al.*, investigated the cytotoxic activity with π - π stacking interactions and charge transfer between the azomethine nitrogen and the metal center [42].

2.4 Anti-Inflammatory Activities

Bharathi *et al.*, have reported the Co(II), Ni(II) and Cu(II) complexes of 2-aminopyridine Schiff bases and observed strong inhibition comparable to diclofenac [43]. Srivastava *et al.*, investigated that Zn(II) complexes stabilize lysosomal membranes and reduce protein denaturation, providing anti-inflammatory protection [44]. Patel *et al.*, synthesized Ru(III) and V(V) complexes that suppressed TNF- α and IL-6 cytokine expression in vitro [45]. Malik *et al.*, have reported the complexes of Cu(II), Ni(II) and Co(II) with Schiff bases derived from salicylaldehyde and 2-aminopyridine or 4-aminoantipyrine reduces the polarity of the metal ion through partial sharing of positive charge with donor nitrogen and oxygen atoms. This reduction enhances lipophilicity and bioavailability, thereby improving the anti-inflammatory response of the resulting complexes, such as $[\text{Cu}(\text{L})_2]$, $[\text{Ni}(\text{L})_2]$ and $[\text{Co}(\text{L})_2]$, where L represents the bidentate Schiff base ligand. Such results confirm the pharmacological versatility of Schiff bases as promising therapeutic scaffolds capable of coordinating biologically active metal ions [46].

2.5 Anticorrosive Activities

Corrosion inhibition by Schiff base ligands and their metal complexes has attracted considerable attention due to their ability to adsorb strongly on metal surfaces through azomethine nitrogen and phenolic oxygen donor atoms. These complexes form adherent protective films that suppress both anodic and cathodic corrosion reactions, often obeying Langmuir-type adsorption isotherms [47, 48].

Rehim *et al.*, investigated the Cu(II) and Ni(II) complexes of 4-aminoantipyrine (AAP) as corrosion inhibitors for mild steel in 2 M HCl, reporting strong adsorption and inhibition efficiency above 85%. The authors attributed inhibition to coordination through nitrogen donor sites and π -electron interactions of the azomethine group [49]. Sastri *et al.*, have reported the Schiff base complexes of transition metals such as Co(II), Ni(II) and Cu(II) follow Langmuir-type adsorption isotherms, forming protective surface films that

reduce metal dissolution [50]. Abd El-Rehim *et al.*, have prepared Cu(II) and Ni(II) Schiff base complexes that acted as mixed-type inhibitors for mild steel corrosion in HCl, reducing both anodic and cathodic currents. Their study confirmed that inhibition arises from electron donation by azomethine and phenolic sites, forming strong coordination layers [51]. Saha *et al.*, synthesized a Zn(II) complex of 2-aminopyridine–5-bromosalicylaldehyde Schiff base, achieving over 90% inhibition efficiency in H₂SO₄. Electrochemical impedance spectroscopy (EIS) and polarization data indicated a synergistic adsorption mechanism involving both physisorption and chemisorption [52]. Badr *et al.*, investigated Ru(III) and V(V) Schiff base complexes as green inhibitors for carbon steel in acidic medium. The complexes formed dense films through combined π -d back bonding and electrostatic adsorption, displaying excellent inhibition (>92%) [53]. Fouda *et al.*, worked on pyridine-based Schiff base complexes of Cu(II), Ni(II) and Co(II) which provide durable corrosion protection by donating delocalized π -electrons to the metal surface. This donation reduces the surface charge density, resulting in reduced metal dissolution and increased surface passivation [54]. Soni *et al.*, have reported Zn(II) and Cd(II) bis-Schiff base complexes that exhibited long-term corrosion resistance in saline and marine environments. The formation of a stable adherent layer was confirmed by SEM–EDS and EIS measurements, highlighting their potential for industrial coatings [55]. Patel *et al.*, investigated Fe(III) and Cr(III) complexes of 2-hydroxybenzaldehyde–p-toluidine Schiff bases, showing >90% inhibition efficiency in NaCl media. The Fe(III) complex was particularly effective due to its high charge density and stronger adsorption energy [56]. Khaled *et al.*, have studied Mn(II) and Co(II) Schiff base complexes derived from salicylidene aniline as inhibitors for mild steel in acidic medium. The Co(II) complex exhibited superior inhibition due to higher molecular planarity, facilitating π -d orbital overlap with the metal surface [57]. Yurt *et al.*, worked on Ni(II) and Cu(II) complexes of N,N'-bis(salicylidene)ethylenediamine (salen), which showed efficient corrosion inhibition in 1 M HCl. Surface characterization revealed a compact monolayer of adsorbed complex molecules that hindered hydrogen evolution [58]. Raja *et al.*, have synthesized Zn(II) and Fe(II) Schiff base complexes derived from vanillin exhibited high inhibition efficiency in H₂SO₄, consistent with mixed adsorption behavior. Quantum chemical analysis supported that inhibition correlates with HOMO energy and charge transfer ability [59]. El-Bagary *et al.*, have prepared Cu(II) and Ni(II) complexes of pyridine–salicylaldehyde Schiff bases and confirmed high surface coverage on steel substrates via AFM and XPS studies, indicating strong coordination bonds with surface Fe atoms [60].

3. Conclusion

Schiff base ligands and their metal complexes exhibit remarkable versatility, showing promising biological and anticorrosive properties. Their strong coordination ability through azomethine nitrogen and phenolic oxygen atoms leads to stable chelates with enhanced bioavailability, lipophilicity and surface adsorption characteristics. These properties contribute to their effective antibacterial, antifungal, anti-inflammatory, anticancer and corrosion inhibition activities. The chelation process reduces the metal ion's polarity, improving membrane permeability and adsorption efficiency. Schiff bases derived from heterocyclic aldehydes such as 5-bromosalicylaldehyde and 2-aminopyridine have shown particularly high potential. Despite substantial progress, further research is needed to explore the structure–activity relationship and optimize biological performance. Overall, Schiff base complexes continue to serve as valuable frameworks for the development of new therapeutic and industrial materials.

4. Acknowledgement

The authors are thankful to Principal, Sadhu Vaswani (Autonomous) College, Sant Hirdaram Nagar (Bairagarh), Bhopal for providing necessary facilities for research work and DST for granting FIST program to the Department and College.

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