

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

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**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,  $^1\text{H-NMR}$ , 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  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  salts were formed complexes [8]. They characterized by elemental, spectral (IR, UV–Vis,  $^1\text{H NMR}$ , 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,  $^1\text{H}$ ,  $^{13}\text{C NMR}$  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,  $^{13}\text{C NMR}$ , mass spectra, XRD and TG/DTA. Synthesized complex were screened antibacterial activity against (*E. faecalis* sp., *S. aureus*, *P. florescens* 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  $\text{N}^1$ -(3-aminopropyl) propane-1,3-diamine and salicylaldehyde. Prepared Schiff base reacts with metal salt [ $\text{Fe}(\text{OAc})_2 \cdot 4\text{H}_2\text{O}$ ] and form complex. They identified by FTIR,  $^1\text{H}$ ,  $^{13}\text{C NMR}$ , 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 ( $^1\text{H}$  and  $^{13}\text{C}$ ), 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,  $^1\text{H NMR}$ , UV-Vis, IR, Magnetic moment,electronic spectra, magnetic susceptibility. Iron complexes were revealed antibacterial activity against (*B.subtilis*, *Staphlococcus aureus*, *Bacillus megatherium*, *Streptococcus- $\beta$ -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 and 2-hydroxy-1 naphthaldehyde. Complex was prepared by  $\text{Fe}(\text{NO}_3)_3$ , ligand and characterized by elemental, FTIR,  $^1\text{H}$ ,  $^{13}\text{CNMR}$ , 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 [ $\text{N}^1$ -(4-methoxy-1,2,5-thiadiazol-3-yl)sulfanilamide, acetylacetone and glycine. Complexes were characterized by elemental, mass, conductivity measurement, IR,  $^1\text{H NMR}$ , 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  $\text{FeCl}_2 \cdot 4\text{H}_2\text{O}$ ,  $\text{H}_2\text{L}$ .Synthesized complexes were characterized by elemental, FTIR, Raman,  $^1\text{H}$ ,  $^{13}\text{C NMR}$ , electronic, mass spectra, conductivity, magnetic susceptibility and show catecholase-like activity [17].

A oxygen-bridged Schiff base iron complex prepared from ligand and  $\text{FeCl}_3$  were synthesized by A.Karahan et al.(2016) and  $\text{H}_2\text{L}$ -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  $\text{FeCl}_3 \cdot 6\text{H}_2\text{O}$  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, <sup>1</sup>H-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 Fe<sub>2</sub>(SO<sub>4</sub>)<sub>3</sub>·xH<sub>2</sub>O. 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(η<sup>5</sup>-cyclopenta-1,3-dien-1-yl)]iron (HL) and 1,1'-phenanthroline[24]. They characterized by elemental, molar conductance, IR, <sup>1</sup>H-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, <sup>1</sup>H, <sup>13</sup>C-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.

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