**VERSATILE IMPORTANCE OF METAL COMPLEXES OF SCHIFF BASE LIGANDS.**

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**Abstract:** The Schiff Base ligand derived from Amines and Carbonyl group such as Aldehydes or Ketones were given very useful activities against antifungal, antibacterial, antidiabetics, anticancer, antiviral, anti-analgesic, anti-depressant, antiplorifutive and also shows DNA binding capacity. Furter study of its derivatives like with transition metal element forms very strong interconjugation with Schiff base ligand and shows impressive activities like antifungal, antibacterial, antidiabetics, anticancer, antiviral, anti-analgesic, anti-depressant, antiplorifutive. This book chapter reveals the review of different Schiff base ligands along with its metal complexes.

**KEY WORDS:** Amines, Carbonyl Group, Schiff Base Ligands, Metal Complex, Anticancer, DNA Binding, Renewable energy source.

**Introduction:**

 The reactions of carbonyl compound like ketones & aldehydes with primary amine was discovered by the researcher Hugo Schiff in 1864. This discovery gave support for further research in many scientific areas [1]. With the help of this discovery different types of Schiff bases and their derivatives have been developed according to their fascinating and valuable properties such as their strength to reversibly bind to oxygen [2], catalytic activity in the hydrogenation of olefins [3], photochromic properties [4-5] and complexing ability towards some poisonous metals [6]. Such complexes are readily collected from diamines and several salicylaldehyde derivatives and are responsive to combinatorial syntheses [7]. Metal Schiff base complexes have been well known for their uncomplicated synthesis, stability, and extensive applications [8–10]. Also considerable attention was devoted in the past decades toward the synthesis and study the different types of Schiff base ligands along with it’s metal complexes owing to their increasing potential in basic as well as applied chemistry [11-13]. The chelates of Schiff bases have been discussed to identify the dependency of their biological efficiency on the linkage of azomethine [14–18]. Many Schiff bases have been used broadly in the field of coordination chemistry, designing molecular ferromagnetisms (DMF), liquid crystals as heterogeneous catalysts [19], biological modelling [20–22], heterogeneous catalysts [23], etc. If we observed the study of Metal complexes of these Schiff base ligands then we can defiantly conclude that the these metal complexes have been successfully used as catalyst in many more biological systems [24], such as dyes [25], analytical chemistry [26],medicinal [27], materials chemistry [28],polymers [29], pharmaceutical fields that comprise miscellaneous therapeutically potent applications [30–32], trace metal analysis and separation [33-34] as well as inorganic and organic synthesis [35].

 In recent days whole world is preferring the renewable sources of energy because of scarcity of fossil fuels as well as material. To fulfill the need of global energy the researcher have devoted their major attention on the energy sources which are easily available in the nature and can be renewable as well as development of renewable energy sources. The mesomorphic non-symmetrical Schiff bases based on the lateral methoxy group in a central core and (E)-3-methoxy-4-(4-methoxyphenyl imino methyl) phenyl 4-alkoxybenzoate have been reported for their potential applications in solar energy [36-37].

Ni (II), Cu (II), Co (II) and Cd (II) forms metal complexes with (E)-N’-((2-hydroxy quinolin-3-yl)methylene)-methylbenzenesulfonohydrazide (Schiff Base) synthesized from the condensation of 2-hydroxyquinoline-3-carbaldehyde and 4-methylbenzenesulfonohydrazide[38]. The novel Schiff base ligands and metal complexes were analysed by numerous spectroscopic techniques i.e.1H NMR, 13C NMR, FT-IR, EPR, UV–Visible and ESI-MS. The synthesized compounds are non-electrolytic shown by Low conductivity data. Magnetic moment of metal complexes of Ni (II), Cu (II) and Co (II) are paramagnetic in nature. The Schiff base ligands and metal complexes were broadcasted for cytotoxicity against human mammary gland cancer cell line (MCF-7) and human lung cancer cell line (A-549) by using MTT [3-(4, 5-dimethylthiazol-2-yl)-2, 5-diphenyltetrazolium Bromide] assay. Metal complexes of Cu (II) complex were found to be additional active than novel Schiff base ligand. They can evolve to use as a chief drug for cancer. Highly active Cu (II) complex was reported that photo-cleavage study with pBR322 DNA.

 

Structure of Quinoline Schiff base ligand and metal complex

Fe (III), Co (II), Mn (II), Ni (II) and Zn (II) these metals form complexes with novel Schiff base ligand acquired by reacting *p*-Hydroxyacetophenone and *p*-methylacetoacetanilide [39]. The Schiff base ligands and metal complexes were signalized by spectral and analytical technique i.e. UV spectroscopy, 1H NMR, IR, 13C-NMR, molar conductance. The metal complexes of Mn (II), Fe (III), Co (II), Ni (II) shows larvicidal activity against larvae of *Cx. Quinquefasciatus* and cytotoxicity against Dalton’s Lymphoma Ascites cell lines from Trypan Blue Exclusion method. High larvicidal activity and anticancer agent shown by Zn (II) complex and they shows antitumor activity against EAC induced as cites tumor and DLA induced solid tumor in Swiss Albino mice.



 Structure of Schiff base ligand

The metal complexes of Fe (III), Cr (III), Co (II), Ni (II), Mn (II), Cu (II), and Cd (II) with novel Schiff base ligand derived from the liquefaction of 2,2-(ethylenedioxy)bis(ethylamine) and imidazole-2-carboxaldehyde[40]. The novel ligands (i.e. Schiff base) along with its metal complexes signalized by C, H, N analysis, magnetic properties, UV, IR spectroscopy, 1H NMR, molar conductivity, thermal analysis, BET surface area and DFT. All complexes adopted octahedral geometry by spectroscopic method. The metal complexes of Cd (II) and Ni (II exhibit antibacterial activity against Aspergillus flavusand Candida albicans respectively. The metal complex of Mn (II) exhibit anticancer activity against breast cancer cell line MCF7. The novel Schiff base ligand essential for fight against the new corona virus by molecular docking. The Mn (II) metal complexes was lower binding energy so its show antiviral activity.

 

 Structure of novel Schiff base ligand



Structure of Metal Complexes

 Structure of metal complexes

The metal complexes of Ni (II), Cu (II), Co (II) and Zn (II) with the new Schiff base ligand 6,6'-((1*E*,11*E*)-5,8-dioxa-2,11-diazadodeca-1,11-diene-1,12-diyl)bis(2,4-dichlorophenol)) derived from the condensation of 1, 8-diamino-3, 6-dioxaoctane and 3, 5-dichloro salicylaldehyde[41]. The metal complex was characterized by analytical and spectroscopic technique i.e. XRD, 1H NMR, FT-IR. The metal complexes show distorted octahedral geometry by XRD study. The Schiff base and metal complexes shows antifungal as well as antibacterial activity against *Aspergillus niger*, *Aspergillus flavus* and *Candida albicans* and *E. coli*, *S. aureus* and *P. aeruginosa* respectively. AO/EB staining assay shows cell death due to apoptosis in MCF-7 cells so Schiff base ligand and metal complex shows cytotoxic activity. MTT 3-(4,5-Dimethylthiazol-2-yl)-2,5-diphenyltetrazolium bromide) assay showed the cytotoxicity of Cu- complex (IC50 = 19 ± 1.1 μg/mL) on human breast cancer MCF-7 cells than Schiff base ligand and other metal complexes.



Synthesis of Schiff base ligand



Structure of metal complexes

The metal complexes of Co(II), Ni(II), Cu(II) and Zn(II) with novel Schiff base ligand derived from the condensation of amoxicillin trihydrate and nicotinaldehyde[42]. The synthesized Schiff base ligand and metal complexes characterized by spectral and physical techniques. i. e. 1H NMR, UV spectra, IR, ESR, SEM, mass spectrometry measurements and elemental analysis, melting point, conductivity respectively. And also analysis by using thermal technique (TGA/DTA), XRD. The metal complexes of Schiff base ligands were screened for antibacterial activity in two various concentrations against *E. coli, P. vulgaris, K. pneumoniae, and S. aureus* this bacterial pathogens.



Structure of novel Schiff base ligand



Structure of metal complexes(M = Co, Ni, Cu, Zn)

The metal complexes of Co(III), Fe(III), Cu(II), and Ni(II) with Schiff base ligand 4‑((E)‑(4‑methylpyridin‑2‑ylimino)methyl)benzene‑1,3‑diol acquired from the liquefaction of 2, 4-Dihydroxy benzaldehyde and 2-amino 4-methyl pyridine[43]. The Schiff base ligands and metal complexes were signalized by spectral and elemental analysis i.e. ESR, FT-IR, magnetic susceptibility and TGA.The metal complex shows square planer and octahedral geometry by ESR data and magnetic susceptibility. The metal complex of Fe (III) shows antifungal activity for the fungi *Aspergillus niger* against *Amphotericine.* The metal complex of Cu (II) shows antibacterial as well as antioxidant activity. Fe (III), Co (III) and Ni (II) metal complexes exhibit removing free radicals properties.



Structure of Schiff base ligand and metal complexes

The metal complexes of Zn (II) with tridentate Schiff base ligand derived from thecondensation of 2-aminobenzimidazole and salicylaldehyde[44]. The metal complex was signalised by mass and 1H NMR spectroscopy, molar conductance, C, H, N analysis, IR. MC measurements suggested that the complex is nonelectrolyticin nature and shows tetrahedral geometry by spectral data. The Schiff base ligands and metal complexes were screened for antimicrobial activity opposed to gram positive andgram negative bacteria.



Structure of Schiff base ligand



Structure of the Zn (II) metal complex

The metal complexes of Co (II), Cu (II), Ni (II) and Zn (II) treated with the Schiff base ligand Indal-4-AAP which was acquired from indole-3-carboxaldehyde and 4-aminoantipyrine[45]. The metal complex was characterized by mass spectroscopy, IR spectroscopy, ESR, magnetic moment, cyclic voltmeter and molar conductance. The metal complex adopted octahedral geometry shown by electronic spectra. The metal complexes of Co (II) and Ni (II) exhibit antimicrobial activity than ligand. The metal complexes of Cu (II), Ni (II) and Zn (II) show complete DNA cleavage activity assayed on pUC18DNA using gel electrophoresis. The biological activity order of metal complexes Ni(II) >Co(II) > Zn(II) >Cu(II) > L.



The metal-complexes like Ni (II), Co (III) & VO (IV) with ligand (Schiff base) which is bidentate (E)-2-((3-(benzyloxypyridinylimino) methyl)-4-bromophenol synthesized from the liquefaction of5-bromo salicylaldehyde & 2-amino-3-benzyloxypyridine[46]. The bidentate ligand (Schiff base) & metal complexes signalised by spectral techniques such as C, H, N analysis, IR, Mass, 1H NMR, 13C-NMR, MC measurement, UV, XRD, magnetic measurements & thermal studies. The metal complexes of Co (III), Ni (II) and VO (IV) exhibit octahedral and square pyramidal geometry respectively by the electronic spectral data and magnetic study. The bidentate Schiff base ligand and their metal complexes screened were antibacterial activity and antifungal activity opposed to Gram positive bacteria *S. aureus* *B. subtilis*, and Gram negative bacteria *E. coli,* *S. typhi* and *A. flavus*, *A. niger*, *C. albicans* and *A. Solanirespectively*. And also exhibit antimicrobial activity against some pathogen.

The bidentate Schiff base ligand and metal complex exhibit crystal packing behavior this is shown by hisrhfeld surface analysis. It is a quantitative way to study the intermolecular interaction of the molecules in a crystal structure.



Structure of Schiff base ligand



Structure of metal complexes

The metal complexes of Cu(II), Co(II), Ni(II), and Zn(II) with novel ligand (Schiff base) *(E)-N*-(pyridine-2-yl)thiophen-2-ylmethylene)hydrazine carbothioamide derived by the liquefaction of thiophen-2-carbaldehyde and 4-(pyridin-2-yl)-thiosemicarbazide[47]. Novel ligand (Schiff base) and metal complexes characterized by elemental analysis, EI-mass spectrum, 1H NMR, 13C-NMR spectrum, FT-IR, UV spectra, magnetic, EPR spectra and thermal analysis. The metal complexes of Ni (II),Co (II), Zn (II) and Cu (II) adopted tetrahedral and square planar geometry respectively by ES & magnetic measurements. They found in thermally stable by thermogravimetric study. Cu (II) complex shows excessive anticancer activity than the ligands well as other synthesized metal complexes by BSA binding activity against HT29 colon cancer cells using MTT assay. The complexes exhibit antibacterial activity than the ligand against diverse bacterial strains.



 Structure of novel Schiff base ligand



Structure of metal complex

The following metals i.e. Ni (II), Co (II), Cu (II) and Zn (II) form complexes with four novel ligands (Schiff base) [48] were investigated such as

* The novel ligand (Schiff base) (E)-N’-(4-(prop-2-yn-1-yloxy) benzylidene) benzohydrazide (**L1**) acquired from the condensation reaction of benzoic acid hydrazide and 4-hydroxy benzaldehyde.
* ThenovelSchiffbaseligand(E)-4-chloro-N’-(4-(prop-2-yn-1-yloxy)benzylidene)benzohydrazide (**L2**) derived from the liquefaction reaction of 4-chloro benzoic acidhydrazide and 4-hydroxy benzaldehyde.
* The novel Schiff base ligand (E)-N’-((2-(benzyloxy)naphthalen-1-yl)methylene) benzohydrazide (**L3**) acquired from the liquefaction of benzoic acid hydrazide and 2-hydroxy-1-napthaldehyde.
* The novel Schiff base ligand (E)-N’-((2-(benzyloxy)naphthalen-1-yl) methylene)-4-chlorobenzohydrazide(**L4**) derived from the liquefaction of 4-chloro benzoic

Acid hydrazide and 2-hydroxy-1-napthaldehyde.

The metal complexes signalized by some analytical and some spectroscopic technique such as 1H and 13C NMR, FT-IR, mass spectroscopy, UV spectroscopy, EPR, TGA, XRD, fluorescence, molar conductance and magnetic susceptibility. The all metal complexes exhibit excellent antioxidant activity and strong free radical scavenging using DPPH method. The Cu (II) complex show higher antioxidant activity. The activity order Cu (II) >Ni (II) >Co (II) >Zn (II) >novel Schiff base ligands. The metal complex show antimicrobial activity opposed to two gram +ve bacteria, S. aureus, S. gordonii and two gram –vebacteria E. coli, P. aeruginosa. The Cu (II) complex show strong poisonous antimicrobial active compound.

The metal complexes of Zn ((II), Ni (II), Co (II) and Cu (II) with Schiff base ligands (E)-4-(3-Hydroxybenzylideneamino)-2, 3-dimethyl-1-phenyl-1, 2-dihydropyrazol-5-one prepared from the condensation reaction of *m*-hydroxybenzaldehyde and 4-amino antipyrine [49]. The metal complexes characterized by spectral techniques such as IR, 13C NMR, 1H NMR and UV spectroscopy. The Zn (II) and Cu (II) complex show antifungal activity against *C*. albicans, A. Niger and C. albicans respectively. The Schiff base ligand and metal complexes shows less cytotoxicity when compared to standard drug molecule against HCT116 (human colorectal carcinoma) cancer cell line by SRB assay. The Cu (II) complex show good cytotoxicity. By EIS technique Ni (II) complex shows outstanding anticorrosion activity than the other metal complexes. And Cu (II) complex show anticorrosion activity less than Ni (II) complex.



Structure of Schiff base ligand

 Structure of metal complexes

The metals i.e. Co (II), Cu (II), Ni (II) and Zn (II) forms complexes with pyridine based Schiff base ligand derived from the condensation reaction of 2-amino-3-hydroxy Pyridine and benzyl[50]. The metal complexes signalised by some techniques like: elemental analysis(CHNS), electronic absorption, magnetic susceptibility, FT-IR, 1H NMR, ESR, ESI-mass spectroscopy, XRD and SEM. The Cu (II) and of Co (II), Ni (II),Zn (II) adopt square planar and tetrahedral geometry respectively. The metal complexes show high antioxidant activity than ligand due to chelation of metal atoms. The metal complexes interacted with DNA by intercalative mode this confirmed by DNA binding analysis. This mode of interaction is confirmed by molecular docking method and anticancer activity is shown against human cancer cell lines by the compounds.



Structure of Schiff base ligand and their metal complexes

**Conclusion:**

 This review of book chapter reveals that Schiff Base Ligands and its derivatives plays vital role in daily life chemistry, drug synthesis, human body activities(DNA), renewable energy sources, medicinal chemistry, biological activities, Anticancer activities etc. This is the main reason that scientist have focused on the Chemistry of Co-ordination chemistry since last two decades. Further there is much more scope in the Co-ordination chemistry due to its unpredictable activities against many of the living problems.

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