

SYNTHESIS AND BIOLOGICAL ACTIVITIES OF SCHIFF BASES AND THEIR DERIVATIVES: A REVIEW OF RECENT WORK

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Abstract—Schiff base metal complexes are derived by the condensation reaction of amine and aldehydic groups. Schiff bases devised by an amino and carbonyl compound which are an important class of ligands which are coordinated with the metal ions via azomethine nitrogen and have been studied extensively. In azomethine derivatives, the C=N linkage is necessary for biological activity, several azomethine have been recognised to possess remarkable antibacterial, antifungal, anticancer and antiviral, antimalarial activities. In the present Era or we can say that in present time the Schiff base metal complexes are lucrative compound for industries as well as important in the medical applications. Schiff bases are the appropriate compound having unrivalled application for both the organic and inorganic chemistry. Schiff base ligands and their complexes are shown influenced application in medicinal applications because of their wide of spectrum of biological activities. This review compiles the antibacterial, antifungal, anticancer and antiviral Schiff bases. An overview of synthetic methodologies used for the preparation of Schiff bases is also described. This review can be summarizing the synthesis, characterization and biological activities of Schiff bases and their derivatives.

Keywords: Schiff bases, Azomethine, Antibacterial, Antifungal, Antiviral.

1. INTRODUCTION

Schiff bases are the compounds or the metal complexes which are widely used in medicinal, pharmaceutical field and for industrial purposes. As per the ancient survey, the Schiff bases are also useful ascribe for their application as a catalyst in a reaction which occur at very high temperature. The activity can help to understand the properties of ligands as well as a metal which can used to synthesize the highly active compounds or the large number of metal complexes.

Basically, the Schiff bases are the ligand, a metal which surrounded by a cluster ions or molecules, which are used for the synthesis of complex compounds. Due to existence of C=O and NH₂ groups, both ketones and amines are very reactive organic compounds. The nucleophilic addition reaction of both ketones and amines formed a very important

class of compounds called as Schiff bases. These are synthesized by a condensation reaction of primary amines and an active carbonyl compound (aldehydes/ ketones). Water is byproduct in this reaction. The general formula of Schiff base is RCH=NR¹, where R & R¹ represents alkyl/aryl substituents).^[1] This review shows the Schiff bases and their metal complexes have the characteristics behavior as a catalyst and their various types of important activities such as antimicrobial^[2] anticancer^[3] antiviral.^[4] In present era the transition metal complexes of Schiff base ligand are very interesting topic for studying for young scientist due to their variety of possible structure for the ligand depending upon the ketones/ amines are used and their specific industrial or biological applications.^[5-11]

To know about the Schiff base metal complexes and their various applications we synthesis a variety of homo and heterocyclic Schiff bases. All the synthesized Schiff bases are characterized by using different physical and analytical tools or techniques such as IR, UV, ¹H NMR and Mass Spectra etc. Schiff base can acclimatize various types of metal complexes which coordinate to synthesize different homo and hetero metal complexes with different structures. Schiff base complexes have important and interesting properties like ability to bind oxygen reversibly, catalysis in hydrogenation of olefins, complexity towards some toxic metals and their photochromic properties.^[12] Schiff bases also consider donor atoms such as N, O, S etc. and these donor atoms of the Schiff bases and their derivatives as mixed ligand complexes can play an important role in biological process in which enzyme were activated by the metal ions.^[13-15] These mixed ligand complexes were derived from the heterocyclic compounds of quinoline and its derivatives.^[16] Quinoline are the most important heterocyclic compounds which are used in the formation of mixed ligand complexes.^[17] These derived derivatives have unique phrenological or important biological applications such antibacterial, antifungal,^[18,19] antiviral.^[20, 21] This review compares the different biological activities and their studies of Schiff base metal complexes.

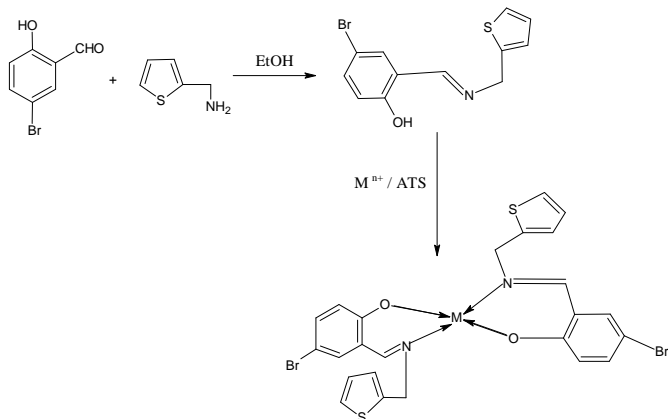
In recent past or in present days Schiff base ligands and their transition complexes have increased significantly interest in students because of some enhancing properties. Some of their compounds are responsible for their unpleasant fragrance or a specific taste thus they are used in various types of beverages like they are used as healthy alcoholic beverages. These types of compounds should be derived from there raw material which are protein, starch and carbohydrates hence these are responsible for the quality of alcoholic beverages as well as their safety products.^[22-24]

2. BIOLOGICAL APPLICATIONS OF SCHIFF BASE METAL COMPLEXES

The enlargement in the branch of bio-inorganic chemistry has expand the interest or engrossment in Schiff base metal complexes, since it has been conceded that many of the Schiff base metal complexes may distribute as modal for important biological applications. Thus, we describe them in following:

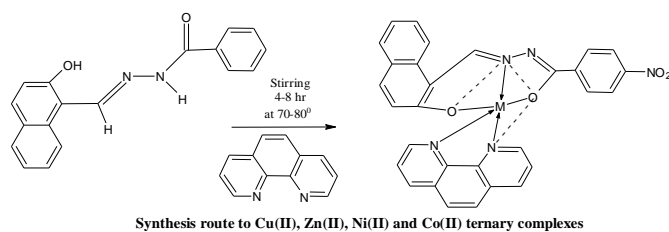
3. ANTIBACTERIAL ACTIVITIES OF SCHIFF BASE METAL COMPLEXES

Schiff base amino acid complexes are obtained from 5-bromosalicylaldehyde (bs) and α -amino acids [*L*-alanine (ala), *L*-phenylalanine (phala), *L*-aspartic acid (aspa), *L*-histidine (his), *L*-arginine (arg)]. Cu(II), Ni(II), Mn(II), Co(II) and Zn(II) metal complexes along Schiff base obtained from the 5-bromosalicylaldehyde and 2-aminomethylthiophene. These Schiff bases and their metal complexes are screened for antimicrobial activities by disc diffusion method antagonistic towards bacteria. Metal complexes display the antimicrobial activities shown in their results. The metal complexes manifest antimicrobial activities and they show magnified inhibitory activity collate with their parental ligands under their condition of experiments. Chelation theory was used to explained the antibacterial activity. The result showed that the tested complexes were reported as antibacterial against Gram-positive and Gram-negative bacterial strains. The complexes are more potent against Gram-positive compare with the Gram-negative bacterial strain. (El-Sharif & Eldebs, 2011)

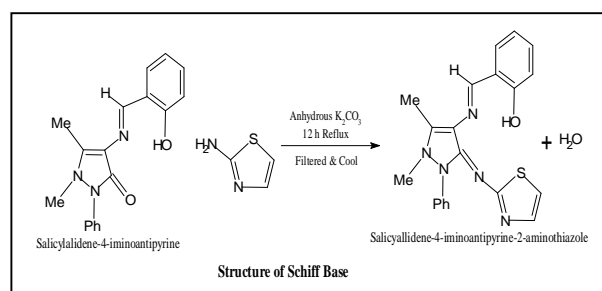


4. ANTIFUNGAL ACTIVITIES OF SCHIFF BASE METAL COMPLEXES

The synthesized Schiff base ligands and there metal complexes were screened against the antifungal activity by well diffusion method (Kirby-Bauer method). The fungal strains of *S. rolfsii* and *M. phaseolina*. The results of the antifungal activity showed that the activity of the synthesized Schiff base ligand and their metal complexes were screened against different types of minimum inhibition concentrations (MIC). The compounds exhibit antifungal activity at the concentration of 1 mg/mL and no antifungal activity were detect at the lower concentration. The result of the antifungal activity showed that the Schiff base metal complexes showed good antifungal activity than the Schiff base ligand. (2017)



The Schiff base metal complexes of new cationic Cu(II), Co(II), Ni(II), VO(II) and Zn(II) are derived from salicylaldehyde-4-imino-2,3 dimethyl-1-phenyl-3 pyrazolin-5-one and 2-aminothiazole. To understand the structural feature of these Schiff base metal complexes with the help of elemental analysis via UV-Vis, ¹H NMR, ¹³C NMR spectroscopies, FTIR, EPR, Fluorescence emission, Powder XRD, FESEM and FAB-Mass spectral measurement. These Schiff base complexes and their various metal complexes are screened against the antifungal activities of chelate against *Candida albicans*, *Rhizoctonia bataicola*, *Aspergillus flavus*, *Aspergillus niger* and *Rhizopus stolonifer* by well diffusion method in which the medium is potato dextrose agar. The result of the screening of Schiff base and their metal complexes against the various fungal strains are described in the minimum inhibitory concentration (MIC). The conclusion of the screening against the antifungal activities showed that the Schiff base metal complexes are more potent in comparison with the Schiff base complexes or we can say that the Schiff base metal complexes shows better result to the Schiff base ligands. (2018DNA)



5. CONCLUSION

In this review articles, the recent progress in the fields of Schiff bases and their derivatives, their structure, characterization and biological applications can be discussed. These ligands and their metal complexes have a significant featured in both industrial as well as in medicinal fields. The Schiff bases are the broad investigator for the applications in industrial fields. Therefore, this class of Schiff base compounds deserve the for investigation in their biological activities. Although the research on the subject of Schiff base and their derivatives is developed, a number of reports disclosing the effect of Schiff base in antimicrobial, antiviral of clinical interest have recently been increasing.

REFERENCES

- [1] Devdatta V. Saraf, Prafullkumar A. Kulkarni, V. G. Deshpande and Seema I. Habib, Heterocyclic Schiff base Cu(II) metal complexes and their X-Ray diffraction study, *European J of Pharm Med Res*, 2017; **4(9)**: 680-683.
- [2] Sulekh Chandra, Seema Gautam, Antibacterial and antifungal activity of Schiff base ligands and their metal complexes- a review, *Int J Chem Pharm Sci*, 2014; **5(2)**: 27-41.
- [3] Parteek Tyagi, Sulekh Chandra, B. S. Saraswat, Deepak Yadav, Design, spectral characterization, thermal, DFT studies anticancer cell line activities of Co(II), Ni(II) and Cu(II) complexes of Schiff bases derived from 4-amino-5-(pyridine-4-yl)-4H-1,2,4-triazole-3-thiol, *Spectrochimica Acta. Part A, Molecular and Biomolecular Spectroscopy*, 2015; 145155-64.
- [4] Anant Prakash, Devjani Adhikari, Application of Schiff bases and their metal complexes- a review, *Int. J Chem Tech Res*, 2011; **3(4)**:1891-1896.
- [5] Senjuti Mandal, Yeasin Sikdar, Dilip K. Maiti, Guru Prasad Maiti, Sushil Kumar Mandal, Jayanta Kumar Biswas, Sanchita Goswami, A new pyridoxal based fluorescence chemo-sensor for detection of Zn(II) and its application in bio imaging RSC Advances, 2015; **5(89)**:72659-72669.
- [6] J. S. Hadi, B. K. Bhkakh, Chaisab, Corrosion, inhibition and biological evaluation investigations of Schiff bases derived from formyl chromone, *Advance App Sci Res*, 2015; **6(5)**:103-112.
- [7] Banabithi Koley Seth, Arpita Saha, Srijan Haldar, Samita Basu, Partha Pritam Chakraborty, Partha Saha, Structure dependent selective efficacy of pyridine and pyrrole based Cu(II) Schiff base complexes towards in vitro cytotoxicity, apoptosis and DNA-base binding in ground and excited state, *J Of Photochemistry and photobiology . B, Biology*, 2016; 162463-72.
- [8] Ikechukwu P. Ejidike, Peter A. Ajibade, Transition metal complexes of symmetrical and asymmetrical Schiff bases as a antibacterial, antifungal, antioxidant and anticancer agents: progress and prospects, *Reviews in Inorganic Chemistry*, 2015; **35(4)**:191-224.
- [9] Abdul Hameed, Mariya al-Rashida, Mahila Uroos, Syed Abid Ali, Khalid Mohammed Khan, Schiff bases in medicinal chemistry: a patent review (2010-2015), *Expert Opinion on Therapeutic Patens*, 2017; **27(1)**:63-79.
- [10] N. Raman, S. Sobha, A. Thamarachelvan, A novel bioactive tyramine derive Schiff base and its transition metal complexes as selective DNA binding agents, *Spectrochimica Acta Part A Molecular and biomolecular Spectroscopy*, 2011; **78(2)**: 888-898.
- [11] Alaah H. Jawad, Jawad K. Shneine, Ahmed Ahmed and Mustafa M. Abdulrasool, Synthesis characterization and evaluation of biological activity of some heterocyclic compound containing 1,2,4-Triazolering, *International Journal of Research in Pharmacy and Chemistry*, 2012; **2(4)**: 2231-2781.
- [12] S. Ajith Sinthuja, Y. Christable Shaji, G. Leema Rose, Synthesis, Characterization and Evaluation of Biological Properties of Transition Metal Chelates with Schiff base Ligands Derived from Glutaraldehyde with L-Leucine, *International Journal of Scientific Research in Science and Technology (IJSRST)*, 2018; **4(2)**:2395-6011.
- [13] Walaah H. Mahmoud, Nessma F. Mahmoud, Gehad G. Mohamed, Z. El-Sonbati, Ashraf A. El-Bindary, Synthesis, spectroscopic, thermogravimetric and antimicrobial studies of mixed ligands complexes, *Journal of Molecular Structure*, 2015; **1095**:15-25.
- [14] A. Z. El-Sonbati, A. A. M. Belal, M. S. El-Gharib, Sh. M. Morgan, Supramolecular structure, mixed ligands and substituents effect on the spectral studies of oxovanadium (IV) complexes of bioinorganic and medicinal relevance, *Spectrochimica Acta Part A*, 2012; **95**: 627-636.
- [15] B. Annaraj, C. Balakrishnan, M. A. Neelakantan, Synthesis, structure information, DNA/BSA binding affinity and in vitro cytotoxic studies of mixed ligand copper (II) complexes containing a phenylalanine derivative and diimine co-ligands, *Journal of Photochemistry and Photobiology B*, 2016; **160**: 278-291.
- [16] Kudrat-E-Zahan M, Haque MM, Ahmmmed L, Ali MS, Islam MS. Studies on the mixed ligand complexes of Co (II), Ni (II) and Cu (II) with phthalimide and heterocyclic amines, *International Journal of Materials Science and Applications*, 2015; **4(2)**:120-3.
- [17] Kulkarni, N.V., Hegde, G.S., Kurdekar, G.S., Budagumpi, S., Sathisha, M.P. and Revankar, V.K., 2010. Spectroscopy, electrochemistry, and structure of 3D-transition metal complexes of thiosemicarbazones with quinoline core: evaluation of antimicrobial property, *Spectroscopy Letters*, 2010; **43(3)**:235-246.
- [18] Sudha N, Selvi G. Synthesis, characterization and biological studies on Fe (II) and Zn (II) quinoline Schiff Base complexes, *International Journal of Chem Tech Research*, 2015; **8**:367-74.
- [19] R Solomon V, Lee H. Quinoline as a privileged scaffold in cancer drug discovery, *Current medicinal chemistry*, 2011; **18(10)**:1488-508.
- [20] Bentzinger G, De Souza W, Mullié C, Agnamey P, Dassonville-Klimpt A, Sonnet P., Asymmetric synthesis of new antimalarial aminoquinolines through Sharpless aminohydroxylation, *Tetrahedron Asymmetry*, 2016; **27(1)**:1-1.

- [21] El-Halim HA, Omar MM, Anwar MN, Preparation, characterization, antimicrobial and anticancer activities of Schiff base mixed ligand complexes, *Journal of Thermal Analysis and Calorimetry* 2017; **130**(2):1069-83.
- [22] Ji Hye Han, Sang Mi Lee and Young- Sun Kim, Effects of Schiff Base Formation and Aldol Condensation on the Determination of Aldehydes in Rice Wine Using GC-MS, *Molecules* 2017; **22**: 618.
- [23] Lago LO, Nicolli KP, Marques AB, Zini CA, Welke JE, Influence of ripeness and maceration of the grapes on levels of furan and carbonyl compounds in wine—Simultaneous quantitative determination and assessment of the exposure risk to these compounds, *Food chemistry*,. 2017; **230**: 594-603.
- [24] Kang HR, Hwang HJ, Lee JE, Kim HR., Quantitative analysis of volatile flavor components in Korean alcoholic beverage and Japanese sake using SPME-GC/MS., *Food Science and Biotechnology*, 2016; **25**(4):979-85.