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Research Paper

Biological Applications of Schiff Base Metal Complexes-A Review

Sandeep R Deshmukh[1], Suresh B Rewatkar[2], Vaishali W. Salve[3]

[1]*Assistant Professor , Rashtrapita Mahatma Gandhi Arts, Commerce & Science College, Saoli, Dist-Chandrapur (Maharshtra), India-441225*

[2]*Dean, Faculty of Science & Technology, Gondwana University, Gadchiroli (Maharashtra) India-442605*

[3]*Research Scholar, Institute of Science, Nagpur (Maharashtra) India-440012*

Abstract:

Schiff bases are synthesized from the condensation of aromatic/ aliphatic primary amines and aromatic/ aliphatic aldehydes and they have good chelating abilities with transition metals, lanthanides and actinides. Metal complexes derived from Schiff bases have attracted the attention of many researchers in recent years due to their wide range of biological applications. The presence of the azomethine group in Schiff bases, as well as its capability to coordinate to various metal ions, is crucial for their biological applications. The Schiff bases derived from various aromatic aldehydes and aromatic primary amines and their complexes with transition metals, lanthanides and actinides were studied and their biological applications were summarized from various reputed journals and discussed in this article.

Keywords: Schiff base, Metal Complexes, Biological applications.

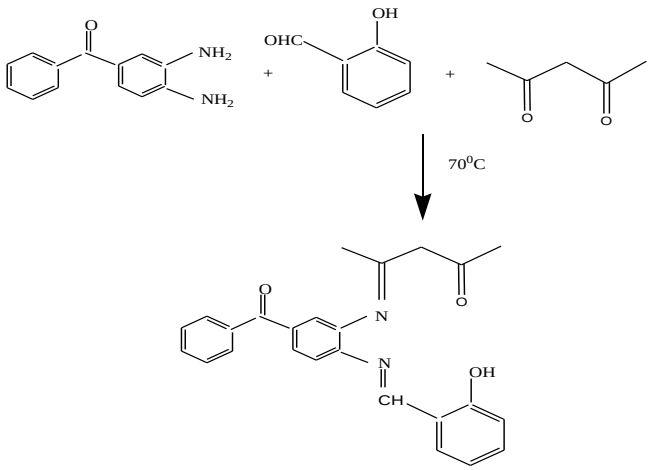
INTRODUCTION

Many Schiff base ligands were produced by researchers all around the world after the Italian chemist Hugo Schiff discovered them in 1864. The Schiff base ligands are obtained by combining the primary amine and carbonyl compounds in a condensation process. A (-C=N-) linkage, also known as an azomethine or imine linkage, is present in the ligand [1]. Schiff bases ligands and their metal complexes have been studied by many researchers as they show a wide range of applications in the field of medicine, catalysis and polymer industry. The Schiff bases and their complexes has been discussed extensively in recent years due to the fact that they are the most versatile compounds in the field of coordination chemistry and have a wide range of biological applications, such as antifungal, antibacterial, antiviral, antitumor, anti-HIV, anti-inflammatory, and antipyretic agents and antioxidant activities[2-3]. Also many metal complexes of Schiff base ligands shows catalytic properties in various reactions in moist condition [4].

This review article summarizes various biological applications of Schiff bases and their transition and inner transition metal complexes.

Biological Applications of Schiff Base and Their Metal Complexes

Co (II), Nickel (II) and Cu (II) complexes of Schiff base derived from condensation of acetyl acetone and salicylaldehyde with 3, 4-diamino benzophenone by refluxing for 2.3 hrs in hot ethanol at 70^0C **Scheme-1**. The antimicrobial activity of the synthesized metal complexes were screened for gram positive and gram negative bacterial species and it was found that metal complexes shows better antimicrobial activity. [5].



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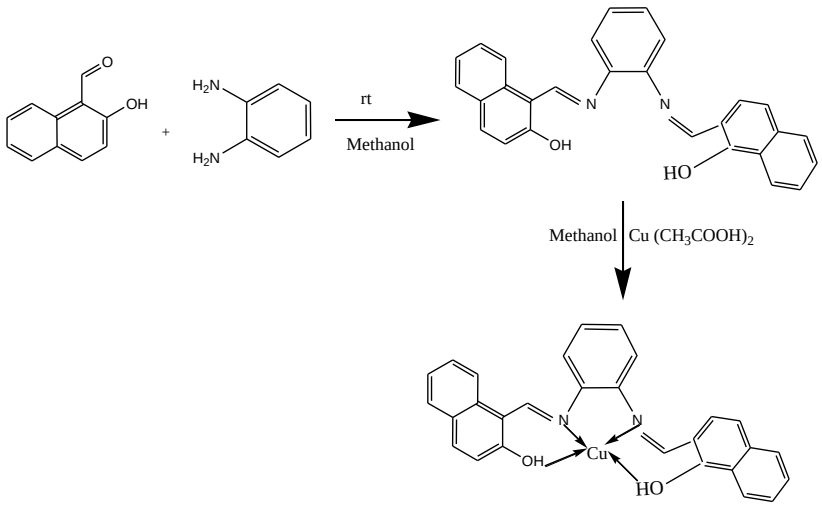
Scheme-1 Schiff base derived from acetyl acetone salicylaldehyde and 3,4-diaminobenzophenone

Hossein Naeimi and colleagues were reported new Schiff base ligand derived by constant stirring the 2-hydroxy-1-naphthaldehyde with 1,2-phenelyne diamine in methanol solvent. The structure of the synthesized ligand was confirmed by various spectroscopic methods and physicochemical studies.

Cu (II) complex of the ligand were synthesized by dissolving ligand and $Cu(CH_3COOH)_2$ in methanol and was stirred at 50^0 C. the synthesized complex were characterized by using different spectroscopic techniques and physical data.Antimicrobial activity for various gram positive and gram negative bacterial strains using micro dilution broth technique and it was investigated from this study that this complex inhibits growth of microbial species. The structure of the synthesized ligand and their metal complex is shown in Sheme-**2** [6].



Scheme-2 Structure of Schiff base ligand and their Cu (II) metal complex

Schiff base ligands prepared by the condensation of 2-hydrazinopyridine with 2-pyridinecarbaldehyde in ethanol and reflux for about 30 min. after synthesis this ligand were characterized using various physicochemical methods and spectroscopic techniques. To this ligand $Ln(NO_3)_2 .6H_2O$ salts (Ln= Nd, Sm) were mixed with sodium acetate and this mixture were stirred in ethanol for 30 min. yellow solids were obtained which were collected and recrystalized using ethanol solvent. The antioxidant activity of the synthesized complexes was done for DPPH and shows the very good antioxidant activity and this activity increases with increasing the concentration of the complexes [7]. Kavitha Andiappan et al.reported a new Schiff base N^2, N^3-bis (anthracen-9-ylmethylene) pyridine-2, 3-diamine, ligand by the condensation reaction between 2, 6-diaminopyridine and anthracene-9-carbaldehyde in 1:2 molar ratio. Spectroscopic measurements confirmed the structure of the synthesized compound. New lanthanide complexes of (Pr, Er and Yb) were synthesized and functional groups of the synthesized complexes were confirmed using UV-visible, FT-IR and fluorescence spectroscopic techniques. Schiff base ligand acted as a bidentate ligand and was structured with metal ions by the two azomethine nitrogens, according to FT-IR spectrum investigations. The cytotoxicity activity of the produced Schiff base- metal complexes was tested against Vero, human breast cancer (MCF7), and cervical (HeLa) anticancer cell lines. In Vero, MCF7, and HeLa cells, Praseodymium-Schiff base complex and Erbium-Schiff base complex effectively triggered apoptosis in a dose-dependent manner. When compared to the

complex of Erbium, the Praseodymium tested Vero cells showed superior biocompatibility [8]. From 3-ethoxy salicylaldehyde and 2-amino benzoic acid, a novel ligand of Schiff base, 3-ethoxy salicylidene amino benzoic acid (ETSAN), has been produced. Ni(II), Co(II), Cu(II), and Zn(II) nitrate/chloride salts were used to make metal complexes of the Schiff base. The confirmation of the newly synthesized ligands and their complexes were done using various spectroscopic techniques.from these investigation it is found that this ligand is tridentate ligand. The antimicrobial studies shows that metal complexes shows comparable activity against tested gram positive and gram negative bacterial strains [9]. Isatin when condensed with aromatic aldehydes gives Schiff base ligands and from studies it was found that these ligands shows better analgesic properties compared to the standard drugs [10]. Many complexes of Copper and Zinc were synthesized from Schiff bases which are prepared by the condensation reaction of benzaldehyde and thiourea as a primary ligand and acetamide as an extra ligand. These complexes were confirmed by IR, NMR and UV-visible spectroscopic methods. The complexes enhanced absorption hypochromicity. The antibacterial activity of the complexes containing the free ligand is higher [11]. In ethanol, sulphadizine and 2-carboxybenzaldehyde produce a novel Schiff base ligand. Cu (II), Co (II), Zn (II), Ni (II), Mn (II), and Fe (II) chloride salts react with this ligand to form transition metal (II) complexes. The produced compounds were characterized using elemental analysis, NMR, and IR spectroscopy methods and when tested for several bacterial strains, these compounds exhibit excellent activity.[12]. New Schiff base with quinoline moiety were synthesized and from them Coppert(II) and Zinc (II) were prepared [13]. 2-aminopyrazine and salicylaldehyde in ethanol produced Schiff base ligands and forms complexes with transition metal salts which were confirmed by various spectral techniques and to evaluate the binding capabilities of the novel drugs, molecular docking experiments were conducted against three protein cancers. The therapeutic efficacy of the Cu(II) complex for (HOP-62) was investigated using various cell lines, and the IC50 of the Cu(II) complex for (HOP-62) was seen to be practical. Zn (II) and Co(II) complexes have low LD50 values, indicating that they are non-toxic at dosages up to 370 mg/kg [14]. Antony A. et al... Reported new SB Ligands from Glycine, Alanine and 3-Amino benzoic acid with Salicylaldehyde these ligands were used to synthesize metal complexes by using metal chloride solution in ethanol. Antimicrobial investigation of these metal complexes shows very good antimicrobial properties [15]. By interacting metallic acetate or metal salts (Ferric chloride Cobalt acetate, Copper acetate, Nickel acetate) with substituted heterocyclic ligand, new heterocyclic methyl-substituted pyridine SB ligands transition metal complexes of Iron (III), Cobalt (III), Copper (II), and Nickel (II) were designed and produced by Jitendra N. Borase and colleagues. Spectroscopic data was also used to characterize all newly synthesized metal complexes, and then they were tested for spectroscopic methods, FT-IR, Electron spin resonance, Magnetic susceptibility, and TGA. The square planer and octahedral geometry of these complexes, as well as their electronic spectra and magnetic susceptibility tests, indicate that they have a structure in which the (N, O) group works as a bidentate ligand. The Freeman Carroll technique was used to calculate the thermal stability, breakdown rate, and thermodynamic characteristics of synthesized metal complexes. In addition, biostatistical data on the antibacterial and anti-oxidant effects of formed metal complexes shows medium to decent results [16]. Amino acids have coordinating sites of –NH2 and –COOH which are condensed with cabonyl compounds to produce Schiff base ligands that are easily coordinated to metallic ions and are functionally engaged in a number of biological processes. The pharmacological actions of most amino acid-derived SB and their metal complexes are diverse [17]. Schiff base ligands derived from condensation of 1-(4- amino-4 phenyl) 3-phenyl triazene-1-ol (hydroxy trizene) and aromatic aldehydes were mixed with Co

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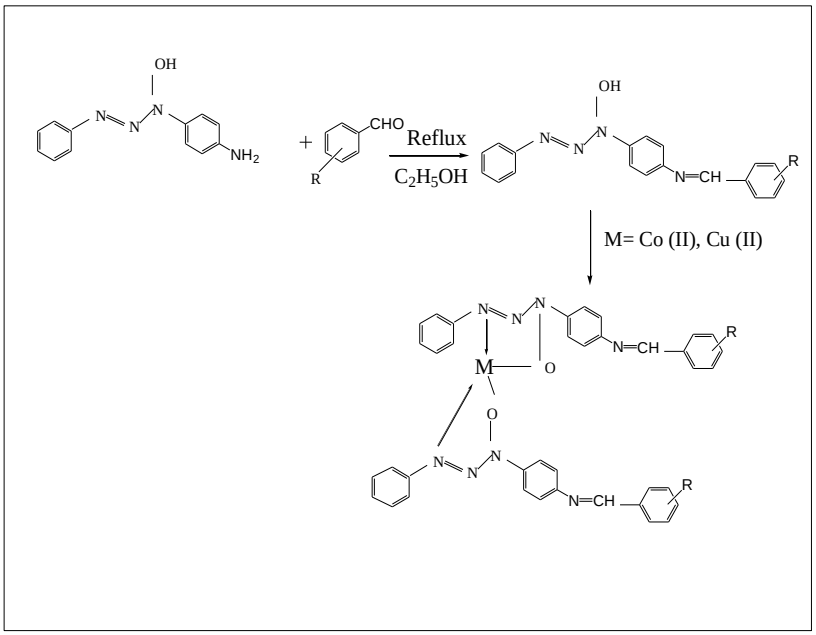
(II) and Cu (II) salts in ethanol to synthesize metal complexes(Scheme-3). Physical and spectral studies like FT-IR, NMR, XRD were used to characterize these complexes. Antibacterial investigations were conducted in vitro against S. aureus, E. coli, and P. Aeruginosa, as well as antifungal activity against C.albicans and A. clavatus. The findings suggest that the complexes have high biological activity [18].



Scheme-3 Synthesis of Schiff base ligands and their Co (II) and Cu (II) metal complexes

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