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Therapeutic Activities of Some Transition Metal Complexes of Schiff Bases Derived from Aminopyridines: A Review

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Abstract: *Schiff base ligands are taken into consideration as an important class of ligands in coordination chemistry, as they are simply synthesized by using condensation of amine with carbonyl compounds. The chelating property of Schiff bases plays a significant role in their therapeutic activities and this could be helpful in the development of different compounds with good biological activities. Aminopyridines are an important class of heterocyclic compounds which have been significantly studied within the last decades due to their interesting therapeutic activities. They exist in isomeric forms: 2-aminopyridine, 3-aminopyridine and 4-aminopyridine. The range of their therapeutic activities has attracted the attention of many researchers. Six membered heterocyclic compounds in arrangement with aromatic moieties played an important role in designing a new class of Schiff base ligands which shows widespread biological behaviour. Present paper summarizes various therapeutic applications of some transition metal complexes of Schiff bases derived from Aminopyridines.*

Keywords: Aminopyridine, Therapeutic, Schiff Bases, Transition Metal, Ligands, Coordination.

I. INTRODUCTION

Schiff bases are the organic compounds carrying imine or azomethine (–C=N–) functional group. Schiff bases are versatile ligands synthesized from the condensation products of primary amines with carbonyl compounds and were first reported by Hugo Schiff in 1864 [1].Schiff base ligands have been extensively studied in the field of coordination chemistry mainly because of their facile synthesis, easy availability, and electronic properties [2]. In recent years, Schiff base coordination chemistry has attracted because of their significance in organic synthesis [3]. The use of Schiff base metal complex in medical field occupied an optimistic role in the field of pharmaceutical research. In this review paper, we are discussing the on-going aspects of therapeutic activities of metal complex [4, 5].

II. AMINOPYRIDINE

Aminopyridine is an organic compound that contains an amino group and an aromatic heterocyclic pyridine. It has the molecular formula, $C_5H_6N_2$ and three isomers: 2-aminopyridine, 3-aminopyridine and 4-aminopyridine [6]. Several derivatives of aminopyridine are used as precursors in the pharmaceutical industries for the preparation of antibacterial and antiviral drugs, herbicides and dyes [7].

III. THERAPEUTIC ACTIVITIES OF TRANSITION METAL COMPLEXES

This review's aim is to have an insight on the therapeutic activities of some transition metal complexes. The summary of the reported work on biological activity of transition metal complexes with Schiff bases has been briefly discussed.

3.1 Anti-bacterial activity

Dhaveethu*et al.,* prepared and characterized a new metal complex of Cr(III), Ni(II) and Cu(II) with 3-aminopyridine and nitrite ions by microwave irradiation technique. The Schiff base ligands were characterized by elemental analyses,

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molar conductance, IR, Far-IR, electronic and EPR studies. On the basis of characterization data, indicated adistorted octahedral geometry for Cr(III) and Cu(II) complexes; distorted tetrahedral geometry for Ni(II) complex. The antibacterial results show that the metal complex shows excellent and moderate activity against *R. planticola, S. flexineri*and *P. aeruginosa*[8].

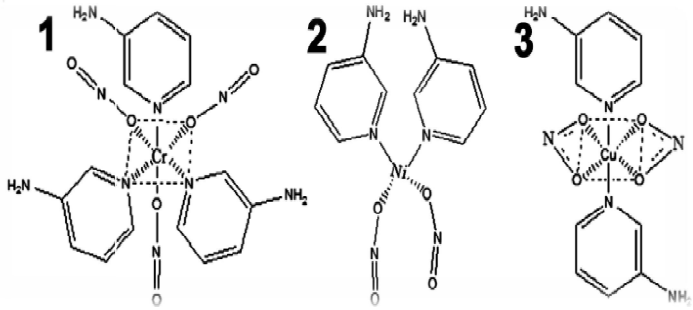

Figure 1: Structures of the complexes

Hossain*et al.,* worked on metal complexes of Mn(II), Fe(II), Co(II) and Cd(II) ions with Schiff base ligand 4-{(pyridin-2-ylimino)methyl}phenol derived from condensation of 2-amino pyridine with 4- hydroxybenzaldehyde. The ligand and complexes characterized by conductivity, magnetic moment, TLC, IR, UV-Visible, thermal analysis and some physical measurements. The metal complexes were screened for their antibacterial activity against pathogenic bacterial strains, *Escherichia coli, Pseudomonas aeruginosa* and *Acetobacteraceti*[9].

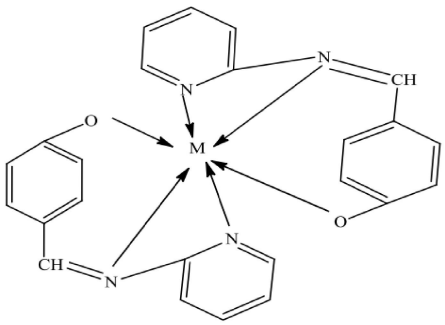

Figure 2: Structure of metal complexes. Where M= Mn(II), Fe(II), Co(II) and Cd(II) and X= Cl^- , SO_4^{-2} ions.

Fakeh*et al.,* prepared a new metal complexof the general formula, $[M(DPPP)(APY)(H_2O)\ Cl_2].xH_2O$, where M = Ni(II), Cu(II),Mn(II), and Fe(II) and x = 0, 1, or 2 molecules of H_2O, DPPP =1,3-bis(diphenylphosphino)propane, and APY= 2-aminopyridine. The complexes were characterized by several techniques using FT-IR, molar conductance, elemental analysis, and UV is spectral data.The ligand and metal complexes were screened for their Anti-bacterial activity againstthree strains of gram-positive *cocci* (*Staphylococcus epidermidis, Enterococcus faecalis, and Staphylococcus aureus),* two strains of gram-negative *(Pseudomonas aeruginosa* and *Escherichia coli)*[10].

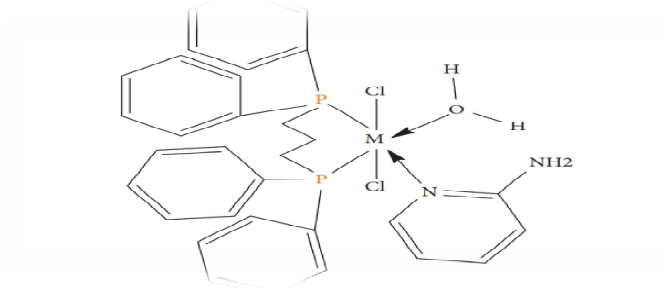

Figure 2: Structure of complexes $[M(DPPP)(APY)(H_2O)\ Cl_2].xH_2O$, where M=Ni(II), Cu(II), Mn(II) or Fe(II) and x= 0, 1, or 2 molecules of H_2O

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3.2 Anti-Fungal Activity

Sani*et al.,* have synthesized transition metal Ni(II) with Schiff bases derived from 2-aminopyridine and 2-methoxybenzaldehyde. The Schiff base is pale yellow, while nickel complexes are light green respectively. The complexes were characterized by solubility test, melting and decomposition temperature determination, FTIR, magnetic susceptibility, molar conductance gravimetric analysis and UV spectroscopy. The antifungal activity study revealed that the Schiff base and its complexes are active against *Candida albicans* at all concentrations [11].

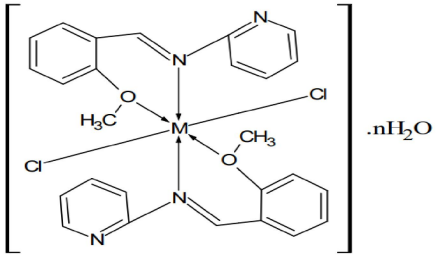

Figure 4: Structure of the Complexes

3.3 Anti-Cancer Activity

John *et al.,* have been synthesized novel Co/Ni/Cu/Zn(II) Schiff base complexes with furfural-MAP derived from furfural and 6-methyl-2-aminopyridine. The complexes were characterized by UV–Vis, IR, mass, ^{1}H NMR, elemental analyses, molar conductance, magnetic, and EPR. *In vitro* anticancer activity of [Cu(II)-(furfural-MAP)$_2$Cl$_2$] has been studied against human ovarian cancer cells, which exhibit promising anticancer activity. Furthermore, cytotoxicity of [Cu(II)-(furfural-MAP)$_2$Cl$_2$] has been analyzed against L929 cells [12].

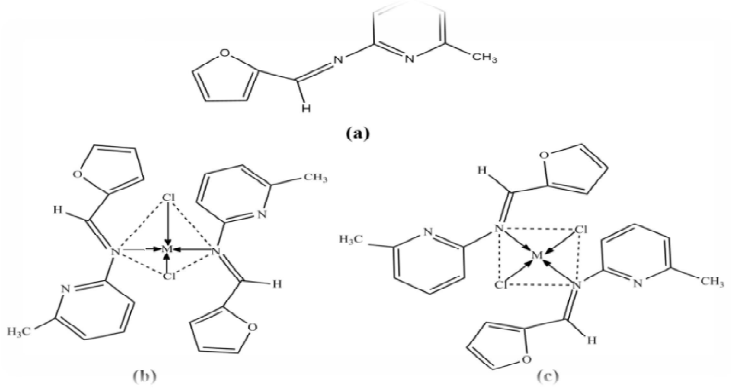

Figure 5: The structures of (a) furfural-MAP, (b) Co(II) and Zn(II) complexes, and (c) Cu(II) and Ni(II) complexes

3.4 Antioxidant Activity

Jafari*et al.,* worked on metal complexes of Co(II), Cu(II), Ni(II), and Zn(II) with Schiff base derived from 2-aminopyridine were synthesized. Molecular structures of complexes were determined by single X-ray diffraction method. The structure and electronic properties of the complexes were analyzed using DFT calculations. All four complexes were studied with respect to their antioxidant activities [13].

Dailami*et al.,* have reported tridentate ligand N–(2–hydroxybenzylidene)pyridine–2–amine by condensation of salicylaldehyde and 2–aminopyridine in absolute ethanol. M(II) complexes (M= Mn and Ni) of the ligand were also prepared. Characterization of the prepared compounds by FTIR spectroscopy, solubility test, melting point, conductivity and magnetic susceptibility measurements. Job's method.The analytical data shows that the metal to ligand ratio is 1:2. Antioxidant activity of the compounds was tested using 2,2'-diphenyl-1-picrylhydrazyl (DPPH) radicals scavenging method. The lower IC50 value (2.27 µg/ml) obtained in the ligand, by probit analysis using SPSS 16.0, indicates its high antioxidant property [14].

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3.5 Antimicrobial Activity

Lovely *et al.,* have synthesized transition metalCu(II), Ni(II), and Co(II) with Schiff bases derived from 4-pyridine carboxaldehyde and 3-amino pyridine complexes .The Schiff base ligand were characterized by elemental analysis, magnetic susceptibility, conductivity measurements, FT-IR, electronic, spectral measurements, XRD studies antimicrobial and nuclease activity studies. The conductance measurements indicate that all the complexes are non-electrolytes. The IR spectra indicate the coordination of pyridine nitrogen and M-N bonds. The powder XRD analysis indicates that the complex is nanocrystalline[15].

Jisha*et al.,* worked on Schiff base ligand, derived from furan 3- carboxaldehyde and 3- amino pyridine and the Ni(II), Cu(II), and Co(II) complexes. The ligand and complexes were characterized by elemental analysis, molar conductance, magnetic moment, ^{1}H NMR, IR, UV-Vis and SEM. The analytical data shows that the metal to ligand ratio is 1:2. Antimicrobial studies indicated that the complexes exhibit more activity than the ligand [16].

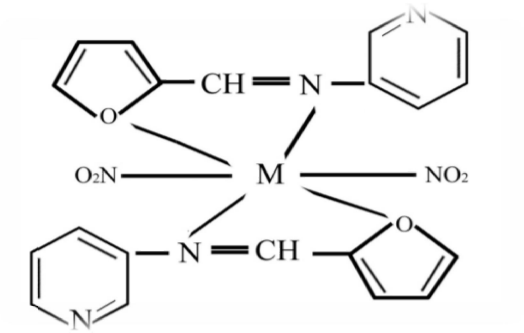

Figure 6: Structure of metal complexes with Ligand L (M=Cu, Co, Ni)

Hossain*et al.,* reported a new Schiff base is derived from salicylaldehyde and 2-aminopyridinewith the metal ionsNi(II), Cu(II), Co and Cd (II). The complexes were characterized by molar conductivity, magnetic susceptibility, elemental analysis, IR, ESR. The elemental analysis data shows the formation of 1:2 [M:2L] complex. The complexes have been tested for their antimicrobial activities against four human pathogenic (two gram-positive and two gramnegative) bacteria. The obtained results showed that only Cu(II) complex exhibited strong activity toward human pathogenic gram positive and gram negative bacteria whereas the Ni(II), Co(II) and Cd(II) complexes showed week to moderate antimicrobial activity compared with standard Kanamycin and Ampicillin [17].

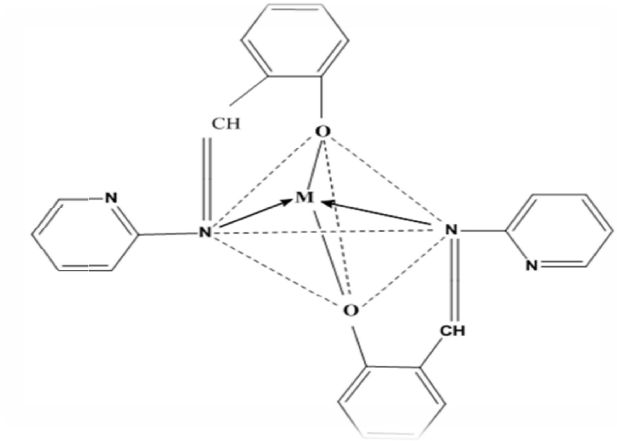

Figure 7: Tetrahedral structure of the complexes

IV. CONCLUSION

Schiff base derived from aminopyridine are explored versatile therapeutic activity in the research field. This review will create new ideas in the field of medicine which helps to produce more new drugs which are specific in action. It

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has been used as an anticancer, antimicrobial, antiviral, antifungal andantioxidantagent in medicine. These moieties have been attributed to a wide spectrum of biological activities in medicine and the environment.

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