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Antimicrobial activities of Schiff Bases: A review

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ABSTRACT: Schiff bases are the most widely used organic compounds in which the carbonyl group is replaced by an imine or azomethine group. These compounds are very important in medicinal and pharmaceutical fields because of their wide spectrum. Most of them show biological activities such as antimicrobial and antifungal activity. This review summarizes the synthesis and antimicrobial activities of Schiff bases and its complexes.

Keywords: Schiff bases, Antimicrobial activities, Organic compounds, Complexes

I. INTRODUCTION

Schiff bases are studied widely due to their synthetic flexibility, selectivity and sensitivity towards the central metal atom; structural similarities with natural biological compounds and also due to presence of azomethine group (-N=CH-) which imports in elucidating the mechanism of transformation and racemization reaction biologically [1,2]. Schiff bases having chelation with oxygen, nitrogen etc. donors and their complexes have been used as drugs and re- ported to possess a wide variety of biological activities against bacteria, fungi, and certain type of tumors and also, they have many biochemical, clinical and pharmacological properties [3,7]. Imine or azomethine groups are present in various natural, naturally derived and non- natural compounds. The imine group present in such compounds has been shown to be critical to their biological activities [8-10]. This review concentrates on the synthesis and microbial properties of Schiff bases and their complexes.

II. ANTIMICROBIAL ACTIVITIES

The Schiff base and metal complexes displayed good activity against the Gram-positive bacteria Staphylococcus aureus, the Gram-negative bacteria *Escherichia coli* and the fungi *Aspergillus niger* & *Candida albicans*. The antimicrobial results also indicated that the metal complexes displayed better antimicrobial activity as compared to the Schiff bases ligand. Chelation tends to make the ligand act as more powerful and potent bactericidal agent [11]. Metal complexes of Schiff bases derived from 2-furancarboxaldehyde and *o*-phenylenediamine and 2-thiophenea carboxaldehyde and 2-aminothiophenol was reported by Gehad Geindy *et al*, These authors have reported the ligand dissociation as well as the metal-ligand stability constants for these complexes. The synthesized ligands, in comparison to their metal complexes were also screened for their antibacterial activity against bacterial species, *Escherichia coli, Pseudomonas aeruginosa and Staphylococcus Pyogones as well as fungi (Candida).* The activity data reveal that the metal complexes are found to be more potent antibacterial than the parent Schiff base ligand against one or more bacterial species. Z.H. Chohan and S. Mushtaq synthesized A series of biologically active pyrazine derived Schiff base ligands have been synthesized by the condensation reaction of 2-aminopyrazine with salicylaldehyde and acetamido benzylaldehyde. Then their Co(II), Ni(II) & Zn (II) complexes have been prepared. The biological evaluation of the simple uncomplexed ligands in comparison to their complexes have been determined against bacterial strains namely *Escherichia coli, Staphylococcus aureous* and *Pseudomonas aeruginosa* [12]. Bidentate complexes of Co(II), Ni(II), Cu(II), Zn(II), Cd(II) and Hg(II) with benzofuran-2-carbohydrazide and benzaldehyde [BPMC] or 3,4-dimethoxybenzaldehyde[BDMePMC] showed biological activities. Co(II) and Cd(II) complexes of [BPMC] are moderately active toward *E. coli* whereas Cu(II), Zn(II) and Ni(II) complexes of [BPMC] and Cu(II) and Zn(II) complexes of [BDMeOPMC] are more active against *S aurious* as compared to free ligands. None of the complexes are active against *A. niger*, but in the case of *A. fumigatus*, Cu(II),Co(II), Ni(II) and Cd(II) complexes of [BDMeOPMC] are more active than the parent ligands [13].

Amino acid Schiff base derived from 2- hydroxy-5-methylacetophenone and glycine and its transition metal complexes showed bacterial activities. The ligand was bacteriostatic against bacterial strains except *Proteus vulgaris*, *Shigella flexneri*, and *Bacillus coagulans.* All complexes are either resistant or less sensitive against *P.vulgaris*. However compared to the antibacterial activity of the standard antibiotic streptomycin, the activity exhibited by the ligand and metal complexes was lower. The metal complexes showed to exhibited higher activity than the free ligand against the same organism under identical experimental conditions, such increased activity of the metal chelates can be explained on the basis of chelation theory [14]. Muhammad Aslam, *et al* [15] synthesized Schiff base by mixing of Aminophenol with 4-chloroacetophenon or 4-hydroxyacetophenone and the reaction mixture was refluxed for 3h with stirring at 70^oC after adding 3-4drops of conc.H_2SO_4. 4-Chloro-2-oxo-2H-chromene-3- carbaldehyde was made to react with different anilines in rectified spirit to yield a series of Schiff bases of the type 4-chloro-3-(substituted-phenylimino)methyl)-2H-chromen-2-one reported by S. Bairagi *et al* [16]. Bag *et al* have synthesized a series of Schiff bases of benzidene with series of substituted aromatic aldehydes and examined the mercuration reaction [17]. Natarajan Raman *et al* [18] have reported the synthesis of a novel 14-membered macrocyclic Schiff base derived from 3-cinnamalideneacetanalide and *o*-phenylenediamine which acts as a tetradentate and strongly conjugated ligand to form a cationic solid complex with Cu(II)/Ni(II)/Co(II) and Zn(II). The ligand and the complexes were characterized by the usual spectral and analytical techniques. The antimicrobial tests were also recorded and gave good results in the presence of metal ions in the ligand system. Hitesh *et al* have reported the synthesis mixed-ligand complexes Mn(II),Co(II),Ni(II),Cu(II),Zn(II) and Cd(II) with biologically active Schiff bases, viz. potassium salt of *o*-hydroxyacetophenone glycine [KHL] and bis(benzylidene) ethylenediamine [A1] or thiophene-o-carboxaldene-p-toluidine [A2]. The mixed-ligand complexes show higher antifungal activity as compared to the free ligands, metal salts, and the control (dimethylsulfoxide) but moderate activity as compared to the standard fungicides (bavistin and emcarb)[19]. Yi-Jun Wei *et al* [20] synthesized a pair of iso structural azido or thiocyanato bridged centre of symmetric dinuclear copper(II) complexes derived from the Schiff base ligand, 4-nitro-2-[(2-diethylaminoethylimino)methyl]phenol. These compounds are characterized by elemental analysis, IR spectra and single X-ray diffraction.

The antimicrobial activities of the complexes have been tested. Mukesh Kumar Biyala *et al.*, [21] have studied the synthesis of mono basic bidendate Schiff base complexes of palladium (II) and platinum (II) from 1H-indol-2,3-dione thiosemicarbazone. These complexes were characterized on the basis of elemental analysis, molecular weight determination, 1H NMR and UV spectral studies. Antimicrobial effects of both the ligands and their complexes on different species of pathogenic fungi and bacteria have been recorded and these are found to possess significant fungicidal and bactericidal properties. Gomathi Vellaiswami & co workers [22] synthesized a novel Schiff base from 3 ethoxy salicyaldehyde & sulpha pyridine. The orange coloured solid mass formed during refluxing was cooled, filtered, washed and dried in a desiccator. The prepared Schiff base was characterized and it was found that it exhibited promising antibacterial and antifungal activity against various microorganisms. The Schiff base 4-chloro-2-(2-morphiolinoethylimino) methylphenolato methanolchloro and its Zn(II) complex were screened for antibacterial activity against two Gram positive bacterial strains (*B. subtilis* method. The Schiff base showed significant activity and *S. aureus*) and two Gram-negative bacterial strains (*E. coli* and P. fluorescence) by the MTT against two Gram-negative bacterial strains with MICof $12.5\mu gmL^{-1}$ but was inactive against two Gram-negative bacterial strains. The Zn complex showed a wide range of bactericidal activities against the Gram-positive and Gram negative bacteria, were potent than, or similar with commercial antibiotics (Kanamycinand penicillin) [23]. Daniel Thangadurai and Son-Ki Ihm [24] have reported the synthesis, characterization, catalytic and antibacterial studies of chiral Schiff base Ruthenium (III) complexes. These authors have tentatively proposed an octahedral structure for all the new complexes. The catalytic and antibacterial activities of these compounds have also been reported. Neutral tetradentate complexes of transition metals with Schiff bases derived from 2- aminophenol/2-aminothiophenol and 1-phenyl-2,3- dimethyl-4(4-iminopentan-2-one)-pyrazol-5-one showed antimicrobial activity against *Staphylococcus aureus, Bacillus subtilis, Klebsiella imeumoniae, Salmonella typhi, Pseudomonous aeruginosa, Shigella flexneri, Aspergillus niger* and *Trichoderma viridi* most of the complexes have higher activity than the free ligand [25].

III. CONCLUSION

Schiff base compounds have been shown to be promising leads for the design of more efficient antimicrobial agents.

Schiff base ligands are considered privileged ligands because they are easily prepared by a simple one pot condensation of an aldehyde and primary amines. In this review, the antimicrobial activities of Schiff base and their complexes are summarized from 1998-2014.

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