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RESEARCH ARTICLE

Cu(II) Metal Complexes of Pyridyl-based Schiff Bases and Their Biological Importance: A Review Study

Anjul Dadoria, Suman Malik, Archana Singh*, Supriya Das

Department of Chemistry, Sadhu Vaswani Autonomous College, Sant Hirdaram Nagar (Bairagarh), Bhopal, Madhya Pradesh, India

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ABSTRACT

Schiff base plays a key role in the evolution of coordination chemistry as they form stable coordination compounds with most of the transition metal ions. Some important transition metals such as Co, Mn, Ni, Zn, and Cu have a significant role in the synthesis of the Schiff base metal complex. The synthesis of Schiff base transition metal Cu(II) complexes using Schiff base as ligands is studied keeping in view the possibility of obtaining coordination compounds of new structure with more stability. They also show excellent biological activities such as anti-inflammatory, analgesic, antibiotic, antioxidative, antifungal, antibacterial, antiviral, and enzymatic activities. The ligand and metal complexes are characterized by elemental analyses, molar conductivity, magnetic moment, FT-IR, UV-Vis, Mass, and ^{1}H-NMR spectrometry as well as thermal analyses. This review paper summarizes to know about the chemistry of different derivatives of substituted Schiff bases and their Cu(II) complexes with their biological importance.

Keywords: Biological activity, Coordination chemistry, Metal complexes, Schiff bases

INTRODUCTION

Schiff bases are a class of organic compounds characterized by the presence of azomethine (-CH=N-) linkage. Due to the lone pair of the sp^2 nitrogen in the azomethine group, Schiff bases have the potential in coordination chemistry as ligands with high-design flexibility and high functionality.[1] They play a vital role in various scientific fields such as biology, medicine, inorganic chemistry, organic, and analytical chemistry. Many Schiff bases and their metal complexes are well known to possess catalytic properties,[2] antibacterial, antifungal, antituberculosis, antihelminthic, anticancer, and antioxidant activities.[3-6] Transition metal complexes which usually contain nitrogen, sulfur, or oxygen as ligand atoms have become increasingly important because these Schiff bases can bind with different metal centers involving various coordination sites and allow successful synthesis of metal complexes.[7] The high affinity for the chelation of the Schiff bases toward oxygen as ligand atoms has become increasingly important because these Schiff bases can bind with different metal centers involving various coordination sites and allow the successful synthesis of metal complexes.[7] The high affinity for the chelation of the Schiff bases toward the transition metal ions is utilized in preparing their solid complexes.[8] Among transition metals, copper has its own unique identification due to its coordinating ability with various ligands to form a variety of geometrical structures such as square planar, square pyramidal, distorted square pyramidal, and octahedral. The copper (II) complexes have also been investigated

***Corresponding Author:**
Archana Singh
E-mail: drsingharchana@rediffmail.com

against a variety of bacterial, fungal, as well as viral strains and showed profound activities against various diseases.[9-11]

PYRIDYL-BASED SCHIFF BASES

Pyridyl is a heterocyclic organic moiety with the chemical formula C_5H_4N. Pyridyl is derived from pyridine by the removal of a hydrogen atom from a ring carbon atom. The physical properties of pyridyl in several important compounds led to a special interest in the study of these compounds in a number of directions. Pyridyl is a colorless liquid and smells like pyridine. In recent years, pyridyl and their derivatives have gained a lot of prominence due to their various biological activities such as antimicrobial, anticancer, anticonvulsant, antitumor, antiHIV-1 activity, antibacterial, and antifungal activity.[12,13]

BIOLOGICAL IMPORTANCE OF COPPER AND COPPER COMPLEXES

Copper is the third most abundant essential trace mineral in the body, after iron and zinc. Copper has been recognized as an essential nutrient since the 1920s.[14] In the past 70 years, much has been learned about the important biological role of copper and copper-dependent enzymes.[15] Copper is a first-row transition metal which is a member of group 11 of the periodic table. Copper(II) metal complexes with various Schiff base ligands possess anti-inflammatory activity, and many popular anti-inflammatory drugs are their copper chelates. Interest in copper complexes as an anti-inflammatory and anti-arthritic drug is evidenced by the large number of reviews and symposia proceedings published in recent years.[16] This review aims at having an insight into the application of Cu(II) complexes of pyridyl-based Schiff bases as antimicrobial agents. The summary of the reported work on the biological activity of Cu(II) complexes with Schiff bases has been briefly discussed.

Ramadan *et al.* reported preparation and characterization of Cu(II) complexes of three tridentate pyridyl hydrazones. The ligands of Schiff base were prepared by condensation of 6-chloro-2-hydrazopyridine with alpha-formyl(L1), alpha-acetyl(L2), or alpha-benzoyl(L3) pyridine. The structural characterization of the compounds prepared was based on elemental analyses, electrical conductance data, magnetic moment measurements, ^{1}H NMR, IR, UV-Visible and ESR spectroscopic methods. The copper(II) complexes have been assigned a monomeric square-planar and a dimeric structure with a chloride bridge in square-pyramidal geometry. In the presence of molecular oxygen, Cu(II) complexes catalyse the oxidative transformation of catechol (benzene-1,2-diol) to the corresponding o-benzoquinone.[17] Raman *et al.* have reported the synthesis of novel N_2O_2 type Schiff base metal complexes of Cu(II) from a new Schiff base ligand derived from 4-aminoantipyrine, salicylaldehyde, and 2-amino-3-hydroxypyridine. The ligand and its complexes have been characterized on the basis of elemental analyses, magnetic susceptibility, FAB mass spectrometry, UV-Vis, IR, ^{1}H-NMR, ESR, and CV spectral studies as well as conductivity data. On the basis of spectral studies, a square-planar geometry for the complexes has been proposed. The *in vitro* antimicrobial activity of the investigated compounds was tested against bacteria such as *Staphylococcus aureus, Escherichia coli,* and *Klebsiella pneumoniae* and fungi such as *Candida albicans* and *Rhizopus stolonifer.*[18] Gupta *et al.* worked on the transition metal complex of Cu(II) with a bidentate ligand bis(2-pyridinecarboxaldehyde) ethylenediamine prepared by the condensation of 2-pyridylcarboxylaldehyde and ethylenediamine. The metal complex has been characterized on the basis of elemental analysis, conductance and magnetic data, infrared, ^{1}HNMR data. From elemental analysis, the complexes have been found to possess 1:2 (metal: ligand) ratio. Octahedral geometry for metal(II) complexes has been proposed. The ligand and metal complexes were screened for their physiological activities against *E. coli, Staphylococcus aureus*, *Bacillus subtilis,* and *Salmonella typhi*.[19] Mishra *et al.* synthesized coordination complexes of Cu(II) with the Schiff bases derived from isatin, 3-chloro-4-floroaniline, and 2-pyridinecarboxaldehyde with 4-aminoantipyrine synthesized by conventional as well as microwave methods. These compounds

have been characterized by elemental analysis, molar conductance, electronic spectra, FT-IR, FAB mass, and magnetic susceptibility measurements. FAB mass data show degradation of complexes. The Schiff base and metal complexes show good activity against the bacteria *Staphylococcus aureus, Escherichia coli,* and *Streptococcus faecalis* and fungi *Aspergillus niger, Trichoderma polysporum, Candida albicans,* and *Aspergillus flavus*.[20] Shamkhy *et al.* reported novel tridentate Schiff base prepared from the condensation of phenyl(pyridin-4-yl)methanone, and the Schiff base was then reacted with transition metal salts of Cu(II) to form coordinated complexes. The novel Schiff base benzyl-2- [phenyl(pyridin-4-yl)methylidene] hydrazinecarbodithioate and the new metal complexes were characterized through various physicochemical and spectroscopic techniques. The FTIR results show that the Schiff base exists in thione form because it contains functional group –NH(C=S)SR, while the metal complexes contain two ligands. Based on the ultraviolet-visible analyses, it shows that the Schiff base shows absorption for n-π * and π-π * while the metal complexes have absorption due to d-d transitions. The result of the magnetic susceptibility measurement indicates the octahedral geometry for $Cu(L_4)_2$.[21] Florencia *et al.* reported that the three novel mononuclear Cu(II) complexes with dipicolinate and pyridyl-based ligands have been isolated and characterized. X-ray diffraction studies accounted for slightly distorted square-pyramidal structures. Their structural and electronic properties have been studied by DFT methods. Electronic UV–Vis spectra were simulated for both dinuclear complexes in the framework of the TD-DFT methodology to assign the origin of the absorption bands. All the complexes were screened for antifungal and antibacterial activity.[22] Jana *et al.* have synthesized mononuclear Cu(II) complex [Cu(L)Cl from a tridentate Schiff base ligand, piperidin-2-ylmethyl-pyridin-2-ylmethylene-amine(L). The single-crystal X-ray complex structure shows a square-pyramidal geometry. The complex was tested against several bacteria and showed good antibacterial activities against almost all of the bacteria.[23] Abdullahi *et al.* have synthesized some aminopyridine- and (aminomethyl)pyridine–salicylaldimine copper(II) complexes. The ligands were prepared by condensing salicylaldehyde and o-vanillin with 2- and 3-amino- and (aminomethyl)pyridine, respectively. The complexes were characterized by micro-analytical, electronic, infrared, and conductivity data. The structures of the Schiff base ligands were further confirmed from ^{1}H- and ^{13}C-NMR spectral data. All the ligands and their Cu(II) complexes were screened for their antimicrobial activity against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli,* and *Candida albicans*.[24] Yuliia *et al*. reported the preparation and characterization of novel copper(II) complexes of 3-(2-pyridyl)-1,2,4-triazole. Magnetic properties reflect Cu-Cu antiferromagnetic interaction. Complexes were characterized by elemental analysis, mass-spectrometry, IR- spectroscopy, and X-ray analysis. Magnetic measurements revealed that both compounds exhibit antiferromagnetic interaction.[25]

CONCLUSION

From the above review, it is clear that pyridyl-based Schiff bases and their Cu(II) complexes possesses a number of biological applications. These complexes have bright future in pharmaceutical as well as chemical science. Metal complexes of Cu(II) were easy to produce, economically viable, and had numerous applications owing to their high catalytic activities, antibacterial, antifungal properties, antitumor, and good biological activities. Review reflects the contribution of Schiff bases to the design and development of novel lead having potential biological activities with special reference to Cu(II) metal complexes of pyridyl-based Schiff bases.

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REFERENCES

1. Tyagi P, Chandra S, Saraswat BS, Yadav D. Design, spectral characterization, thermal, DFT studies and anticancer cell line activities of Co(II), Ni(II) and Cu(II) complexes of Schiff bases derived from 4-amino-5-(pyridin-4-yl)-4H-1,2,4-triazole-3-thiol. Spectrochim Acta A Mol Biomol Spectrosc 2015;145:155.
2. Jacobsen EN, Kakiuchi F, Konsler RG, Larrow JF, Tokunaga M. Enantioselective catalytic ring opening of epoxides with carboxylic acids. Tetrahedron Lett 1997;38:773-6.
3. Bekhradnia A, Forouzani M, Shahamat Z. Synthesis of a novel fluorescent schiff base as a possible Hg and Ag ions selective sensor. Res Pharm Sci 2012;7:5.
4. Martins CV, da Silva DL, Neres AT, Magalhaes TF, Watanabe GA, Modolo LV, *et al.* Curcumin as a promising antifungal of clinical interest. J Antimicrob Chemother 2009;63:337-9.
5. Husain MI, Shukla MA, Agarwal SK. Search for potent anthelmintics. Part VII. Hydrazones derived from 4-substituted 7-coumarinyloxyacetic acid hydrazides. J Ind Chem Soc 1979;56:306-7.
6. Shaker N, Fatma H, El-Salam A, El-Sadek BM, Kandeel EM, Baker SA. Anionic schiff base amphiphiles: Synthesis, surface, biocidal and antitumor activities. J Am Sci 2011;7:427-36.
7. Alexander V. Design and synthesis of macrocyclic ligands and their complexes of lanthanides and actinides. Chem Rev 1995;95:273-342.
8. Quiruga AG, Ranninger CN. Review contribution to the SAR field of metallated and coordination complexes: Studies of the palladium and platinum derivatives with selected thiosemicarbazones as antitumoral drugs. Coord Chem Rev 2004;248:119-33.
9. Gao EQ, Liao DZ, Jiang ZH, Yan SP. Synthesis, crystal structure and magnetic properties of novel copper(II)–nickel(II) complexes of macrocyclic oxamides. Polyhedron 2001;20:923-57.
10. O'Brien P, Stafford C, Young LC. Isomerism of mixed ligand copper(II) complexes containing 1,10-phenanthroline and oxalate. J Inorg Chim Acta 1988;147:3-4.
11. O'Brien P. Isomers of α-amino acids with copper(II). Part VI. Novel equilibria at high pH in copper(II):Amino-acid solutions. Trans Met Chem 1980;5:314-5.
12. Morrison and Boyd. Organic Chemistry. 6th ed., Vol. 9741. Hoboken: Prentice Hall; 2004. p. 997-820.
13. Chohan ZH, Pervez H, Rauf A, Khan KM, Supuran CT. Antibacterial cobalt (II), copper (II), nickel (II) and zinc (II) complexes of mercaptothiadiazole--derived furanyl, thienyl, pyrrolyl, salicylyl and pyridinyl Schiff bases. J Enzyme Inhib Med Chem 2006;21:193-201.
14. Hart EB, Steenbock H, Waddell J, Elvehjem CA. Iron in Nutrition. VII. Copper as a supplement to iron for hemoglobin building in the rat. J Biol Chem 1978;77:797-812.
15. Sorenson JR. Characterization of a mononuclear copper carboxylate complex: bis(acetylsalicylato) bis(pyridine) copper(II). Med Biol 1985;63:40-3.
16. Sorenson JR. Copper complexes offer a physiological approach to treatment of chronic diseases. Prog Med Chem 1989;26:437-568.
17. Ramadan AE, El-Mehasseb IM. Synthesis, characterization and biomimetic oxygenations of manganese(II), iron(III) and copper(II) pyridyl hydrazone complexes. Transit Met Chem 1998;23:183-9.
18. Raman N, Johnson Raja S, Joseph J, Dhaveethu Raja J. Synthesis, spectral characterization and DNA cleavage study of heterocyclic schiff base metal complexes. J Chil Chem Soc 2007;52:1138-41.
19. Gupta YK, Agarwal SC, Madnawat SP, Narain R. Synthesis, characterization and antimicrobial studies of some transition metal complexes of schiff bases. Res J Chem Sci 2012;2:68-71.
20. Mishra AP, Mishra R, Jain R, Gupta S. Synthesis of new VO(II), Co(II), Ni(II) and Cu(II) complexes with isatin-3-chloro-4-floroaniline and 2-pyridinecarboxylidene-4-aminoantipyrine and their antimicrobial studies. Mycobiology 2012;40:20-6.
21. Shamkhy ET. Preparation and characterization of new schiff base derived from pyridine and its metal complexes. Int J Curr Res Chem Pharm Sci 2016;3:118-23.
22. Luzardo F, Álvarez N, Kremer C, de Camargo AS, Gancheff JS. New complexes of Cu(II) with dipicolinate and pyridyl-based ligands: An experimental and DFT approach. Spectrochim Acta A Mol Biomol Spectrosc 2017;183:45-52.
23. Jana K, Maity T, Mahapatra TS, Das Mohapatra PK, Debnath SC, Das S, *et al*. A square pyramidal copper(II) complex of a schiff base ligand: Synthesis, crystal structure, antibacterial and DNA interaction studies. Transit Met Chem 2017;42:69-78.
24. Sobola Abdullahi O, Watkins Gareth M, van Brecht B. Synthesis, characterization and biological study of Cu(II) complexes of aminopyridine and (aminomethyl)pyridine Schiff bases. J Serbian Chem Soc 2018;83:809-19.
25. Petrenko YP, Khomenko DM, Doroshchuk RO, Shova S, Novitchi G, Piasta K, *et al*. Synthesis, crystal structure and magnetic properties of new copper(II) complexes based on 3-(2-pyridyl)-1,2,4-triazole. Inorganica Chim Acta 2020;500:119216.