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Biological Activities of Metal Complexes of Schiff Bases – A Review

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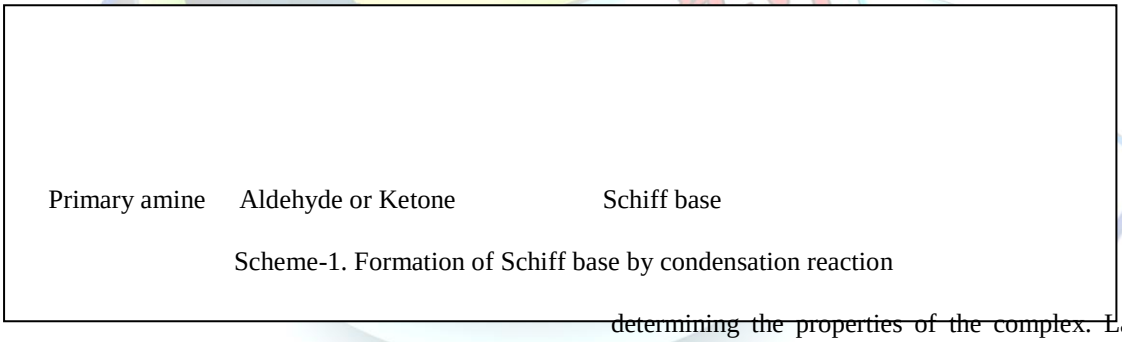
Abstract: Schiff bases have ability to form complexes with transition and inner transition metals and therefore regarded as very important class of organic compounds. Schiff bases serve as special ligands because they are readily synthesized by condensation reactions of aldehyde derivatives with imines. However their production is simple, their modest manufacturing technology and wide range of applications in areas such as coordination chemistry, analytical chemistry, catalysis and medicinal chemistry make them unique compounds. Various bioactivities such as anticancer, antineoplastic, analgesic, antifungal, antiviral, antioxidant, antibacterial, antipyretic, antiproliferative and anti-inflammatory etc. of schiff bases and their metal complexes are being studied. This review highlights synthesis as well as biological applications of various schiff bases and their metal complexes.

Keywords: Schiff bases, bioactivities, analgesic, antineoplastic, antipyretic, antiproliferative,

I. INTRODUCTION

Schiff bases which are the product of condensation of primary amines with carbonyl compounds are described by Hugo Schiff in 1864[1,2]. Schiff bases are synthesized by the condensation of aldehydes or ketones with primary amines and such compounds contain azomethine group (HC=N).They are also called as imines or azomethines and are typically represented by the formula R'R"C=NR where R', R" and R are alkyl or aryl groups[3].



Primary amine Aldehyde or Ketone Schiff base

Scheme-1. Formation of Schiff base by condensation reaction

II. IMPORTANCE OF SCHIFF BASE AND IT'S METAL COMPLEXES

Schiff bases form metal complexes with transition metal ions very efficiently and they act as very good chelating ligands[4,5]. The metal ion incorporated in schiff base complex is essential in determining the properties of the complex. Large number of transition and inner transition metals form schiff base metal complexes by combining with bi, tri and tetra dentate schiff bases having donor atoms like nitrogen and oxygen [6, 7]. The schiff bases and their metal complexes are widely used in regio-selective ring opening of epoxides[8] and as a membrane in ion selective electrode [9-13]. The schiff bases and their metal complexes also finds use in versatile catalytic reactions for organic synthesis [14-17]. The schiff bases and their metal complexes are also used in transistor [18], in defense as gas generating agents [19] and pyrotechnic mixtures [20]. Schiff bases are regarded as an important class of organic compounds in the medical, pharmaceutical, and biological fields. Broad range of biological activities including antiproliferative, anti-inflammatory, antifungal , antibacterial , antimalarial , antipyretic and antiviral properties were exhibited by schiff bases and their metal complexes[21-24].

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IMPORTANCE OF TRANSITION METAL COMPLEXES

Transition metal complexes and metal based complexes possess the ability to co-ordinate with ligands in a three dimensional configuration, thereby perform various functions.

1) Transition metal complexes in cancer treatment :

Transition metal complexes are very useful in medicinal chemistry. The medicinal use of transition metal complexes in leukemia and cancer has been reported since the 16th century. In 1960, the inorganic complex, cisplatin was discovered which is still one of the best selling anti cancer drug in the world. Metal complexes formed with other metals such as copper, tin, gold , ruthenium and iridium show significant antitumor activity in animals.

2) Transition metal complexes as anti-bacterial agent :

Various transition metal complexes have been used for years as anti-bacterial agent. In general, sulfonamide copper(II) complexes exhibit antibacterial activity against both Gram (positive) and Gram (negative) bacterial types [25]. Zinc Diabetes mellitus is characterized by high blood sugar levels known as hyperglycemia and caused because of insulin deficiency and insulin resistance. Ingestion of chromium metal complexes shows a significant reduction in glucose levels [29]. In addition, zinc (II) complexes are effective in lowering blood glucose levels in type 2 diabetes in animals [30].

III. PREVIOUS RELATED STUDIES

(II) complexes of amino acids with antibacterial activity have been developed.

3) Transition metal complexes as anti-fungal agent :

Large numbers of transition metal complexes have been used as anti-fungal agent. Zinc (II) complexes of sulfadrugs such as sulfadiazine and sulfamerazine also proved to be effective anti-fungal agents against *Aspergillus* and *Candida sp.* Moreover, the activity of the complexes were higher than that of the free ligands, but lower than that of the drug ketoconazole [26] . The cobalt (II) complex also exhibits antifungal activity. Anti-fungal activity against *Aspergillus sp.* and *Penicillium sp.* was also found for Copper (II) complexes of *p*-amino acetophenone benzoylhydrazone [27].

4) Transition metal complexes in neurological disorder :

Complexes of transition metals also play a key role in the treatment of various neurological disorders. Transition metals such as zinc and copper act as transmitters in neuronal signalling pathways [28].

5) Transition metal complexes in Diabetes:

Abubakar Abdullahi Ahmed, Hassan Usman Ali, Abdullahi Idi Mohammed[31] synthesized schiff base derived from 4-methoxybenzaldehyde and *o*-aminobenzoic acid (Scheme-2) . They also synthesized Ni (II) metal complex of schiff base (Figure-1). This study gives a square planar geometry for the complex.

Scheme-2

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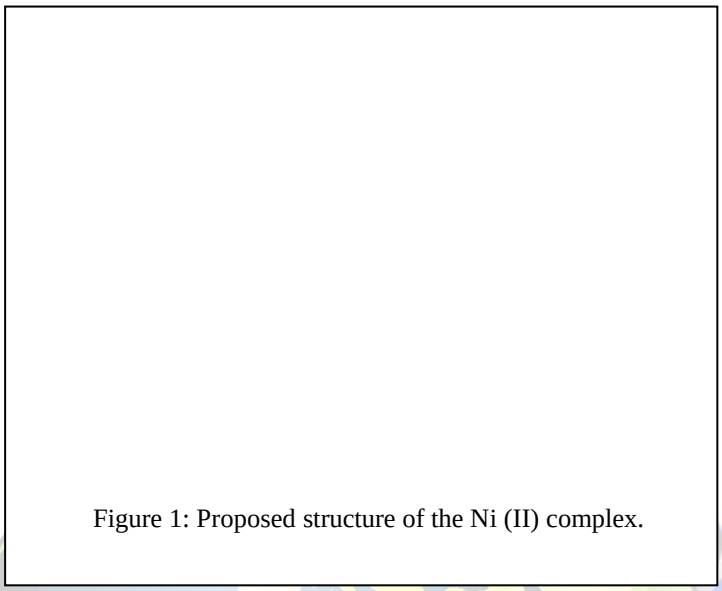

Figure 1: Proposed structure of the Ni (II) complex.

Synthesis of schiff bases with substituted benzylidine aminobenzoic acid was done by Govindaraj V, Ramanathan S, Murgasen S[32](Figure- 2 & 3) .They also synthesized Ni(II) metal complexes with the ligands L^1 and L^2 (Figure- 4&5).

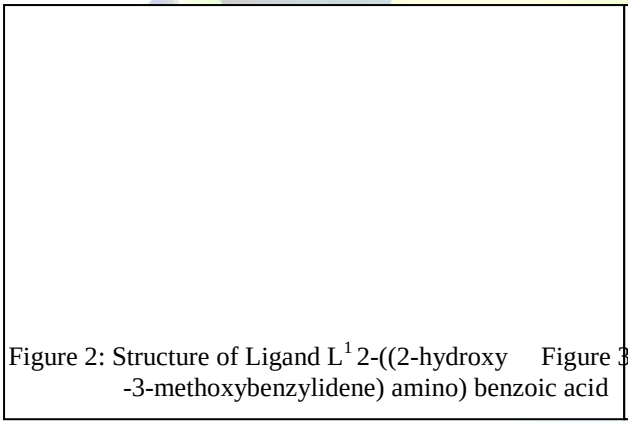

Figure 2: Structure of Ligand L^1 2-((2-hydroxy -3-methoxybenzylidene) amino) benzoic acid

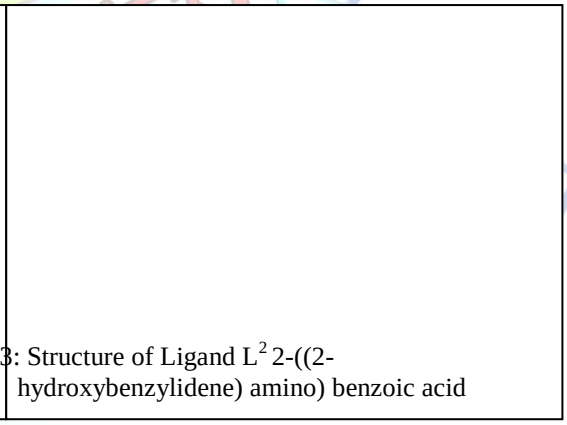

Figure 3: Structure of Ligand L^2 2-((2-hydroxybenzylidene) amino) benzoic acid

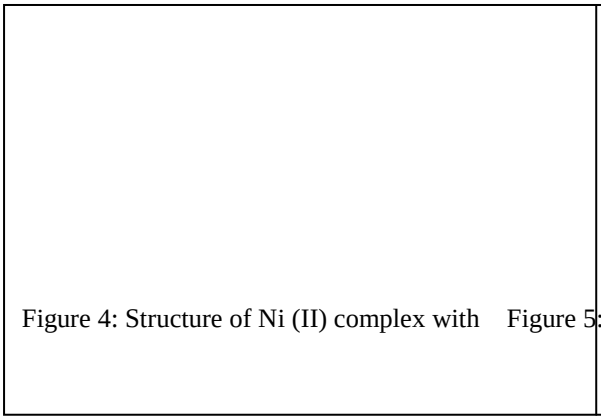

Figure 4: Structure of Ni (II) complex with

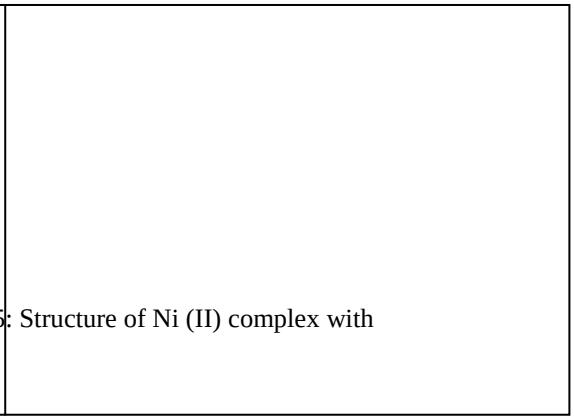

Figure 5: Structure of Ni (II) complex with

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ligand L^1, $[Ni(L^1\text{-}2H)(H_2O)_3].H_2$

ligand L^2, $[Ni(L^2\text{-}2H)(H_2O)_3].H_2O$.

Synthesis of two novel schiff bases namely 1-(cyclopentyliminomethyl)napthalen-2-ol and 4-nitro-2(cyclopentyliminomethyl)phenol was done by Guo[33] (Scheme- 3&4). These schiff bases were synthesized by the reaction of cyclopentylamine with 2-hydroxy-1-naphthaldehyde and 5-nitrosalicyaldehyde , respectively in methanol. He also synthesized two new complexes by using Zn metal (Figure- 6&7) . The schiff bases and it's Zn metal complexes exhibit stronger antibacterial activity against *E.coli* and *P. fluorescens* but weaker antibacterial activity against *B.subtilis* and *S.aureus* than Penicillin. The Zn metal complexes of these schiff bases exhibit greater activities against all the bacteria than the schiff base ligands.

Scheme-3

Scheme-4

Figure 6

Figure 7

Two novel schiff bases were synthesized by Cai[34] (Scheme-5). Cai also synthesized two Cu metal complexes of schiff bases (Figure- 8&9). These two complexes exhibit same activities against *B. subtilis, E.coli., P. putida*. Complex II shows stronger activity for *S. aureus* than complex I.

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Scheme-5

Figure 8

Figure 9

Nassar M. Y., Ahmed I. S., Dessouki H. A. and Ali S. S.[35] synthesized three schiff bases from 2,5-dihydroxyacetophenone (Scheme-6). They also synthesized Cu^{+2}, Zn^{+2}, Cd^{+2} and Hg^{+2} complexes of these schiff bases (Figure- 10-12) . These schiff bases have antifungal activity against one yeast (*C.albicans*) and antibacterial activities against one gram positive bacteria *(S. aureus*) and three gram negative bacteria (*E.coli, K. pneumonia and P. vulgaris*). Third compound exhibits less activity than first and second compound. Metal complexes of these schiff bases also shows antimicrobial activities.

Compound (L_1); X= -H, Z= $-CH_3$
Compound (L_2); X= -OH, Z= -H
Compound (L_3); X= $-OCH_3$, Z= -H

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Scheme-6

Figure 10

Figure 11

M = Cu, Zn, Cd and Hg
Figure 12

IV. CONCLUSION

As schiff bases form complexes with transition metals, they are very important organic compounds. They also shows pharmacological properties and has industrial and medicinal applications. This literature study proved that schiff bases and their metal complexes show better biological activity. Therefore, we decided to synthesize 2-(salicylideneamino) benzoic acid as ligand and it's metal complexes for the future study of biological activities such as antioxidant , antibacterial and antifungal activities.

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