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A Short Review on Biological Evaluation of Novel Schiff Base Complexes with Divalent Transition Metals

[1]Rajeev Pradhan

[1]Department of Chemistry, P.K.Roy Memorial College, Dhanbad, Jharkhand

Abstract

Schiff's bases are appropriate ligands that can be produced by condensing 1^{o} amines with C-O groups such as CHO and =O. This process of condensation leads to the production of Schiff's bases. Due to their involvement in a wide variety of biological activities, these compounds are of great importance to the pharmaceutical and medical sectors. The great majority of them have antibacterial, antifungal and anticancer properties. Under the majority of experimental conditions, Schiff's base ligands can react with metal salts to produce metal complexes. A lot of research has been done to try to figure out how Schiff's base ligands change the biological activity of transition metal complexes. This article provides a summary of the biological actions of new Schiff base compounds incorporating divalent transition metal.

Keywords: Transition metal complexes, Anti-microbial, Anti-inflammatory.

1. INTRODUCTION

Hugo Schiff, a German-American scientist, made the initial discovery of Schiff bases in the year 1864. These are the products that are made when carbonyl compounds and amines combine. They are also called imines or azomethine because of the (-HC=N-) functional group. In this particular instance, the nitrogen atom acts as a bonding molecule for the complexation process. In order for azomethine derivatives to exhibit any kind of biological action, the C-N bond is required and different azomethine have been demonstrated to exhibit potent antibacterial, antifungal, anticancer and antimalarial characteristics [2-5].

These days, chemicals formed from Schiff base are considered to be of utmost relevance. Crystalline and fundamentally simple in composition, Schiff bases predominate among bases. This is available at a lower cost [6-8]. Synthesis of the ligand as well as its charged or neutral metal complexes is a straightforward process. These complexes have the ability for being more

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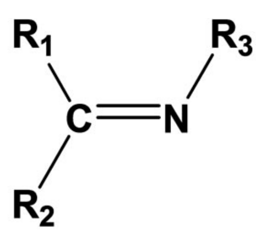
effective cancer treatments than conventional anti-cancer medications like cis-platin. Zn(II) complexes assist in promoting a more rapid recovery from wounds [9,10]. At room temperature, In a range of organic solvents, Schiff bases are miscible, but water is the only solvent that they are insoluble in [11].

This ring form is likely biologically active because it has a high aromaticity, which makes it more stable in living organisms and less toxic to vertebrate animals, like humans. Schiff bases have a large range of other fantastic uses besides these two as well, such as being used as dyes, agrochemicals, chemosensors, catalysts, chemotherapeutics, anticorrosives, and polymers [12–14]. Schiff bases have a broad range of applications within the chemical sector of the economy. There is a significant amount of interest in the fields of biochemistry and other material sciences, organic and inorganic chemistry, as well as schiff bases [15].

The biological evaluation of Schiff base ligand (L) and its complexes with transition metals was finished by testing its antifungal, antioxidant, and anti-inflammatory effects. TMCSB have been the subject of a significant amount of research about its antibacterial [16], anticancer, antioxidant, antitubercular [17], anticorrosion, antidiabetic, antiviral [18], and antiulcer [19] characteristics.



R_1, R_2 and / or R_3=alkyl or aryl

Fig. 1: General Schiff Base Structure

Schiff's bases are a significant form of ligand in field of co - ordination chemistry, and they can be utilized in many different ways [20, 22]. When these ligands and metal ions come into contact with each other, they form complexes with different shapes that could be active in biological systems [23]. A geometrical constraint is frequently imposed by the -system in a Schiff's base,

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and this system also has an effect on the electrical structure. Scholars have been interested in Schiff's bases' thermochemical properties because they can bind through NO or N_2O_2 donor atom sets [24]. This ability has caught the attention of many scientists.

Schiff's bases are a class of ligands that can connect to a variety of metal ions to form complexes that, in both theory and practice, have advantageous features. This group of ligands is versatile and can change shape [25]. In the last few decades, a lot of research has been done on Schiff's base ligands and the metal complexes they form. Salicylaldimines, which can be made from salicyldehyde and primary amines and are possible O, N-donors, are very popular because they can chelate many different things [26]. This type of Schiff's base is made by putting together various types of amines and C-O compounds.

2. Biological Activities of Schiff Bases

Schiff bases are often bivalent or trivalent ligands that can combine with transition metals to make very stable complexes. These complexes can be created by mixing the Schiff base with the transition metal. The formation of bonds between carbon and nitrogen is an essential step in the synthesis of organic molecules, and this step is accomplished via Schiff base reactions.

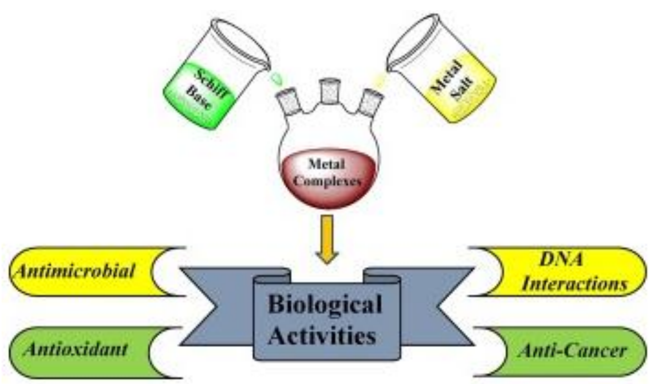

Fig. 2: Biological Activities of Schiff Bases *(Source: https://www.sciencedirect.com/science/article/abs/pii/S1387700321002653)*

Prashanthi et al. [27] studied Ni(II) mixed ligand complexes of 1,10-phenanthroline with distinct Schiff bases (Fig.-4). Many various types of bacteria were used to test how well these mixed ligand complexes killed bacteria. It was found that the antibacterial process of binary complexes was much lesser than that of their tertiary counterparts. This is because the complexes have a

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bigger smooth surface and systems that makes stacking stronger. Changes in the capacity of different complexes to kill dangerous bacteria and fungus could be caused by either variations in the ribosomes of microbial cells or the inability of microbial cells to let things in or out.

Neelakantan et al. (2010) [28] studied several mixed ligand complexes of Mn(II), Co(II), Cu(II), Ni(II), and Zn(II) with o-vanillidene-2-aminobenzothiazole and 1,10-phenanthroline. Also, the chelates described above were mixed with o-vanillidene-2-amino-N-(2-pyridyl)-benzene sulfamide to make Schiff base metal complexes. On many strains of bacteria, fungi and yeast, the bioactivity of free compounds and their Schiff base ligand complexes was tested. The metal complexes had much more powerful impacts than that of the free compounds.

M. Revanasiddappa (2008) [29] investigated the production and characteristics of 1,4(2'-hydroxyphenyl-1-yl) di-imino azine 1,4(2'HPDA) complexes with 1st row transition metals.These results are explained. Element analysis, molar conductance, magnetic studies, infrared, one-half nuclear magnetic resonance, and ultraviolet-visible research have all been used to describe the complexes. [M1,4(2'HPDA)2 2H2O] and [M'L2] are their formulations, where M = Mn(II), Fe(III), Co(II) and Ni(II) and M' = ZrO(II), VO(II), Zn(II), Cd(II) and Hg (II). It has been determined whether or not the metal complexes exhibit any antibacterial or antifungal activity. Antibacterial and antifungal activity has been observed in both the ligand and the complexes.

Nidhal M. Hassan et al. (2013) [30] evaluated the divalent transition metal cations Co(II), Ni(II) and Cu(II) in a new ionic liquid constituted of Al(NO3)3.9H2O/urea at a mole ratio of 1:1.2 and found that they could mix and demonstrated weak co-ordination interactions with ionic liquid species. This was seen when the electronic spectra of these cations changed in intensity or in how they acted when compared to the spectra of the same cations in water and when thiocyanate was added to replace them. It was thought that basic ionic liquid species would have a low ionic strength.

Cezar Spinu [31] investigated Co (II), Ni (II), and Copper (II) complexes of the form ML2Cl2, where M is Co(II), Ni(II), or Cu(II) and L is a Schiff base produced by combining 2-thiophenecarboxaldehyde with either propylamine, N-[2-thienylmethylidene]-1-propanamine (TNAP) or ethylamine. Magnetic susceptibility data, electronic and ESR spectra, a distorted

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structure, a tetrahedral geometry and a D4h symmetry are all things that should be present in the Cu(II) and Ni(TNAE)2Cl2 complexes. The IR and NMR spectra of the complexes show how the nitrogen and sulfur atoms are linked to the metal atom in the middle. The complexes are not electrolytic according to conductance measurements, while $Ni(TNAP)_2Cl_2$ is 1:2.

Anu Kajal and colleagues (2013) [32] investigated the hypothesis that Schiff bases are produced when primary amines react with carbonyl compounds. It was discovered that Schiff bases are a useful pharmacophore which can be used to make a broad variety of lead compounds with biological activity. This was figured out. In these compounds, you can find a functional group called an imine or an azomethine (-C=N-). Schiff bases have many useful biological effects, such as being anti-inflammatory, antibacterial, antituberculous, anticancer, antihelmintic, antiglycation and antidepressant. In the organic synthesis process, as well as catalysts, pigments, dyes, and intermediates are also made. Schiff bases are employed to create corrosion inhibitors, polymer stabilizers, and polymer stabilizers.

C. Batiu (2005) [33] focused at the 4-(4-ethoxy-phenylhydrazono)-1-phenyl-3-methyl-1H-pyrazolin-5 compound (4H) –one was the ligand (H-EMPhP). Its complexes with cu(II), cobalt(II) and Ni(II) were made and their thermal and spectral characteristics were discussed. The bidentate ligand is the azocoupling product (H-EMPhP) that also can do the azo-hydrazone tautomerism. This means that it works with both N2 in the azogroup of its common anion and O2 in the pyrazole ring of the same anion.

Nitu et al. [34] reported nine new compounds of the types [ML1Cl2], [ML2Cl2], and [ML3Cl2] 12-membered tellurium bearing tetraazamacrocyclic ligands]. These complexes were made with the help of the 1,3-diaminoprop. To find out what these complexes are like, the elements were studied, the conductivity was measured, the magnetic susceptibility was measured, and IR spectra, electronic absorption spectra and proton magnetic resonance spectra were taken. The most likely structure for each of these metal complexes is a structure with eight sides.

Zhou et al. [42] reported that they made N, N'-(Z-allylidene-1,3-diyl)bisamino acid methyl esters that are 17 new Schiff's bases. These Schiff's bases display a moderate amount of analgesic effect against the tail flick mouse model. Rana et al. [43] have provided a comprehensive analysis of the most important examples of Schiff bases, which demonstrate analgesic, anti-

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inflammatory, and non-ulcerogenic properties. Schiff bases of gossypol have been shown to possess potent antiviral activity [44]. The Schiff base formed from chitosan and carboxymethyl-chitosan demonstrates a high level of antioxidant activity [45]. Several Schiff bases were created, described based on their spectrum data and tested for antibacterial activity in vitro against gram-positive bacteria, gram-negative bacteria and fungi [46].

2.1 Antimalarial activity

Malaria is a disease that does not receive sufficient attention, despite the fact that it continues to create a great deal of trouble for the public's health. About 500 million individuals are estimated to be afflicted with the sickness on a yearly basis, and between 1 and 3 million of those people are estimated to die as a direct result of the illness [35]. Young children make up the vast bulk of individuals who perish in countries located south of the Sahara. Malaria is caused by a parasite called Plasmodium, which can show up in one of four different ways (P. falciparum, P. vivax and P. malariae). Female Anopheles mosquitoes [36] that are part of the genus Anopheles pass Plasmodium from one host to another.

2.2 Antibacterial activity

The majority of the increase in mortality rates from viral infections is attributable to germs that have developed resistant to a significant number of different medications. The fact that there are currently no treatments that have been demonstrated to be effective is the key element that is contributing to this problem [37, 38]. In the realm of medicine, there is no question that the research and development of new antibacterial medications that utilize novel modes of operation and are also more effective is of the utmost significance [39]. More and more evidence suggests that Schiff bases may be able to eliminate microorganisms. N-(salicylidene)-2-hydroxyaniline (4; Fig. 3) is one example of a compound that inhibits the growth of Mycobacterium TB H37Rv and has a minimum inhibitory concentration value of 8 lg/mL [40].

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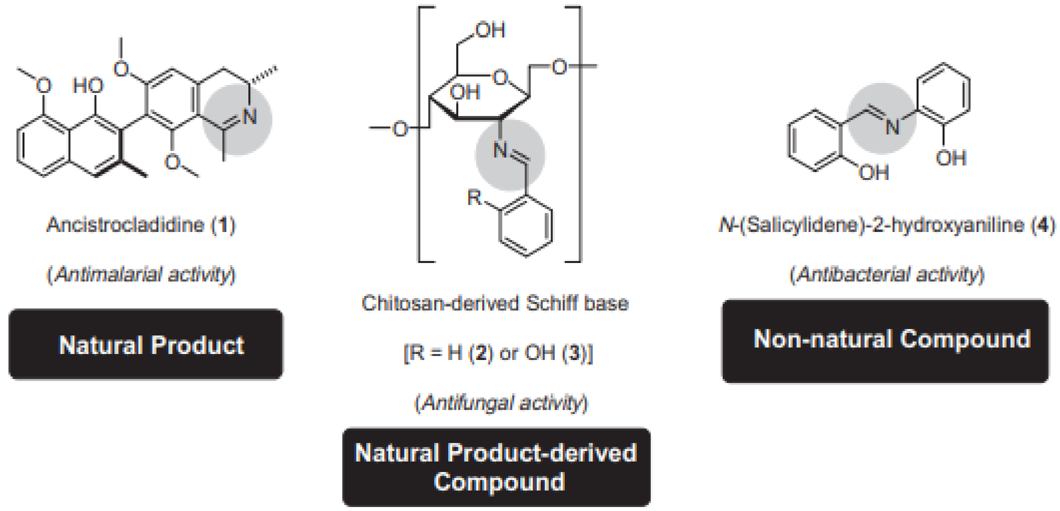

Fig. 2: Examples of Schiff bases those are bioactive. Each molecule is shaded where there is an imine or azomethine group.

2.3 Schiff base anti-cancer activity:

Cancer is the umbrella word for a group of diseases in which an abnormal clump of cells grows and spreads without any discernible pattern or order. The term "malignant neoplasm" is another term that can be used to refer to cancer. It is still the diagnosis that scares people the most, and it is still a huge public health concern all over the world. After heart disease, it is the 2nd major cause of mortality in both developed and developing nations. It's also the second leading cause of death around the world. At the moment, surgery to remove the tumor and chemotherapy are the two most common ways to treat cancer. On the other hand, the chemotherapeutic treatments that are available now do not work as well as they need to in order to cure cancer, and they also have a lot of bad side effects. For the past fifty years, the primary goal has been to produce new drugs with the idea of improving the effectiveness of cancer treatment. In recent years, it has come to light that a considerable number of Schiff bases and derivatives of these bases contain anticancer qualities. These bases have been the subject of much research in recent decades.

3. Catalytic Applications

The environment at the coordination center can be changed in Schiff base metal complexes by adding different ligand substitutes. For the purpose of fine-tuning structure and reactivity, this entails that a broad range of steric and electronic characteristics could be given [47, 48]. It is well

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known that Schiff bases can react with p and d-block metals to form metal complexes and that these metal complexes can function as extremely potent catalysts in a variety of crucial synthesis and other processes [49–52]. A lot of Schiff base complexes like Rh and Pd, must be used to make high-quality polymers. Katsuki focused solely on the investigation into the asymmetric catalysis of the salen transition metals and the related Schiff-base ligands.

Gupta and Sutar looked at the catalytic activity of both simple transition metals and complexes with polymers attached to them. They then put together a summary of what they found. They have demonstrated that the Schiff base complex can be utilized as catalyst for oxidation process, hydrogenations, polymerizations, different coupling processes, and ring closures [54].

3.1 Transition Metal Complexes of Schiff's Base in Catalysis

The development of humanity has been considerably aided by processes accelerated by transition metals. This invention has benefitted a number of very significant industries, including the plastic and agricultural industries. The pharmaceutical sector has benefited greatly from the development of various transition metal catalysts. Obtaining mechanistic insights is a crucial step in the development of novel and more potent catalysts. This thesis presents a number of various approaches for looking into the mechanics of transition metal-catalyzed processes [55].

Schiff's base complexes have different activities depending on the ligands they contain, the number of coordination sites they have, and the metal ions they contain. There are a variety of homogeneous catalytic processes in which Schiff's base complexes play a vital role. According to the findings of previously published research, a few of Schiff's base transition metals have the potential to function as catalysts. Chiral Schiff's base complexes have an extraordinarily high degree of selectivity in processes such as oxidation, hydroxylation, aldol condensation, and epoxidation. Aromatic Schiff's bases or their metal complexes have the potential to speed up reactions involving the oxygenation, hydrolysis, electro reduction, decomposition, and oxygenation of alkenes.

CONCLUSION

Schiff bases are important parts of many different medicines. They are one of the most significant kinds of compounds. Transition metal Schiff base complexes have been getting lots of

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attention lately. This is mostly because they could be used to make new medical therapies and have many uses in the biological field. But it is essential to maintain studying the biological characteristics of these complexes of transition metals which have already made, as well as making new complexes with different properties. The study of Schiff bases is a subfield of chemistry that is still in its infancy as a topic of investigation. The therapeutic chemicals formed from Schiff bases and the metal complexes of those bases are among the most important forms of chemical compounds. This is due to the essential property of structural variation that both of these types of molecules share in common.

Schiff's bases are, in a general sense, ligands with two or three dentate groups that can form quite stable complexes with transition metals. Schiff's bases are used to study transition metal complexes in particular. Some of these materials are used to make liquid crystals. Schiff's base reactions can help form carbon-nitrogen bonds, which can be significant step in organic synthesis. Schiff's bases are believed to serve a significant role as an intermediate in numerous unique enzymatic reactions, especially those where an enzyme interacts with an amino or C-O group on substrates. Schiff's bases are used in processes when an enzymes reacts with an amino or C-O group on the substrate. Schiff's base, which is another name for the biochemical process of producing an imine, is thought to be one of the most significant types of catalytic reactions. In this step, the primary amine of an enzyme, which is generally a lysine residue, binds to a C-O group on a substrate. This results in the formation of an imine. An imine is produced as a result of this procedure. The novel Schiff's base ligands and their complexes are thoroughly evaluated in this paper.

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