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A review on versatile applications of novel Schiff bases and their metal complexes

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ABSTRACT

Metal complexes synthesized from Schiff bases and furthermore Schiff bases are versatile in nature. Such types of compounds were prepared from the condensation of an amino compound with carbonyl compounds (aldehyde or ketone) during which the carbonyl group is replaced by an imine or azomethine group. Schiff bases and their derivatives are widely employed in industries, polymers, dyes and medicative and pharmaceutical fields and additionally exhibit biological activities like antibacterial, antifungal, anti-inflammatory, antimalarial, antiviral, and antipyretic properties. Many Schiff base metal complexes exhibit glorious catalytic activities in numerous mechanisms. Their several applications in homogenous and heterogeneous catalysis were according troughout last decade. Several Schiff base complexes were helpful for their application as catalysts in reactions involving at high temperatures because of the high thermal and moisture stabilities. This text totally based on literature review with examples of the most promising applied Schiff bases and their complexes in several areas, summarizing the applications of Schiff bases and their numerous derivatives and complexes.

Keywords: *Schiff base, Metal complex, Antifertility, Oxygen affinity, Imine.*

1. INTRODUCTION

Schiff base contains the imine group (–RC=N–). Schiff bases named after Hugo Schiff (1964), had been synthesized by condensation of aldehyde- or ketone (RCOR′) like compounds where R, R′ is either an alkyl or aryl group with primary amine ($R–NH_2$) amine in which the carbonyl group is changed by using an imine or azomethine group[1]. Schiff bases are known because of their strong coordinating nature as a family of ligands[2]. The Schiff base is very versatile in nature, as those compounds could have unique substituents and they can be unbridged or N,N′-bridged. Usually Schiff bases have NO or N_2O_2 donor atoms but oxygen can be replaced with sulfur, nitrogen or selenium atoms[3].

Schiff bases are great intermediates for the synthesis of numerous bioactive compounds. Moreover, they may be said to expose a variety of biological activities including antibacterial, antifungal, antifertility, dioxygen coordination, anti cancer and herbicidal activities[4-11]. In other words, they may be essential material for synthesis of various Schiff base ligands which used as chiral auxiliaries in asymmetric synthesis. Schiff base metal complexes have also been utilized in oxidation reactions[12].In view of these facts that, Schiff base isessential in medical chemistry, food industry, dye industry, fungicidal, analytical chemistry, catalysis, agrochemical and biological activities. In this paper, we will explain which the simple techniques to synthesize Schiff bases and the significance of Schiff bases.

Schiff bases represent a class of ligands which have been studied in coordination chemistry. Schiff base ligands are without problems easily prepared and synthesized complexes with almost all metal ions. In the recent years, there have been many reports published on their biological activities such as antibacterial, antifungal, anticancer, antioxidant, anti-inflammatory, antimalarial and antiviral activity. Schiff base metal complexes are also known for their important biological roles along within photosynthesis and transport of oxygen in mammalian and other respiration systems[13].

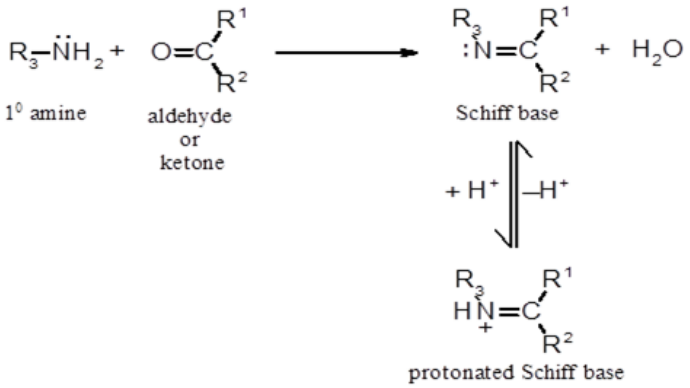

Figure 1. General path for preparation of Schiff bases.

These complexes also exhibit a significant role in agriculture, pharmaceutical and industrial chemistry. It has been determined that depending at the solvent, molybdenum(VI) Schiff base complexes may be four, five or six coordinate.

2. BIOLOGICAL SIGNIFICANCE OF SCHIFF BASE COMPLEXES

This paper reviews the role of Schiff bases and their metal complexes as anti-bacterial, anti-fungal, antifertility oxygen affinity, antiviral, anti-cancer, dyes, antioxidant, anti-inflammatory and agents.

2.1. Anti-bacterial activity.

Schiff base (derived from condensation of thenil with 2,3-diamino-5-bromopyridine and their cyclization with β-diketones) metal complexes synthesized from 2-thiophene carboxaldehyde

and 2-aminobenzoic acid (HL) and Fe(III) or Co(II) or Ni(II) or Mo(VI) confirmed antibacterial activity towards *Staphylococcus aureus, Enterobacter aerogenes, Salmonella typhi* and *Bacillus subtilis*[14].Fe(III), Cu(II) and Mo(VI) complexes caused inhibition for *Escherichia coli*. The importance of this lies inside the truth that these complexes could be applied in the treatment of some diseases caused by *Escherichia coli*. But, Fe(III), Co(II), Cu(II) and Mo(VI) complexes have been specialized in inhibiting Gram-positive bacterial strains (*Enterobacter aerogenes* and *Bacillus subtilis*). The importance of this special property of the investigated Schiff base metallic complexes lies in the reality that, it could be implemented properly in the remedy of infections caused by any of these particular strains[15]. Metal complexes of a singular Schiff base derived from condensation of sulphametrole and varelaldehyde were screened against bacterial species (*Escherichia coli* and *Staphylococcus aureus*). The newly prepared Schiff base and its metal complexes confirmed a better impact on *Escherichia coli* (Gram-negative bacteria) and *Staphylococcus aureus* (Gram-positive bacteria)[16].

Schiff base 2-Aminomethylthiophenyl-4-bromosalicylaldehyde and its metal complexes were investigated for their antimicrobial activities the uses of the disc diffusion method against bacteria. The outcomes of antimicrobial interest prove that the metal complexes exhibit antimicrobial properties and they show strong inhibitory activity compared to the parent ligand under experimental conditions. The antibacterial activities had been explained on the idea of chelation theory. The consequences confirmed that tested complexes were more active against Gram-positive than Gram-negative bacteria. It could be concluded that antibacterial activity of the compounds is associated with cell wall structure of the bacteria.

Tridentated Schiff bases and their metal complexes display antibacterial activities against *Escherichia coli, Staphylococcus aureus, Bacillus subtilis* and *Bacillus. Pumilus*[17,18]. Some Schiff bases obtained from amino acid, aldimines, pyrazine and Schiff bases derived from heterocylic-ketone display antibacterial activity[19-25]. Metal complexes of Mo(IV) and Mn(II) with hydrazine carboxamide and hydrazine carbothiamide show antibacterial activity against *Staphylococcus aureus* and *Xanthomonas compestris*[26]. Schiff bases (benzimidazole, furaldehyde, thiazole, pyridine, benzyldithio -carbazate, glucosamine and pyrazolone) display antibacterial interest[27-35]. Schiff bases synthesized from Isatin have anti-HIV activity and antibacterial activity. Metal complexes of Salicylidene derivatives and neutral tetradentate indicate antibacterial activities against *Salmonella typhi, Staphylococcus aureus, Kelbsiella pneumonia* and *Bacillus subtilis*[36-39]. Organo-silicon (IV) complexes and organo-lead (IV) complexes with nitrogen donor ligands of sulpha drugs and organo-silicon (IV) complexes with bidentate Schiff base show antibacterial activities[40-42].

2.2. Antifungal Activities.

Metal complexes with Schiff bases obtained from o-phthalaldehyde and amino acids viz., glycine L-alanine, L-phenylalanine, (where metal, M= Cu(II), Co(II), Ni(II) and Mn(II)) have been synthesized, then tested against fungi. It is confirmed that Cu(II) and Ni(II) complexes show inhibition closer to all the studied microorganisms. Although, Co(II) and Mn(II) complexes display less inhibition and VO(II) complexes have no activity towards the microorganisms[43-45]. Metal complexes of Cr(III), Mn(III), and Fe(III) in ethanolic medium with Schiff base ligand prepared from 1,4-dicarbonyl-phenyldihydrazide and chromene-2,3-dione (2:2) synthesized and then tested for their antifungal activities to assess their inhibiting capacity. The antifungal experimental consequences of the compounds have been in comparison with the same old antifungal drug (Miconazole) at the same concentration. All the complexes showed enormous antifungal activity against Aspergillus species. Despite the fact that, they show lesser interest in opposition to rhizoctonia species than standard drug miconazole. The Cr(III) and Fe(III) complexes are wonderful fruitful towards Penicillium species than the standard drug. From the data it has been found that the antifungal activity depends upon the metal ion and varies in the following order Cr > Fe >Mn[46].

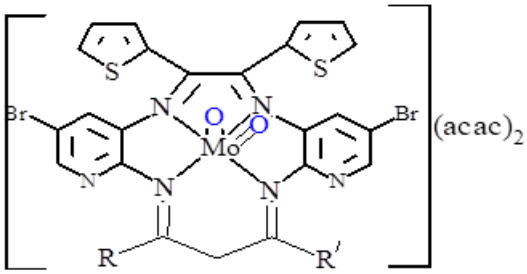

Figure 2. Proposed structure of Molybdenum complexes with Schuff base.

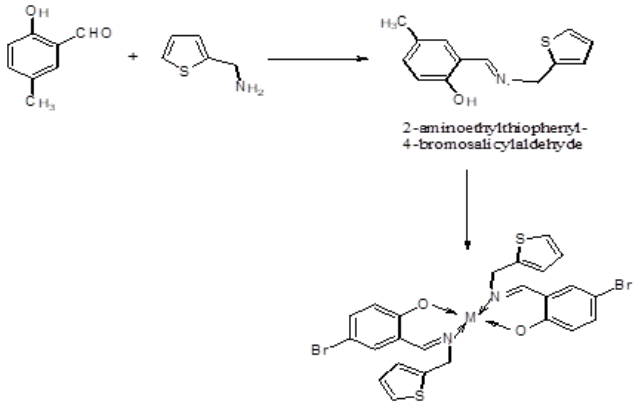

Figure 3. Proposed structure of Schiff base ligand and its metal complex as where M=Cu(II), Ni(II).

Metal complexes of As (III), Sb (III), and Bi (III) with o-tolylammonium di-thiocarbamate are antifungal in opposition to *Aspergillus niger* and *Alternaria alternata* [47]. Mo and Mn complexes test disease (caused by *Alternaria alternata*) in brinjal crop. Schiff bases like phenyl-azo-thiazole or benzothiazole and their metallic complexes show microbiological activity towards *Aspergillusniger* and *Alternariaalternate* [48].Pyrandione Schiff bases show physiological activity in the direction of *Aspergillusniger*[49]. Thiazole and benzothiazole Schiff bases offer powerful antifungal activity[50]. Presence of methoxy, halogen and napthyl groups enhance the fungicidal activity towards Curvularia. Metal complexes (metal M= Ni(II), Cu(II), and Zn(II)) obtained from Schiff base of salicylaldehyde and O,O-di-methyl thiophosphoramide are effective chemical substances to kill *Tetranychus bimaculatus*[51].

2.3. Antifertility Activity.

Schiff base of bis(3-oxo-2-butylidene)propane-l,3-diamine and metal complexes of Sn(II) may also modify reproductive

physiology. Oral direction of various complexes to rats appreciably reduced sperm concentration of testes and epididymis. The motility of cauda epididymal sperms become additionally decreased remarkably[52]. Massive reduction in the sperm motility of cauda epididymis turned into tested in all experimental groups. This may be due to an intrusion with enzyme reactions along with the oxidation phosphorylation uncoupling[53,54]. Schiff base of hydrazine carboxoamide and metal complexes of MoO_2(VI) and Mn(II) might adjust the reproduction system[25]. Schiff base linkages with pyridoxal from lysine to analine or histidine smash enzyme activity in protein[55].

2.4. Oxygen Affinity.

Synthetic dioxygen carriers are extensively studied. Examples are salen, porphyrin, tertiary phosphine and phthalocyanine complexes of Co, Mn, Fe, Mo and Cu have been observed to bind the dioxygen reversibly[56,57]. The activation of molecular oxygen with salen-type complexes changed into examined by way of Tsumaki in1930[58].

The cobalt(II) complexes with N,N'-bis (salicylidene)-2,2'-dimethyl-1,3-propanediimine ligand derivatives, termed CoSaldmpr have oxygen absorption activities[59]. Those complexes gave remarkable effects in 1-methyl-2- pyrrolidinone (NMP) solution. 2- cyanopyridine (2 M) taken as axial base and their complexes, loading of Co(3-methoxySaldmpr), measured in (g O_2/g solution) remain approximately 35% higher than Co(3-methoxy-Salen) for at least four sorption (absorption/ desorption cycles). Oxygen sorption processes for Mn(II), Co(II) and Ni(II) square planar complexes of tetradentate Schiff base ligands obtained from condensation of ethylenediamine with salicylaldehyde, o-hydroxyacetophenone or acetyl acetone in DMF and chloroform solvents had been observed. The sorption processes have been continued inside the presence/absence of axial-base in 1:1 molar ratio of (pyridine:metal(II) complexes). Here axial base is pyridine. Complexes in DMF exhibit important oxygen affinity than in chloroform solvent. Co(II) complexes confirmed great sorption processes in comparison to Mn(II) and Ni(II) complexes. The presence of pyridine axial base glaringly enhance oxygen affinity. This type of substance may be used as a catalyst in oxidative addition reactions in the organic chemistry and petrochemicals, that is reproducible and is considered eco-friendly[60].

Oxo-molybdenum chemistry is of tremendous significant due to the fact such units are found in the active sites of the majority of molybdo-enzymes. In order to mimic the biological systems, a number of oxomolybdenum complexes had been prepared and examined. The geometry of such form of molybdenum coordination compounds is distorted octahedron of the basis of spectral studies. In geometry the ONO tridentate ligand occupies a meridional position with two anionic oxygen donors together trans and cis to the oxygen centers of the cis-dioxo group. The applications of cis-MoO_2(ONO)-type complexes had been suggested inside the literature involve oxo transfer reactions like sulfoxidation, epoxidation and phosphine oxidation reactions[61].

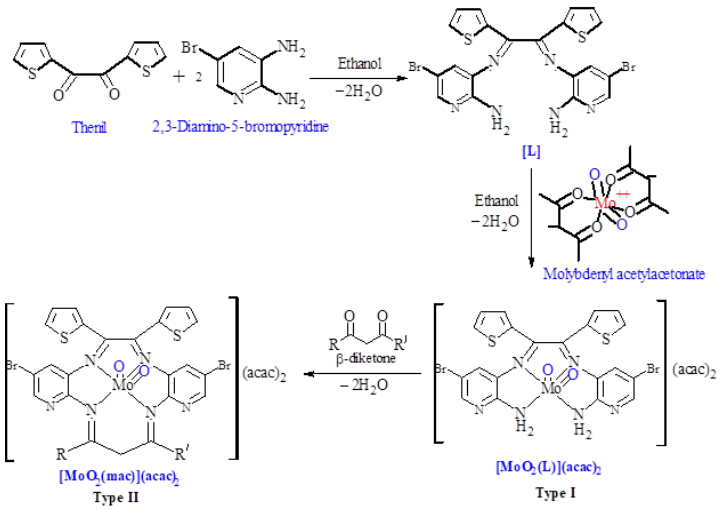

Figure 4. Scheme for preparation of tetradendatemacrocyclic complexes of dioxomolybdenum(VI) complexes.

Where, L = thenil+ 2,3-diamino-5-bromopyridine; mac = macrocyclic ligands carried out from condensation of L with β-diketones in presence of dioxmolybdenum(VI) cation; R = CH_3, C_6H_5, C_4H_3S, C_6H_5; R' = CH_3, CH_3, CF_3, C_6H_5; respective with β-diketones = (i) acetylacetone, (ii) benzoylacetone, (iii) thenoyltrifluoroacetone, (iv) dibenzoylmethane.
Scheme taken from D P Rao*et al*, *Biointerface Research in Applied Chemistry*, 4(1), 2014, 678-684

2.5. Antiviral Activities.

Salicylaldehyde Schiff bases of 1-amino-3-hydroxy-guanidine tosylate are an excellent template for the layout of new antiviral complexes[62]. Gossypol Schiff bases exhibit excessive antiviral activity[63]. Ag(I) complexes show inhibition towards *Cucumber mosaic* virus. Glycine salicylaldehyde Schiff base Ag(I) complexproduced powerful results up to 74.5% towards *C. mosaic* virus[64]. 1-amino-3-hydroxyguanidine tosylate-derived Schiff bases and 2-(3-allyl-2-hydroxybenzylidene)-N-hydroxyhydrazinecarboximidamide derivative turned into powerful towards mouse hepatitis virus (MHV)[62].

2.6. Anticancer Activity.

Cancer is a serious public health problem all over the international as the most feared diagnosis. It is the second most reason of human loss of life after cardiac diseases in developing in addition to developed countries[65]. Cancer is a disease in which a group of cells displays out of control growth[666-68]. In present, the primary treatment for most cancers consists of surgery and chemotherapy, however the remedial effects of the existing chemotherapeutic drugs aren't advanced and they have considerable side effects. The development of greater effective drugs for most cancer sufferers has been a main attempt over the last five decades. In cutting-edge years, numerous Schiff bases derivatives and complexes have been discovered to be associated with anticancer properties.

Aryl-azo Schiff show off anticancer activity[69].Schiff base of indole-2-carboxaldehydes exhibit inhibitor activities to K B cell lines[70].Several Schiff bases and their metal complexes (metal, M= Co, Ni, Cu and Zn) own antitumor properties[71-72]. Such type of metal complexes synthesized from salicylaldehyde, 2,4-dihydroxy-banzaldehyde, glycine and L-alanine. The sequence of reactivity of these agents with metal is Ni> Cu >Zn >Co[73]. Salicylidiene anthranilic acid show antiulcer interest and copper

complexes with Salicylidiene anthranilic acid have a great antiulcer interest[74].

The preparing of extra powerful, target particular metal drugs, less toxic and evaluate their anticancer properties, an order of Ru(II) and Ru(III) complexes having 4-hydroxy-pyridine-2,6-dicarboxylic acid and PPh_3/$AsPh_3$ have been synthesized[75].

2.7. Dyes.

Chromium complex with azomethine, cobalt complex with Schiff base, unsymmetrical complex 1:2 chromium dyes provide fast colors to leathers, food packages, wools etc. Metal complexes with azo groups are applied for dying cellulose polyester textiles[76-78]. Some metal complexes are applied for mass dye polyfibers[79]. Cobalt complex of Schiff base (viz. salicylaldehyde with diamine) has better mild resistance and storage capacity and does no longer degrade even in acidic gases (CO_2). Novel tetradentate Schiff base behaves as a chromogenic reagent for assessment of Ni in some natural food samples[80].

Two low-dimensional oxime-containing Schiff base copper (I/II) complexes with iodineecopper cluster $[Cu^{I}_2I_4]^{2-}$ bridges, namely $\{[Cu^{II}_4I_3(pop)_4]_2(Cu^{I}_2I_4)\}.(CH_3CN)_2.H_2O$ (2) and $[Cu^{II}_4I_2(pop)_4(Cu^{I}_2I_4).(CH_3CN)]_n$ (3) (Hpop = 2-(hydro-xyimino)-N`-[1-(2-yridyl)ethylidene] propane-ydrazone), were prepared from the reaction of [2x2] grid-like compound $\{[Cu^{III}(pop)]_4\}_2.4H_2O$ (1) with equivalent $Cu^{I}_2I_2$ (iodineecopper clusters) under solvothermal condition and characterizated by means of elemental analysis, infra-red spectrum, thermogravimetric analysis, and X-ray single-crystal/powder diffraction. The results exhibit that 2 is 0-D discrete structure from group of one $[Cu^{I}_2I_4]^{2-}$ unit and two [2 x2] molecular grids 1 via μ_3-I atom coordinating to Cu(I) /Cu(II) atoms. But, compound 3 shows 1-D wave-like chain, that's shaped by using coordination of μ_2-I atoms from $[Cu^{I}_2I_4]^{2-}$ units with Cu(II) atoms in [2x 2] molecular grids (1). Moreover, catalytic experiments showed that compounds 2 and 3 have promising visible-light-driven catalytic interest in degrading various organic dyes[81].

2.8. Antioxidant Activity.

Free radicals are built beneath certain environmental conditions and during normal cell functions in the body. Antioxidants play acritical role to protect the human body towards harm by reactive oxygen species. The capacity of Schiff bases and their metal complexes to scavenge free radicals is an important property[82]. Present time a whole lot of Schiff-base metal complexes were investigated as antioxidants.

Five kinds of Schiff bases of chitosan and carboxymethyl chitosan (CMCTS) had been synthesized and the antioxidant interest was studied using superoxide and hydroxyl radical scavenging. Drastic differences between the Schiff bases of chitosan and carboxymethyl chitosan have been observed. It can be related to the contents of the active hydroxyl and amino groups in the molecular chains. The scavenging impact increases with increasinggrowth inside the concentration of the Schiff[83]. In present time, synthetic or artificial antioxidants are typically used due to the fact they're effective and budget friendly than natural antioxidants. Present-day a number of Schiff base metal complexes had been synthesized as effective scavengers of ROS, acting as antioxidants.

The antioxidant capacities of Schiff base ligand N-(4-phenylthiazol-2-yl)-2-(thiophen-2-ylmethylene) hydrazinecarboxamide and its Cu(II), Co(II), Ni(II) and Zn(II) complexes have been evaluated by DPPH technique. The Schiff base ligand and its Cu(II), Co(II) complexes have exhibited a wonderful antioxidant activity, whereas Ni(II) and Zn(II) complexes have shownmoderate activity. The scavenging activity depends upon concentration[84]. Schiff base ligand and its copper complex exhibit necessary free radical scavenging action, this could ensue to the presence of >NH groups. It should give an electron or hydrogen atom to DPPH and produce a stable free radical[85]. The Tin (II) chloride complexes with many Schiff base derivative of 2-Hydroxy-1- naphthaldehyde (HN) have been synthesized and screened for their antioxidant activities by DPPH technique. All the complexes showed great antioxidant activities and better antioxidant activities than their corresponding ligands[86-88].

Schiff bases of Sulphanilamide and its complexes with elements like Cu, Zn and Cd metals have been tested as an antioxidant. The Cu and Zn metal complexes show moderate antioxidant activity. Whereas the metal complexes of Cd reveal potent antioxidant activity[89]. The complexes have noticeable antioxidant interest due to the coordination of metal with the condensed ring system. Condensed ring system will increase its capability to stabilize unpaired electrons and, thereby, to scavenge free radicals[83,90].

3. CONCLUSION

Schiff bases are notified as a very dominant group of organic compounds due to their capability to form complexes with transition metal ions and of their biological properties. Schiff bases and their metal complexes had been widely used for industrial applications. However, the antioxidant activities of this group of compounds deserve greater research. It shows when plant pathogens are considered. Moreover, inside the primary of the studies on this subject, the number of reports proving the consequences of Schiff bases on pathogens of clinical interest has been increasing. I've reviewed Schiff bases, which have a terrific capability for the formation of complexes with metal ions, demonstrating that these Schiff bases and their metal complexes have antioxidant interest. Metal complexes of Schiff bases are exquisite selective and top oxygen carriers. The synthesis of latest macrocyclic Schiff base ligands and their use as chelates will implementation the platform for applications of such antioxidants.

Transition metal complexes with Schiff bases were of much interest over the recent years, in huge scale due to its numerous applications in biological processes and tremendous applications in designing new healing agents. Moreover, still, there may need to explore the biological properties of earlier prepared Schiff base transition metal complexes and to synthesize new complexes with more properties. Schiff bases and their metal complexes were exhibits to design of more efficient chelates. Advent on this field would require analyses of the structure and activity relationships of the Schiff bases in addition to the mechanism of action of these Schiff bases and their metal complexes.

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