P: ISSN NO.: 2394-0344 RNI No.UPBIL/2016/67980 VOL-3* ISSUE-12* (Part-2) March- 2019
E: ISSN NO.: 2455-0817 *Remarking An Analisation*

# Schiff Bases and Their Co-ordination Complexes as Antimicrobial Agents: A Review

**Renu Saraswat**
Associate Professor,
Dept. of Chemistry,
Meerut College,
Meerut, U.P., India

**Devesh Sarsawat**
PGT,
Dept. of Chemistry,
Eicher Public School,
Faridabad, U.P., India

**Meenakshi Yadav**
Assistant Professor,
Dept. of Chemistry,
Meerut College,
Meerut, U.P., India

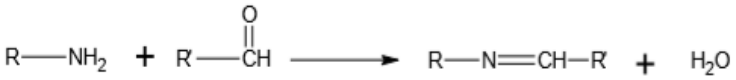
**Abstract**

Schiff bases (also known as azomethines) are the most versatile ligands that are widely used in coordination chemistry as they are potentially capable to coordinate with many transition metals and combine with their different oxidation states. Schiff bases are prepared by the condensing primary (aromatic) amines with aldehydes or ketones as a result of which azomethine (imino) moiety (-CR=N-) is formed .Because of the synthetic flexibility, relative ease of formation and electron donating natural property of C=N group, schiff bases generally act as excellent chelating agents and usually result in the formation of five or six membered ring with the metal ion. There has been an increasing interest towards investigation of the coordination behaviour of schiff bases during the recent years due to the effect of certain transition elements on the biological activity of schiff base compounds and their natural chemical behaviour as multidentate ligands. Many schiff base complexes with transition metal have exhibited a broad spectrum of biological activities which include antibacterial, antitubercular, antiparasitic, antiviral, antifungal, analgesic, antiinflamatory and catalytic activity. This review summarizes some of the important applications of azomethines and their coordination complexes as powerful antimicrobial agents.

**Keywords:** Schiff Bases, Antimicrobial Activities, Ligand, Coordination Complexes.

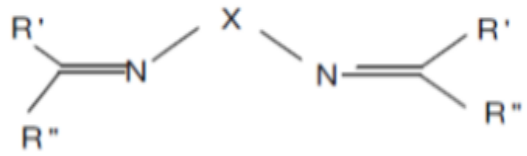
**Introduction**

Schiff bases constitute an important class of ligands in coordination chemistry[1,2] that are derived by the condensation of aliphatic or aromatic aldehydes with aromatic amines and form coordination complexes with a number of transition metals .Metal complexes of schiff bases are widely studied due to their selectivity ,ease of formation and sensitivity towards the transition metal ion. Schiff bases of aliphatic aldehydes are unstable and readily get polymerized but in contrast schiff bases of aromatic aldehydes are more stable on account of their effective conjugation system. Schiff bases are the organic compounds having a carbon -nitrogen double bond as functional group with a general formula RR′C=NR″, where R and R′ represent hydrogen, an alkyl group or an aryl group and R″ is an alkyl or aryl. Schiff bases of aromatic amines are also known as anils. Basic character of the schiff bases play an important role in the formation and stability of the complexes. The nitrogen atom in imines is basic in nature and shows pi-acceptor properties .Majority of Azomethines are found to be stable in basic or alkaline solutions.




Primary amine Aldehyde Schiff base

The bridged Schiff's bases contain many functional groups which are capable to transform according to the requirement. Bridged Schiff's bases have following structure




Bridged Schiffs base (X is alkyl or aryl group)

Schiff base ligands with a variety of donor atoms (like nitrogen, oxygen etc) exhibit some impressive modes of coordination with transition metals and it is the azomethine linkage that is responsible for the biological activities[3] of these compounds. Hydrogen bonding of the schiff bases through their imino group with the biological system[4] may be resposible for their antimicrobial activities.

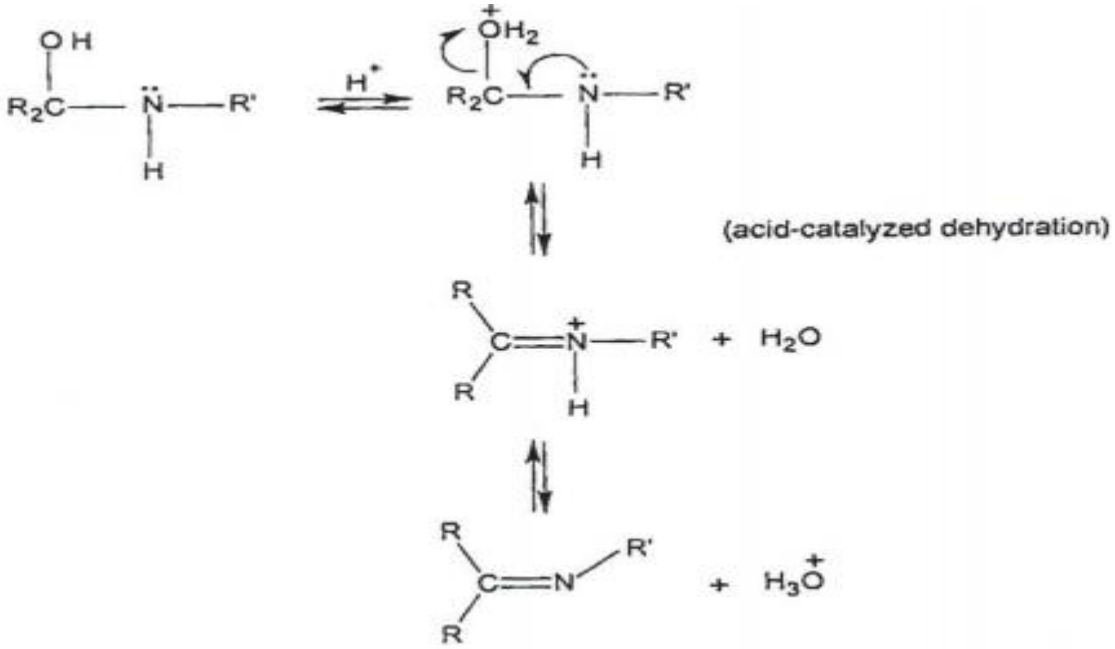
Imine complexes as biological models helps us in understanding the frameworks of many biomolecules and processes occurring inside the living organisms. Schiff bases having imine group helps to illustrate the mechanism of racemization and transamination reactions occurring in biological system[5]. Several azomethine derivatives were found to possess remarkable antibacterial, antifungal, antiviral, antioxidant, anti-inflammatory, anticancer and diuretic activities[6,7]. However with increasing incidences of infectious bacterial and viral diseases, there has been more emphasis on the discovery of some new , more reliable and effective antimicrobial drugs with low side effects. Schiff base chemistry is drawing the attention of many researchers during past few decades because of their application in various fields like and dye industry, catalysis, analytical chemistry, food and biological studies. Due to the various analytical, biological, industrial applications and the versatility of Schiff bases and their coordination complexes it seems highly desirable to further explore this field. In this review some important applications of a few schiff bases and their coordination complexes as powerful antimicrobial agents have been discussed in brief.

**Aim of the Study**

The study is made with the purpose of summarizing the work done on the antimicrobial activities of the natural and non natural Schiff bases and their complexes and to further explore these compounds and synthesize new drugs with diverse biological activities for the mankind.

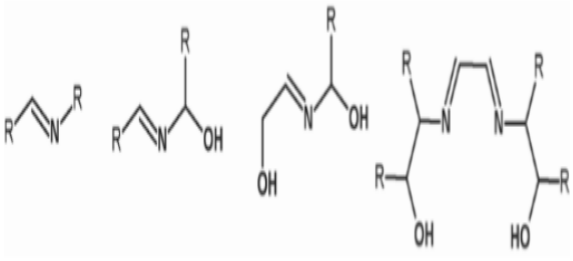
**Mechanism of Formation of Schiff bases**

Schiff base formation is a type of neucleophilic addition reaction on aldehyde or ketone groups. Here amino group is a nucleophile. It is important to mention that schiff base formaton from a carbonyl compound is a reversible process that takes place through acidic as well as basic catalysis under thermal conditions. In the first step of mechamism amino group reacts with the carbonyl (>C=O) compound to form an unstable adduct called Carbinolamine. This carbinolamine then looses water either by an acid or by a base catayzed pathway .Carbinolamine being an alcohol looses water and its dehydration is acid catalyzed .In Schiff base formation reaction the rate determining step is the loss of water from carbinolamines, therefore the reaction is acid catalyzed. Because of the basic nature of amino group concentration of acid should not be high. Protonated amine becomes non-nucleophilic hence the equilibrium is shifted towards the left and formation of carbinolamine is stopped. Therefore, many of the Schiff bases synthesis reactions are carried out at the pH that is slightly acidic. The dehydration (i.e loss of water) of carbinolamines may also proceed in the presence of base. The reaction is quite similar to that of E2 (bimolecular) elimination of alkyl halides or haloalkanes. The reaction is a two steps process proceeding via an anionic intermediate. Formation of schiff base is indeed a series of two sort of reactions first is an addition reaction and the second one is an elimination reaction. Sometimes the schiff bases can hydrolyze back to their respective carbonyl compound and amine by an aqueous acid or base. Iminium salt ($R_2C=N+R_2$) gets rapidly hydrolyzed by water therefore they have to be prepared under strictly anhydrous conditions .The ease of hydrolysis of iminium salt has been used in converting primary amines into secondary amines which involves firstly the conversion into the aldimine ($R_1CH=NR_2$) which is then followed by alkylation in to the iminium salt [$R_1CH=N+R_2$ ($R_3$) X- ] and finally by its hydrolysis to give the secondary amines ($R_2NHR_3$). Imines hydrolysis is an important step in various reactions like Stephen, Sonn-Muller, Sommelet and Gattermann aldehyde synthesis.




**Denticity of Schiff Bases**

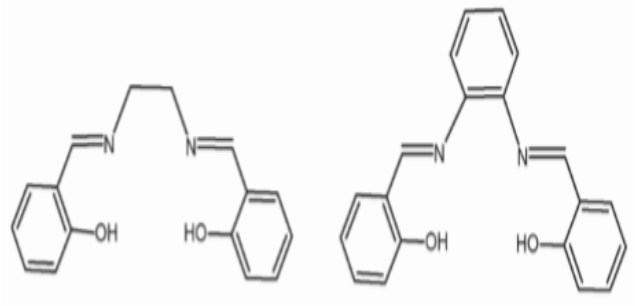
Ligands are classified on the basis of number of donor atoms (atoms that can donate a lone pair of electrons) present in them and are known as unidentate (one donor atom), bidentate (two donor atoms), tridentate (three donor atoms), or quadridentate (four donor atoms) ligands. Whenever a polydentate ligand bonds within the same metal ion through two or more coordination sites, a closed ring complex is formed. This process of ring formation is known as chelation and ring formed is known as chelate ring. In 1920 Morgan and Drew introduced the term 'chelate' derived from *chele* (Greek word) for the complexes containing closed rings. Schiff bases primarily owes nitrogen atoms as donor, though many other type of donor atoms like oxygen, Sulphur may also be present to make the ligand act as bi-, tri-, tetra- or polydentate. Donor nature of the ligands mainly depends on the type of carbonyl compound used as well as the nature of amine used.



**Schiff Bases of Changing Denticity; From Monodentate to Tetradentate, Groups R May Be Varingly Substituted**

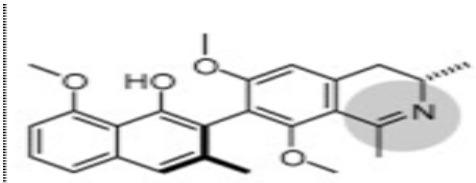
A number of Schiff base with tetradentate ligands that are derived from salicylaldehyde (sal) and ethylenediamine (en) have been reported in the recent years .The $N_2$ $O_2$ donor Schiff bases form a family of compounds, salen or salophen, which possess a wide variety of applications in asymmetric catalysis[8]. Similarly a huge number of tridentate Schiff bases of NNN , ONS, ONN, NNS or ONO donors are reported that can be used in the formation of complexes and such type of Schiff base complexes have been found varying applications in medicinal field such as antiviral agents, antibacterial agents, local anaesthetics, and antispasmodics .

**Tetradentate Schiff Base Ligands Salen and Salophen**

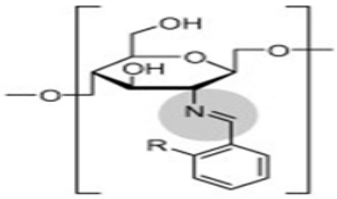


**Antimicrobial Activities**

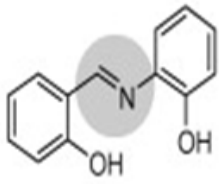
Antimicrobial agents tend to reduce or completely block the growth and multiplication of bacteria and as such these are helpful in the treatment of a number of infectious diseases. Schiff bases have shown to possess a wide number of biological activities that includes antifungal, anticancer and antibacterial, antimalarial, antiproliferative, anti-inflammatory, antiviral, and antipyretic [9].Biological activities of various natural, natural-derived, and non-natural compounds are due to the presence of Imine or azomethine (C=N linkage) present in such compounds. This sort of complexes were explored vigorously in the past few years and the results of such studies have been discussed in many review[10-11].



Ancistrocladidine(1)
(Antimalarial Activity)
**Natural-Product**



Chitosan- derived schiff base
R=H(2) or OH(3)(Antifungal activity)
**Natural Product derived- compound**



N-(Salicyldene)-2-hydroxyaniline(4)
(Antibacterial Activity)
**Non- Natural Product**

Ancistrocladidine (1) Chitosan- derived schiff base N-(Salicyldene)-2-hydroxyaniline (4) (Antimalarial Activity) R=H(2) or OH(3) ( Antifungal Activity) (Antibacterial Activity)
**Natural-Product Natural Product Derived-Compound Non- Natural Product**

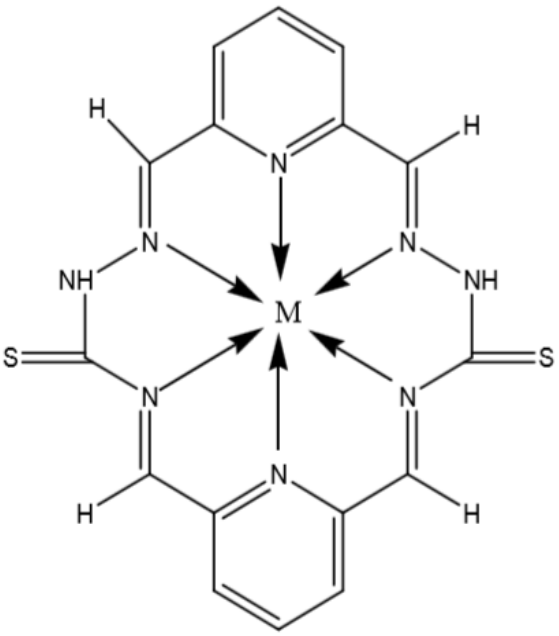
The Schiff bases and their coordination complexes have been found to show good activity against the Gram-positive bacteria *S.aureus*, the Gram-negative bacteria *E. coli* and the fungi *Candida albicans* and *Aspergillus niger*.The results of studies of antimicrobial activities revealed that the coordination complexes show better antimicrobial activity in comparison to the Schiff base ligand. Ligand become more strong and potent bactericidal agent[12] due to chelation.

**Fields of Application of Schiff Bases**

1. Halogen and nitro compounds of Schiff bases are found to possess antibacterial, antiviral, antifungal and antitumor activities. Some derivative of Schiff base & Beta- Lactam acts as good antimicrobial agents [13].
2. Schiff base ligand & metal complexes of sulphur &nitrogen good antibacterial agents [14].
3. The crown ether ligands of schiff bases have shown to possess a very good prospective to act as anti microbial agent [15].
4. Some Copper (II) coordination complexes of Schiff bases with bipyridyl and phenanthroline have been found to be more active towards controlling the fungal diseases in human as well as in plants [16].
5. Schiff's bases and their coordination complexes with transition metal ions containing thiazole were found to be have a broad scope of biological activities.
6. Similarly a considerable number of coordination complexes of schiff base with transition metals like Zn, Co and Cu etc were found to show a huge number of antimicrobial activities[17].

Schiff base coordination complexes of Cr(III), Co(II), Ni(II) and Cu(II) obtained from 2, 6-pyridine dicarboxaldehyde-Thiosemicarbazone (PDCTC) were prepared by microwave as well as standard or traditional methods. In conventional method the preparation of metal complex was done by the mixing equal moles of metal salt solutions in the methanol followed by addition of sodium acetate (metal: ligand) in the ratio of 1:1. The complex precipitated was further filtered and then washing was done with ether.Ethanol was used for the recrystallization of the complex and finally it was dried in a desiccator over the anhydrous $CaCl_2$ under the condition of reduced pressure whereas in microwave method the metal salts and ligands were mixed in 1:1 ratio of metal and ligand in a grinder. The Schiff base and its coordination complexes exhibited excellent activity against the Gram-positive bacteria *S. aureus*, the Gram-negative bacteria *E.coli* and the fungi *Candida albicans & Aspergillus niger.* The results of antimicrobial studies indicated that the coordination complexes show better antimicrobial activity when compared to that of Schiff bases ligand. Chelation makes the ligand to act as more powerful bactericidal agent [18](Fig. 1)

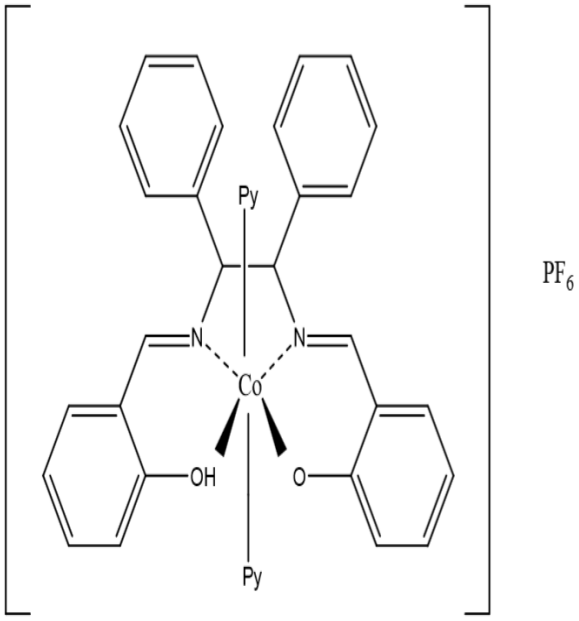
**Fig. 1 [Schiff base coordination complex derived from 2, 6-pyridine dicarboxaldehyde-Thiosemi carbazone (PDCTC)]**




Schiff base coordination Complex from 2 - Hydroxy-3methoxy-5-nitrobenzaldehyde was

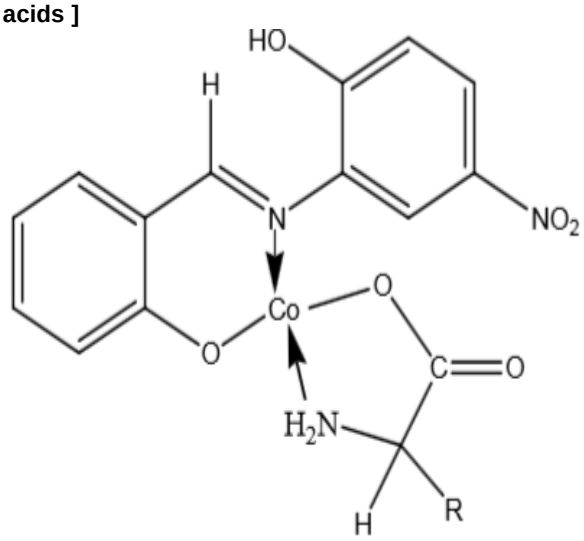
synthesized [19] by K.R.Joshi and coworkers & the newly prepared complex was tested for its antibacterial activities. It was found to be very effective antibacterial agent. Coordination complexes of Schiff bases derived from o phthalaldehyde and amino acids like glycine, l-alanine , l-phenylalanine [20] were synthesized by Neelakantan et al. Antimicrobial activities of these coordination complexes were tested in vitro against various microorganisms by the modified disc diffusion method. Complexes of Cu(II) and Ni(II) showed inhibition towards all the microorganisms that were taken for study whereas Complexes of Co(II) and Mn(II) showed less inhibition and the complexes of VO(II) were not at all active towards the studied microorganisms. Four new tetradentate schiff base coordination complexes ($N_2O_2$ type) of Co(III) were synthesized[20] by the condensing salicylaldehyde derivatives with meso-1,2 diphenyl-1,2-ethylenediamine (mesostilbenediamine). The in-vitro antimicrobial activity of the above mentioned complexes was tested against a number of human pathogenic microorganisms [Fig.2].

**Fig.2 [Schiff base coordination complexes derived from 2 -Hydroxy-3-methoxy- 5-nitrobenzaldehyde ]**



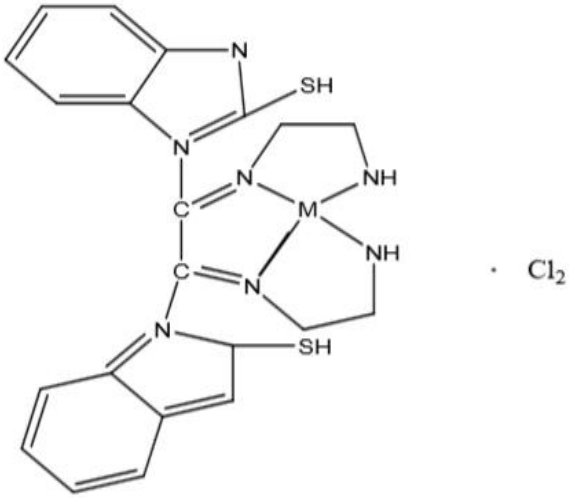

Schiff base coordination complexes of Co(II) derived from 2-amino-4 nitrophenol-N-salicylidene with amino acids were prepared by Ajay R.Patil & coworkers [21]. The schiff base complexes and some complexes of mixed ligands were initially examined against a number of strains of microorganisms to make a study of their biological effects [Fig.3]. These compounds were found to possess very good antibacterial and antifungal activity. Coordination complexes were found to show more activity when compared to the activity of ligand. This indicated that on introducing a metal ion the antimicrobial activity increases.

**Fig.3 [Co(II) complexes of schiff base derived from 2-amino-4-nitrophenol-N-salicylidene with amino acids ]**



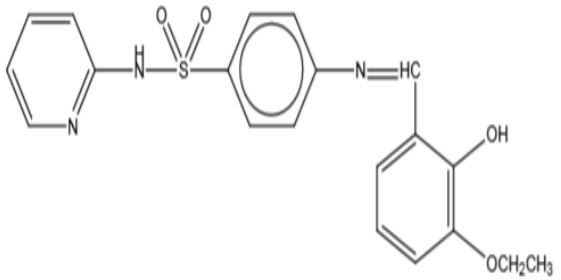

Schiff base ligand was synthesized by the condensation of 2-mercaptobenzimidazole and diethyloxalate by Farukh Arjmand & co -workers [22].The ligand was allowed to react with bis(ethylenediamine)CuII/ NiII complexes to yield complexes [Fig. 4 ].The antibacterial and antifungal studies of the prepared compounds were carried out against *S. aureus, E. coli* and *A. niger*. All the compounds tested were shown to be the active against bacterial and three fungal pathogens.

**Fig.4 [Schiff base derived from condensation of 2-mercaptobenzimidazole and diethyloxalate]**



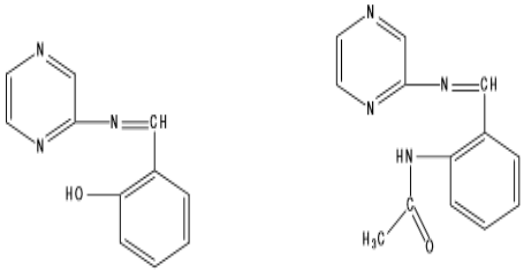

A new Schiff base which was derived from sulpha pyridine and 3 ethoxy salicyaldehyde was prepared by Gomathi Vellaiswami & his co workers [23]. The solid mass of orange colour that was produced during refluxing was collected and then subjected to cooling, filteration and washing, finally it was dried in a desiccator. This Schiff base synthesized by Gomathi Vellaiswami & co workers was found to exhibit excellent antibacterial and antifungal activity against variety of microorganisms [Fig.5].

**Fig.5 [Schiff base ligand, 4-(3-ethoxy-2-hydroxybenzylideneamino)-N-(pyridin-2yl) benzenesulfonamide prepaired from sulfapyridine and 3-ethoxysalicyl aldehyde ]**



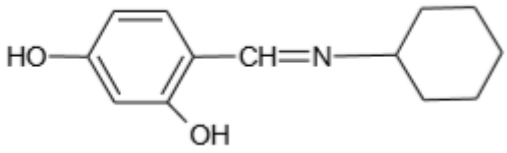
A number of pyrazine-derived biologically active Schiff base ligands were prepared by the condensation reaction of 2-aminopyrazine with acetamidobenzylaldehyde and salicylaldehyde (Fig .6). Then their metal complexes with Co(II), Ni(II) & Zn (II) have been prepared. The prepared ligands and their coordination complexes were subjected to the determination of their biological activity against bacterial strains namely *Staphylococcus aureous, Escherichia coli and Pseudomonas aeruginosa*[24].

**Fig.6 [Schiff base ligands derived from the condensation reaction of 2-aminopyrazine with salicylaldehyde and acetamidobenzylaldehyde]**



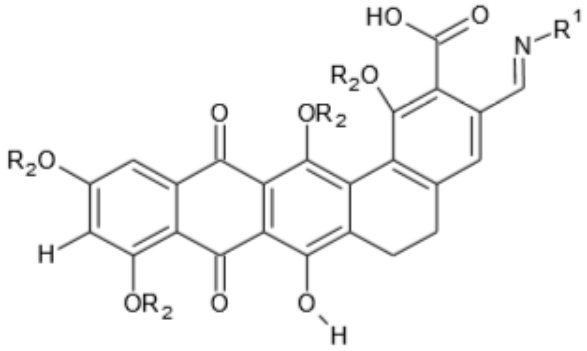
Schiff bases derived by the condensation reaction of 4-hydroxy salicylaldehyde with cyclohexamine (Fig 7) have been prepared by Kim and coworkers and found it a potent inhibitor of Escherichia coli with antimicrobial activity [25].

**Fig. 7 [schiff base ligand derived from the condensation of 4-hydroxy salicylaldehyde and cyclohexamine]**



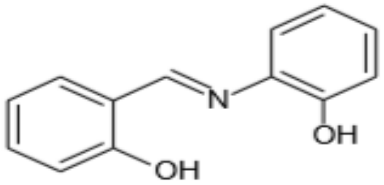
Madurahydroxylactone schiff' bases are the imines that are prepared from natural products. These are secondary metabolites of the plant Actinomadura rubra[26]. The imines (Fig .8) are the excellent examples of the Schiff bases of this class, all compounds derived Madurahydroxylactone were found effective in the in-vitro inhibition of *M. flavus, B. subtilis, S. lutea, and S. aureus growth* [27].

**Fig.8 [Madurahydroxylactone schiff's base derived from natural products.]**



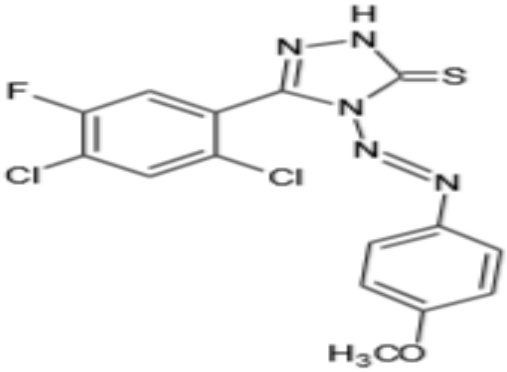
Some phytopathogenic fungi like Alternaria brassicicola & Alternaria brassicae badly affect the production of many crops of cruciferae family (cauliflower, turnip, cabbage, broccoli ,rape, mustard, and radish).It was found that N-(Salicylidene)-2-hydroxyaniline(Fig. 9) control the growth of these fungi by 67–68% [28] when it is used at a concentration of 500 ppm.

**Fig. 9 [Schiff base derived from N-(Salicylidene)-2-hydroxyaniline]**



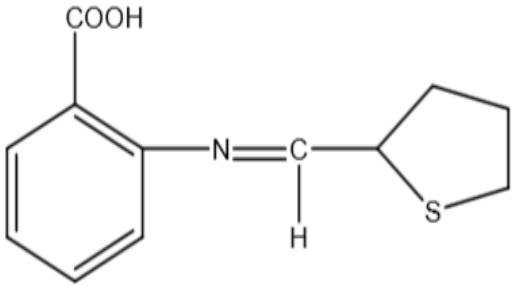
Schiff's bases prepared from 2, 4-dichloro-5-fluorophenyl moiety e.g compound(Fig .10) have exhibited to control the growth of fungi that are of clinical interest, such as *Aspergillus flavus, Aspergillus fumigatus*, *Penicillium marneffei* and *Trichophyton mentagrophytes*,. The minimum inhibitory concentration (MIC) values for these compounds was found to be optimum in the range of 6.3–12.5 µg/mL, showing that they are as powerful as the drug fluconazole [28] is.

**Fig. 10 [Schiff's bases derived from 2, 4-dichloro-5-fluorophenyl moiety]**



Schiff base derived from 2-nitro benzoic acid and 2-thiophene- carboxy- aldehyde was synthesized by A.V.G.S. Prasad & co-workers. Metal complexes of this Schiff base were also synthesized using the salts of Mn (II) and Co (II) in an alcoholic medium. Various spectroscopic methods were used to confirm the chemical structures of the Schiff-base ligand and its coordination complexes [Fig. 11]. These schiff bases and their coordination complexes were tested for their Antibacterial as well as antifungal activities by disc diffusion method and the results were discussed. The experimental results showed that the coordination complexes of schiff bases are more powerful in antibacterial and antifungal activities [29].

**Fig.11 [Schiff base derived from 2-thiophene-carboxy- aldehyde and 2-nitro benzoic acid ]**




**Conclusion**

Schiff bases and their metal complexes are one of the most important class of chemical compounds that have been explored extensively for their biological activities and has shown to be promising leads for the design of more efficient antimicrobial agents. Mortality rate of the diseases caused by the infectious bacteria is increasing day by day because of the multiple resistance of bacteria towards the antibiotics .Similarly there is a significant increase in the incidences of fungal infection in last few years which is life threatening as fungal infections are limited not only to the surface tissues. Therefore, the search for antimicrobials is a never-ending task and it is an urgent medical need to develop new and more effective antibacterial and antifungal drugs..Concisely, Schiff bases are among the molecules which have therapeutic prospects for the treatment of a number of infectious human diseases. Hence there is strong need to explore these compounds and synthesize new drugs with diverse biological activities for the mankind.

**End Notes**

1. *V Ambike, S Adsule , F Ahmed. "Copper conjugates of nimesulide Schiff bases targeting VEGF, COX and Bcl-2 in pancreatic cancer cells," Journal of Inorganic Biochemistry. 2007; 101(10):1517-1524.*
2. *Ashok N Patange, Uttam M Yadav, Pratik A Desai, Pravin U Singare. Synthesis of some Novel Halogenated Platinum (II) Complexes of Active Schiff's Base Ligand Derived from 5-Bromo Isatin and Evaluation of their Antibacterial Activity, World Scientific News. 2015; 10:32-43*
3. *S Chandra , D Jain ,A.K Sharma and P.Sharma. Molecules, 2009;14, 174.*
4. *Enis Nadia, Md Yusof, Thahira Begum SA, Ravoof, Edward RT, Tiekink. Abhimanyu Veerakumarasivam, Karen Anne Crouse, Mohamed Ibrahim Mohamed Tahir and Haslina Ahmad,Synthesis, Characterization and Biological Evaluation of Transition Metal Complexes Derived from N, S Bidentate Ligands, Int. J. Mol. Sci. 2015; 16:11034-11054.*
5. *Ashraf Mahmood K.,Wajid A.:Synthesis ,Charcterization and Biological Activity of Schiff Bases.IPCBEE 2011,10,1-7.*
6. *P. Panneerselvam, R.R. Nair, G. Vijayalakshmi, E.H. Subramanian,S.K. Sridhar, Eur. J. Med. Chem. 40 (2005) 225.*
7. *J. Wang, Z. Lioh, H. Wang, X. Jih, Y. Liu, J. App. Poly. Sc. 123(6)(2011) 3242.*
8. *E. N. Jacobsen, M. L. Güler and W. Zhang, J. Am. Chem. Soc., 1991, 113, 6703–6704*
9. *P. Przybylski, A. Huczynski, K. Pyta, B. Brzezinsk i, F. BartlBiological properties of schiff bases and azo derivatives of phenolsCurr Org Chem, 13 (2) (2009); pp. 124-148*
10. *C.E. Powell, M.G. Humphrey, Coordination Chem. Reviews. 248(2004) ;725.*
11. *Anita Rani1*, Manoj Kumar1, Rajshree Khare2 and Hardeep Singh Tuli3 Journal of Biological and Chemical Sciences (JBCS) (2015); vol.2, no. 1, 62-91*
12. *Mohammed Fakruddin Ali Ahmed and V. Mahammad Yunus, Oriental Journal Of Chemistry, Vol. 30, No. (1), 2014,;Pg. 111-117.*
13. *S. Meenachi et al, A Review of Chemistry and Biological Importance of Schiff Base,International Journal of Scientific Research and Reviews, IJSRR 2014 ISSN: 2279–0543, 3(1),pp 08- 18.*
14. *Cleiton M. da Silva, Daniel L. da Silva, Luzia V. Modolo, B. Alves Cleide V.B. Martins Aˆ ngelo de Fa´ tima, Schiff bases: A short review of their antimicrobial activities Journal of Advanced Research, (2011); 2, 1–8.*
15. *A. Kaura, Lalit Sharma and V. J. Dhar , Antimicrobial Study Of Schiff Bases And BetaLactam Derivatives, Int. J. Chem. Sci.: 2011, 2009-2015, 9(4), ISSN 0972-768X.*
16. *B.K. RAI and Rachana Kumari, Oriental Journal Of Chemistry, ISSN: 0970-020 X , CODEN: OJCHEG, 2013; Vol. 29, No. (3),Pg.1163-1167.*
17. *S.Chandraleka, G.Chandramohan, D. Dhanasekaran, P. Meenakumari and A. Panneerselvam Antifungal activity of amino acid schiff base Copper (II) complexes with phenanthroline and bipyridyl, International Journal of Chemical and Analytical Science, ISSN: 0976-1206, 2011, 2(10), 1235-1240.*
18. *Mohammed Fakruddin Ali Ahmed and V.Mahammad Yunus,Microwave Synthesis & Antimicrobial Activity of Some Cu(II),Co(II),Ni(II) & Cr(III) complexes with Schiff base 2,6-pyridinedicarboxaldehyde Thiosemicabazone,Oriental Journal Of Chemistry(An International Open Free Access, PeerReviewedResearchJournal) ISSN: 0970-020 X CODEN: OJCHEG, 2014;Vol. 30, No. (1): Pg. 111-117*

19. *K. R. Joshi, A. J. Rojivadiya and J. H. Pandya, Synthesis and Spectroscopic and Antimicrobial Studies of Schiff Base Metal Complexes Derived from 2-Hydroxy-3-methoxy-5nitrobenzaldehyde Hindawi Publishing Corporation International Journal of Inorganic Chemistry,Volume 2014; Article ID 817412, 8 pages, http://dx.doi.org/10.1155/2014/817412.*
20. *E. Akila, M. Usharani, P. Maheswaran and R. Rajavel,Schiff base : A Review on their Antimicrobial Activities, International Journal of Advanced Scientific & Technical Research,ISSUE 3, VOL. 5,Sept-oct.2013; ISSN 2249-9954,pp: 457-469.*
21. *Ajay R. Patil, Kamini J. Donde, Sambhaji S. Raut, Vishwanath R. Patil and Rama S. Lokhande,Synthesis, characterization and biological activity of mixed ligand Co(II) complexes of schiff base 2-amino-4-nitrophenol-n-salicylidene with some amino acids Journal of Chemical and Pharmaceutical Research, ISSN : 0975-7384, CODEN(USA) : JCPRC5,2012; 4(2):14131425.*
22. *Anju Das Manikpuri,Synthesis and antimicrobial studies on therapeutically significant Schiff bases of Salicaldehyde and sulfonamides,Research Journal of Pharmaceutical, Biological and Chemical Sciences, ISSN: 0975-8585, Volume 1 Issue 2 Page No. 21.*
23. *Gomathi VellaIswami & Selvameena Ramaswamy,Synthesis,Spectral characterization & antimicrobial Screening of novel Schiff base from Sulfa Drugs, International Journal of Pharmacy and Pharmaceutical Sciences, ISSN-0975-1491, 2014; Vol 6, Issue 1.*
24. *Z.H. Chohan and S. Mushtaq, Pakistan Journal of Pharmaceutical Sciences. 13(1), 21(2000);*
25. *L.D.S. Yadav, B.S. Yadav, V.K. Rai, Tetrahedron Lett. 45 (2004)5351.*
26. *L.X. Zhang, Y. Liu, L.H. Cia, Y.J. Hu, J. Yin, P.Z. Hu, Thermochim.Acta. 440 (2006); 51.*
27. *J.Y. Lee, K.W. Jeong, J-U. Lee, D-I. Kang, Y. Kim, Bioorg. Med. Chem. 17 (2009); 1506.*
28. *H. Nakano, H. Haroda, T. Funaoka, K. Akashi, Chem. Abstr. 78 (1973) ;43086.*
29. *A.V.G.S. Prasad, P. Venkateswara Rao, P.S.S. Prasad, Spectral and Biological studies of Manganese (II) and Cobalt (II) Complexes with Schiff Base Derived from 2Thiophenecarboxylaldehyde and 2-nitrobenzoic Acid,International Journal for Pharmaceutical Research Scholars (IJPRS), ISSN No: 2277 – 7873, 2014; V-3, I-1,pp 91-94.*