

Studies on Schiff Base with its Complexes on Synthesis, Characterization, Biological Activity

Jyoti Sihag¹ Divya Prakash²

^{1,2} Department of Chemistry, Amity School of Applied Sciences, Amity University Rajasthan, Jaipur (India)

Abstract:-The Schiff base (C=N double bond) is synthesized by the reaction of amine and carbonyl compound (aldehydes or ketone). Schiff base are multilateral ligand and offer a resilient series of ligand, who capable to co-ordinate with different metals. The Schiff base, strong candidate in medicinal field as a drug because they exhibit activity against various microorganisms such as bacteria, fungi and cancer cells etc.. The Schiff base and its iron complexes show biological activity like antibacterial, antifungal, antiviral, antileishmanial, antioxidant, cytotoxic, radical-scavenging activity and anticancer etc. The coordination of metal with Schiff base enhances the biological activity of Schiff bases. These synthesized Schiff base and metal complexes, characterized by various spectroscopic and analytical techniques. At present time, these complexes are highly demanding in medicinal field due to its effective activity against cancer cells and microorganisms. This review mainly aims to provide an extensive overview of the various methods used for the preparation of Schiff bases and Schiff base metal complexes, characterization with their biological activities.

Keywords:-Microorganism, Multilateral Ligand, Antioxidant.

I. INTRODUCTION

A condensation process, in which the nucleophilic nitrogen atom of amine, attack on the electrophilic carbon atoms of aldehydes and ketones. In end product, the C=O group is replaced by a C=N group. This product is known as Schiff base/ imine/Azomethine group/Anils. Schiff base, named after Hugo Schiff is a compound and the general structure of Schiff base is $R_2C=NR^*$

Where $[R^* \neq H]$ and $[R^* = \text{alkyl or aryl group}]$, $[R = \text{May be H}]$

Iron metal ion enhances (most cases) the biological activity of different Schiff base ligands. The Schiff base ligand in which N, O-donor atoms are present act as monodentate, bidentate and chelate /bridging agent with metal ions. The Schiff base ligand and its Iron complexes were screened in vitro for their antibacterial, antifungal, antitoxic and anticancer activity.

II. SYNTHESIS, CHARACTERIZATION AND BIOLOGICAL ACTIVITY OF SCHIFF BASE AND ITS IRON COMPLEXES

Laila H. Abdel Rahman et al. (2013) have synthesized iron complex containing the Schiff base were prepared by the 5-bromo-2-hydroxybenzaldehyde, amino acid (L-alanine, L-phenylalanine, L-aspartic acid, L-histidine, L-arginine) solution and complexes were synthesized by SB ligand and $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ and determined by elemental, IR, UV-Visible, conductivity, magnetic susceptibility, the stoichiometry and screened for antibacterial activity against *E.coli*, *P. aeruginosa* and *B. cereus*. [1].

Laila H. Abdel-Rahman et al. (2013) have synthesized the metal complexes of Schiff base ligands from the 2-hydroxy-1-naphthaldehyde [2] and 5-bromosalicylaldehyde [3], the amino acid (ala, phala, aspa, his or arg) solution. The metal complexes prepared by ligand and $FeSO_4 \cdot (NH_4)_2SO_4 \cdot 6H_2O$ and characterized via elemental, thermo gravimetric analysis, molar conductance, IR, electronic, mass spectra and the stability constant. They were screened for antibacterial against *E.coli*, *P. aeruginosa*, *B.cereus* and *P.purpurogenium*, *A.flavus* and *T.rosium* (fungus).s

Fe (II) complexes with N-(2-hydroxyethyl)-5-nitrosalicylalimine was synthesized by Selma Celen et al.(2013).The tridentate Schiff base was prepared by 2-hydroxy-5-nitrobenzaldehyde ,ethanolamine and identified by elemental, UV-vis, IR, NMR spectra. The antimicrobial activities of ligand and metal complex were evaluated against *C. jejuni*, *E. aerogenes*, *E. coli*, *L.monocytogenes*, *P.aeruginosa*, *P.vulgaris*, *S.aureus*, *S.marcescens*, *S.sonnei*, *K.pneumoniae*, *C.albicans*, *A.flavus*, *A. niger*, *Penicillium expansum*, *P. lanosum* and *A.alternata* [4].

M.I. Khan et al. (2013) were prepared Schiff base by the condensation of 4-dimethylamino -benzaldehyde and 4-aminobenzoic acid and complex were identified by UV/Vis, FTIR, NMR, Mass Spectra, XRD, TGA, SEM and screened antibacterial activity against *P.aeruginosa*, *K. pneumoniae*, *E.coli*, antifungal; *A.flavus*, *A.fumigatus*, *A.niger*, *F.solani* and anti-leishmanial ; *Leishmania major*, *L.tropica* and *L.donovani* [5].

Ehab M. Zayed et al.(2013) were prepared SB by the condensation of bisaldehyde (2,2'(ethane-1,2-diylbis(oxy))dibenzaldehyde, hydrazine carbothioamide and the metal complexes by iron chloride, the organic ligand .They analyzed by elemental, magnetic measurements, electronic, IR, ¹H-NMR, mass spectra, Molar conductance, Magnetic susceptibility, TG,DTG,DTA. Both show high antibacterial activity for Gram-positive than Gram-negative bacteria [6].

Omima M.I. Adly et al.(2013) have synthesized ,the Schiff base was prepared by AHTD , ethylenediamine and the metal salt, lithium hydroxide ,SB ligand was mixed to synthesize metal complexes[7] and Magdy Shebl (2013) have synthesized the Schiff base by o-acetoacetyl -phenol,1,2-diaminopropane and isatin. Reactions of the ligand with FeCl₃.6H₂O salts were formed complexes [8]. They characterized by elemental, spectral (IR, UV–Vis, ¹H NMR, ESR and mass), magnetic and molar conductance. Fe (III) complexes were showed high activity towards S.aureus, E.coli.

Nabel A. Negm et al.(2013) have prepared the tannic Schiff base were synthesized by tannic acid-glycine derivatives, benzaldehyde[9] and Abdel-Nasser M.A. Alaghaz et al.(2014) [10] have synthesized schiff base by the condensation of ethylenediamine with [5-(4-sulfanilamido -phenylazo salicylaldehyde)]. These Schiff base react with metal salt of Fe(III),metal complex was formed and characterized by elemental, FT-IR, ¹ H , ¹³C NMR and show antimicrobial activity against Gram positive, Gram-negative bacteria and fungi.

M.L. Sundararajan et al.(2014) have synthesized schiff base by 5-bromo salicylaldehyde and 3,4-(methylenedioxy)aniline. The metal chloride or nitrate react with Schiff base, metal complexes was formed and characterized by elemental analysis, molar conductance, FTIR, UV–Vis, ¹³C NMR, mass spectra, XRD and TG/DTA. Synthesized complex were screened antibacterial activity against (E. faecalis sp., S. aureus, P. floescens sp., E. coli, and Klebsiella sp.), antifungal activity against C. albicans, Fusarium sp., Trichosporon sp. and antioxidant activity [11].

Noureddine Charef et al.(2014) have synthesized metal complex of Schiff base by N¹ -(3-aminopropyl) propane-1,3-diamine and salicylaldehyde. Prepared Schiff base reacts with metal salt [Fe(OAc)₂.4H₂O] and form complex. They identified by FTIR, ¹ H, ¹³C NMR, mass, UV–Vis spectra and elemental analysis and Fe(II) complex was show DPPH radical-scavenging activity ,antioxidant activity[12].

Hina Zafar et al.(2015)have prepared metal complex by metal ions, 2-acetyl pyrrole and 1,3-diaminopropane and characterized by elemental analyses, ESI – mass, NMR (¹ H and ¹³C), IR, XRD, electronic, EPR spectral, magnetic susceptibility and molar conductance measurements. Fe complex were showed antibacterial activity against S. pyogenes and K. Pneumonia [13].

A novel series of transition metal complexes of Fe(III) containing the Schiff base derived from condensation of S-methylthio carbazate and cinnamaldehyde were synthesized by Md. Kudrat-E-Zahan et al (2015). The complex was characterized by IR, ¹H NMR, UV-Vis, IR, Magnetic moment,electronic spectra, magnetic susceptibility. Iron complexes were revealed antibacterial activity against (B.subtilis, Staphlococcus aureus, Bacillus megatherium, Streptococcus-β-haemolyticus, Escherichia coli, Shigella dysenteriae, Shigella sonnei, Shigella shiga) and antifungal activity against (Aspergillus Candidus, Penicillium Marneffeii, Candida Albicans, Aspergillus niger)[14].

Reem K. Shah et al.(2015) have synthesized homo-binuclear Fe (III) complexes and Schiff base derived from p-phenylenediamine and2-hydroxy-1 naphthaldehyde. Complex was prepared by Fe(NO₃)₃, ligand and characterized by elemental, FTIR, ¹H, ¹³CNMR, UV–Vis, XRD, SEM, molar conductance. Average drug-like activity was estimated for complexes [15].

Carmen M. Sharaby et al. (2016) have synthesized, the metal complexes by ferric chloride/ ferrous sulfate, Schiff base and mixed ligand complexes prepared by HL, glycine and metal salts and a novel sulfonamide Schiff base ligand resulted from the condensation of sulfametrole [N'-(4-methoxy-1,2,5-thiadiazol-3-yl)sulfanilamide, acetylacetone and glycine. Complexes were characterized by elemental, mass, conductivity measurement, IR, ¹H NMR, UV-vis, solid reflectance, magnetic susceptibility, TGA and DTA. The Schiff base ligand, its complexes were screened against S. aureus, B. subtilis, S. typhimurium , E.coli, yeast; Candida albicans and fungi; A. fumigates [16].

A tetradentate Schiff base and its [FeL]complexes, were synthesized by Neslihan Beyazit et al.(2016).Schiff base was prepared by 6-formyl-7-hydroxy-5-methoxy-2-methyl benzopyran-4-one and 2-aminobenzylamine.Complex was prepared by FeCl₂.4H₂O, H₂L.Synthesized complexes were characterized by elemental, FTIR, Raman, ¹ H, ¹³C NMR, electronic, mass spectra, conductivity, magnetic susceptibility and show catecholase-like activity [17].

A oxygen-bridged Schiff base iron complex prepared from ligand and FeCl₃ were synthesized by A.Karahan et al.(2016) and H₂-4-MeOL1 ligand prepared from 2,2-dimethyl-1,3-diaminopropane and 2-hydroxy-4-methoxybenzaldehyde. The bridged complex was characterized by single crystal X-ray diffraction and screened antibacterial activity against – B.subtilis, S. aureus, E.coli, Klebsiella pneumonia [18].

Kiran R. Surati et al.(2016) have synthesized Schiff bases by ethylenediamine or o-phenylenediamine and 3-Methyl-5-oxo-1-(p-tolyl)-4,5-dihydro-1H-pyrazole-4-carbaldehyde. The complex synthesized by FeCl₃.6H₂O and characterized by elemental analysis, IR, NMR, mass, molar conductivity,

magnetic measurement, TG, DTA, DSC, Massbauer and XRD [19].

Complex of nano-sized Fe (II) with Schiff base, synthesized from 2-amino-3-hydroxypyridine and 3-methoxysalicylaldehyde were prepared by Laila H. Abdel-Rahman et al. (2016). The compounds characterized by Elemental analyses, TGA, conductivity, IR, UV–Visible and complexes showed antimicrobial activity against bacteria (*E.coli*, *M.luteus*, *Serratia marcescens*) and fungi (*A.flavus*, *G.candidum*, *F.oxysporum*) and the cytotoxic effect against colon carcinoma cells (HCT-116 cell line), hepatic cellular carcinoma cells (HepG-2) [20].

Walaah H.Mahmoud et al.(2016) have synthesized the metal complex resulted from the condensation of o-benzoyl benzoic acid and 4-aminoantipyrine. The metal complexes prepared by reaction of metal chloride and HL. They characterized by elemental, magnetic susceptibility, molar conductivity, ¹H-NMR, mass, UV–visible, FTIR, ESR, thermal and XRD. Complexes showed anticancer activity against breast cancer cell line (MCF7), antibacterial against *Staphylococcus aureus* and *Bacillus subtilis*, *E.coli* and *N. gonorrhoeae* and antifungal against *Candida albicans* [21].

A hydrazine Schiff base, prepared from pyridine 2-carbaldehyde, 4-hydroxy benzohydrazide was given by Behrouz Shaabani et al.(2016). Fe complex was synthesized by HL, azide ligand and Fe₂(SO₄)₃·xH₂O. The complexes were characterized by elemental analysis, FT-IR, UV, XRD and the both complex were screened antimicrobial activities against bacteria *Enterobacter faecalis*, *Staphylococcus aureus*, *Enterobacter aerogenes*, *E.coli*, *Klebsiella pneumoniae*, *Proteus mirabilis* and anticancer activities for MCF-7 cell line (breast cancer)[22].

Hanan F. Abd El-Halim et al. (2016) have synthesized mixed ligand complexes by Schiff base, 1, 1'-phenanthroline and metal salt. The Schiff base was prepared by condensation of oxamide, furan-2-carbaldehyde and 1,10-phenanthroline[23]. W.H. Mahmoud et al.(2017) have described the mixed ligand complexes of the ferrocene based ligand were synthesized by Fe(III) ions, (Z)-(4-(1-(2-carboxycyclohexa-2,4-dien-1-yl)imino)ethyl)[bis(η⁵-cyclopenta-1,3-dien-1-yl)]iron (HL) and 1,1'-phenanthroline[24]. They characterized by elemental, molar conductance, IR, ¹H-NMR, mass spectra, TG/DTG and screened against *S.pneumoniae*, *B.subtilis*, *P.aeruginosa*, *E.coli*, *Aspergillus fumigatus*, *Candida albicans*.

Laila H. Abdel-Rahman et al.(2017) synthesized Schiff base from 2,3-diaminopyridine and 2-hydroxy-1-naphthaldehyde and estimated by elemental analyses, FTIR, magnetic measurements, molar conductivity, TGA, DTA. Both complexes were screened against *e.coli*, *B.subillis*, *S.aureus*, *A.flavus*, *T.rubrum*[25].

Mustafa Yıldız et al.(2017) have synthesized Schiff base formed by polyethyleneimine hydrochlorid, methanol, KOH, the 3-methoxy-5-nitrosalicylaldehyde and characterized by FT-IR, ¹H, ¹³C-NMR, LC-MS and UV-Vis spectra and show antifungal effect on *C. albicans*, *C. tropicalis* (H) and *B. subtilis* (S)[26]

M. S. Hossain et al.(2017) have derived Fe metal complex and 4-((pyridin-2-ylimino) methyl)phenol synthesized by 2-amino pyridine, 4-hydroxybenzaldehyde and characterized by conductivity, magnetic moment, TLC, IR, UV-Visible, TGA and DTG IR, UV spectra and screened for antibacterial activity against *e.coli*, *Pseudomonas aeruginosa*, *Acetobacter aceti*[27].

Omima M.I. Adly et al.(2017) have reported the Schiff base prepared by o-acetoacetylphenol, 2-hydroxybenzohydrazide and characterized by elemental, IR, NMR, electronic, ESR, mass spectra, conductivity, magnetic susceptibility, TGA, DTG. The Schiff base was screened against *Staphylococcus aureus*, *Salmonella typhimurium*(H), *Bacillus subtilis*(L), *Candida albicans*, *Aspergillus fumigatus*(I) and Fe complex was screened against *C. albicans*[28].

III. CONCLUSION

Schiff base and its complexes have a lot of applications like clinical, analytical, pharmacological, biological properties against microorganisms and cancer cells. The Schiff bases and its iron complexes are playing an important role in pharmacological field in form of drug because the biological activity results indicate that Schiff base and iron complexes show activity against for many bacteria such as gram positive and gram negative bacteria, fungi etc. Experimental data exhibit that the complex, restricts the growth of cancer cells. These Complexes also show activity like antileishmanial, antioxidant, cytotoxic against colon carcinoma cells and hepatic cellular carcinoma cells, DPPH radical-scavenging activity and catecholase-like activity. These complexes can be used for resistance against bacteria, fungi and cancer cells for medical purpose.

REFERENCES

- [1]. Laila H. Abdel-Rahman et al.(2013), "DNA binding ability mode, spectroscopic studies, hydrophobicity, and in vitro antibacterial evaluation of some new Fe(II) complexes bearing ONO donors amino acid Schiff bases", *Arabian Journal of Chemistry*, Volume 10, pp S 1835-S 1846.
- [2]. Laila H. Abdel-Rahman et al.(2013), "Design, characterization, teratogenicity testing, antibacterial, antifungal and DNA interaction of few high spin Fe(II) Schiff base amino acid complexes", *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Volume 111, pp 266-276.

- [3]. Laila H. Abdel-Rahman et al.(2013), “Metal based pharmacologically active agents: Synthesis, structural characterization, molecular modeling, CT-DNA binding studies and in vitro antimicrobial screening of iron(II) bromosalicylidene amino acid chelates”, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Volume 117,pp 366-378.
- [4]. Selma Celen et al. (2013), “Synthesis, spectroscopic characterization, and antimicrobial activities of Ni(II) and Fe(II) complexes with N-(2-hydroxyethyl)-5-nitrosalicylaldimine”, *Journal of Coordination Chemistry*, Volume 66, pp 3170–3181.
- [5]. M.I. Khan et al. (2013), “Spectral, XRD, SEM and biological properties of new mononuclear Schiff base transition metal complexes”, *Inorganic Chemistry Communications*, Volume 35, pp 104–109.
- [6]. Ehab M. Zayed et al. (2013), “Thermal and spectroscopic investigation of novel Schiff base, its metal complexes, and their biological activities”, *Journal of thermal analysis and calorimetry*, Volume 116,pp 391-400.
- [7]. Omima M.I. Adly et al. (2013), “Synthesis, spectral characterization, molecular modeling and antimicrobial activity of new potentially N₂O₂ Schiff base complexes”, *Journal of Molecular Structure*, Volume 1054–1055, pp 239–250.
- [8]. Magdy Shebl(2013), “Synthesis, spectroscopic characterization and antimicrobial activity of binuclear metal complexes of a new asymmetrical Schiff base ligand: DNA binding affinity of copper(II) complexes”, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Volume 117,pp 127-137.
- [9]. Nabel A. Negm et al.(2013),“Synthesis and Inhibitory Activity of Schiff Base Surfactants Derived from Tannic Acid and Their Cobalt (II), Manganese (II) and Iron (III) Complexes Against Bacteria and Fungi”, *Journal of Surfactants and Detergents*, Volume 16,pp 767-777.
- [10]. Abdel-Nasser M.A. Alaghaz et al. (2014), “Synthesis, spectral characterization, thermal analysis, molecular modeling and antimicrobial activity of new potentially N₂O₂ azo-dye Schiff base complexes”, *Journal of Molecular Structure*, Volume 1074, pp 359-375.
- [11]. M.L. Sundararajan et al (2014), “Synthesis of metal complexes involving Schiff base ligand with methylenedioxy moiety: Spectral, thermal, XRD and antimicrobial studies”, *Spectrochimica Acta Part A: Molecular and Biomolecular Spectroscopy*, Volume 131,pp 89-93.
- [12]. Noureddine Charef et al.(2014),“Synthesis, characterization, X-ray structures, and biological activity of some metal complexes of the Schiff base 2,2' -(((azanediylbis (propane-3,1-diyl))bis(azanylylidene))bis(methanylylidene))diphenol”, *Polyhedron*, Volume 85,pp 450-456.
- [13]. Hina Zafar et al. (2015),“Synthesis, characterization and antimicrobial studies of Schiff base complexes”,*Journal of molecular structure*, Volume 1097,pp 129-135.
- [14]. Md. Kudrat-E-Zahan et al. (2015),“Synthesis, characteristics, and antimicrobial activity of some complexes of Mn(II), Fe(III) Co(II), Ni(II), Cu(II), and Sb(III) containing bidentate Schiff base of SMDTC”, *Russian journal of general chemistry*, Volume 85,pp 667-672.
- [15]. Reem K. Shah et al.(2015), “Elaborated studies on nano-sized homo-binuclear Mn(II), Fe(III), Co(II), Ni(II), and Cu(II) complexes derived from N₂O₂ Schiff base, thermal, molecular modeling, drug-likeness, and spectral”,*Journal of thermal analysis and calorimetry*, Volume 123,pp 731-743.
- [16]. Carmen M. Sharaby et al.(2016), “Synthesis, Structure Characterization and Biological Activity of Selected Metal Complexes of Sulfonamide Schiff Base as a Primary Ligand and some Mixed Ligand Complexes with Glycine as a Secondary Ligand”, *Journal of molecular structure*, Volume 1134,pp 208-216.
- [17]. Neslihan Beyazit et al.(2016), “ Synthesis, characterization and catecholase-like activity of new Schiff base metal complexes derived from visnagin: Theoretical and experimental study”. *Journal of Molecular Structure*, Volume 1119,pp 124-132.
- [18]. A.Karahan et al.(2016), “A dinuclear oxygen-bridged Schiff base iron (III)complex derived from N,N'-bis(4-methoxy-2-hydroxybenzylidene)- 2,2-dimethylpropane-1,3-diamine”, *Journal of Structural Chemistry*, Volume 57, pp 731-736.
- [19]. Kiran R. Surati et al. (2016), “Schiff base pyrazolone complexes of iron (III): synthesis, characterization, antimicrobial and antioxidant activity”,*Medicinal chemistry research*, Volume 25,pp 2742-2751.
- [20]. Laila H. Abdel-Rahman et al.(2016), “ Some new nano-sized Fe(II), Cd(II) and Zn(II) Schiff base complexes as precursor for metal oxides: Sonochemical synthesis, characterization, DNA interaction, in vitro antimicrobial and anticancer activities”, *Bioorganic Chemistry*, Volume 69,pp 140-152.
- [21]. Walaa H. Mahmoud et al.(2016) , “Preparation, geometric structure, molecular docking thermal and spectroscopic characterization of novel Schiff base ligand and its metal chelates”,*Journal of Thermal analysis and calorimetry*, Volume 217,pp 2149-2171.
- [22]. Behrouz Shaabani et al. (2016),“Chromium(III), manganese(II) and iron(III) complexes based on hydrazone Schiff-base and azide ligands: Synthesis, crystal structure and antimicrobial activity”, *Journal of Coordination Chemistry*, Volume 43.
- [23]. Hanan F. Abd El-Halim et al.(2016),“Synthesis, spectral, thermal and biological studies of mixed ligand complexes with newly prepared Schiff base and 1,10-phenanthroline ligands”, *Journal of Molecular Structure* , Volume 1146,pp 153-163.
- [24]. W.H. Mahmoud et al. (2017),“Mixed ligand complexes of the novel nanoferrocene based Schiff base ligand (HL): Synthesis, spectroscopic characterization, MOE studies

- and antimicrobial/anticancer activities, *Journal of Organometallic Chemistry*, Volume 848, pp 288-301.
- [25]. Laila H. Abdel-Rahman et al.(2017),“Synthesis, characterization, DFT calculations and biological studies of Mn(II), Fe(II), Co(II) and Cd(II) complexes based on a tetradentate ONNO donor Schiff base ligand”, *Journal of Molecular Structure*, Volume 1134, pp 851-862.
- [26]. Mustafa Yıldız et al. (2017),“Synthesis, characterization, and application of a novel water-soluble polyethyleneimine-based Schiff base colorimetric chemosensor for metal cations and biological activity”, *Sensors and actuators B :Chemical*, Volume 252, pp 55-61.
- [27]. M. S. Hossain et al.(2017),“Synthesis and characterization with antimicrobial activity studies on some transition metal complexes of N, O donor novel schiff base ligand”,*Journal of scientific research*, Volume 9, pp 209-218.
- [28]. Omima M.I. Adly et al.(2017), “Synthesis, spectroscopic characterization antimicrobial and antitumor studies of mono-, bi- and tri-nuclear metal complexes of a new Schiff base ligand derived from o-acetoacetylphenol”, *Journal of molecular structure*.