WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 7.523
Volume 6, Issue 11, 312-320. Review Article ISSN 2277– 7105

ANTIMICROBIAL APPLICATION OF SCHIFF'S BASE AND IT'S METAL COMPLEXES: A REVIEW

R. G. Mahale* and Deepak V. Nagarale

Department of Chemistry, S.S.V.P.S.'s L.K. Dr. P.R. Ghogrey Science College, Dhule, North Maharashtra University, Jalgaon(MS), India.

Article Received on
29 July 2017,
Revised on 19 August 2017,
Accepted on 10 Sep. 2017
DOI: 10.20959/wjpr201711-9596

***Corresponding Author**
Dr. R. G. Mahale
Department of Chemistry, S.S.V.P.S.'s L.K. Dr. P.R. Ghogrey Science College, Dhule, North Maharashtra University, Jalgaon(MS), India.

ABSTRACT

In last decades Aliphatic, Aromatic and heterocyclic compounds containing one or two heteroatoms are gain attention of researchers knowing importance of Schiff's base and its application in pharmaceuticals and drug manufacturing as well as in the synthetic compounds of biological interest.[1] Here we reviewed some synthetic methods, Schiff's base and its complexes formed from condensation of the carbonyls and amines keeping its application regarding biological activity in global prospective. Schiff bases are a popular class of compounds with interesting biological properties. Schiff bases are also versatile metal complexing ligands and have been used to coordinate almost all d-block metals as well as lanthanides and found various application were patented its therapy of Schiff bases.[2]

KEYWORD: Antimicrobial Activity, Schiff's Base, Metal Complex, Inorganic preparations, Pharmaceutical.

INTRODUCTION

Metal-drug complexed compounds are more popular nowadays due to their greater biological activity than uncomplexed ligands of some drugs.[3] In most of cases, it was found that Metal ions affects the action of drugs and in many cases enhance the efficacy of drugs on coordination. Therapeutically, Schiff bases and their metal complexes have been reported to exhibit a wide range of biological activities such as antibacterial including antimycobacterial, antifungal, antiviral, antimalarial, antiinflammatory, antioxidant, pesticidal, cytotoxic, enzyme inhibitory, and anticancer including DNA damage.[4] Metal ions play an important role in different biological processes[5] and they may act as site specific. Biological activity of

metal ions depends on their concentration, they may either promotes the health of the organism or cause toxicity.[6] It was found that metal chelate possess Several biological activity viz., antibacterial, anti-fungicidal, antiviral and anticancer activity.[7] In many cases, it has also been found that the metal-drug complex possess more antimicrobial activity than the uncomplexed ligand themselves.[8] Antimicrobial resistance is fast becoming a global concern with rapid increases in multidrugresistant bacteria. Some previously treatable pathogens are now becoming untreatable, for example methicillin-resistant Staphylococcus aureus (MRSA) and vancomycin-resistant enterococcus (VRE). MRSA (resistant to methicillin, cephalosporins, all beta lactams and occasionally gentamicin, erythromycin and trimethoprim/sulfamethoxazole) VRE (resistant to vancomycin, ampicillin, and gentamicin). To overcome the alarming problem of microbial resistance to antibiotics, the discovery of novel active compounds against new targets is a matter of urgency.[9] Among these novel metal complexes derivatives which show considerable biological activity may represent an interesting approach for designing new antibacterial drugs. This may be due to the dual possibility of both ligands plus metal ion interacting with different steps of the pathogen life cycle.[10]

Metals have played an significant role in biological systems over the years. Many are important to our diets in varying quantities, although people have only recently realized their significance. Introducing metal ions into a biological system may be carried out for therapeutic or diagnostic purposes, although these purposes overlap in many cases. Metals not only provide path for synthesis, but they also introduce functionalities that enhance drugs action.[11-14]

Schiff bases constitute some of the most valuable groups of biomolecules. Some schiffs base can made using Vilsmeier-Hack reactions.[15-18] First reported in 1864 by Hugo Schiff, these compounds gained notoriety due to the ease way of preparation from commercially available inexpensive aldehydes/ketones and primary amines. The azomethine linkage (C-N) allows rapid access to vast libraries of structurally diverse molecular hybrids with interesting biological properties, including antifungal, antibacterial, antimalarial, anti-inflammatory, antiviral, antioxidant, pesticidal and in vitro inhibitory effect against experimental tumor cells. The electrophilic carbon and nucleophilic nitrogen in C-N core confer to Schiff bases the possibility to interact with several nucleophilic and electrophilic biological species, which can lead to enzymes inhibition or DNA replication impairment. Then, Schiff bases are

promising as lead compounds for the rational design of novel cytotoxic and cytostatic small molecules with a mechanism of action that may differ from that of clinically approved anticancer agents.[19-21]

Mausin Khan et al Ciprofloxacin is a derivative of quinolone. Quinolones possesses antibacterial activity and they are structurally related to Nalidixic acid. Various modification has been done in quinolone moiety to enhance antibacterial activity and reduce resistance shown in fig-1.[22]

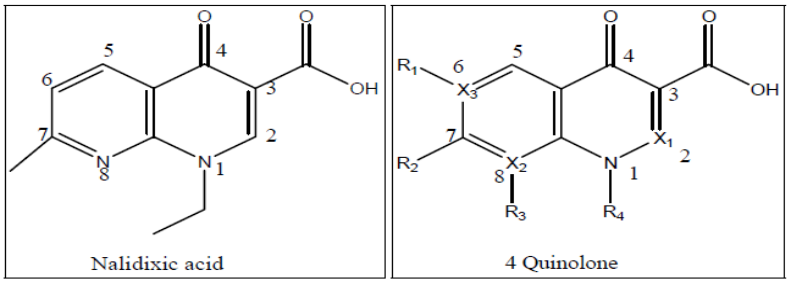
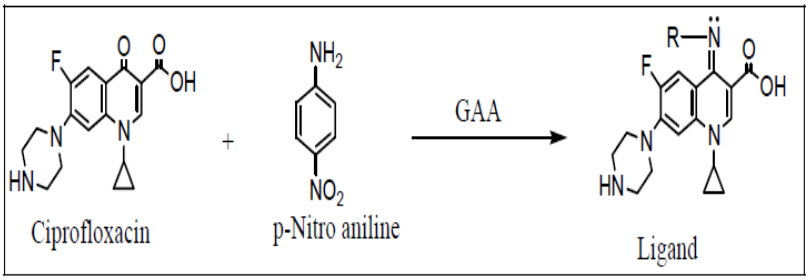


Fig. 1.

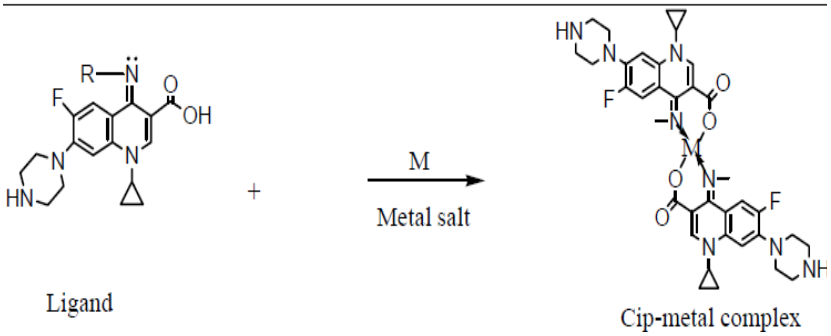
Step I Synthesis of ciprofloxacin imines[23]

Reactions Metal complexes of ciprofloxacin



Scheme. 1: Reactions Metal complexes of ciprofloxacin.

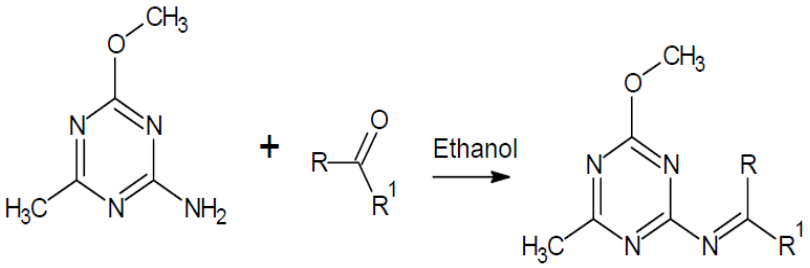
Step II -Synthesis of metal complexes



Scheme. 2: Synthesis of metal complexes.

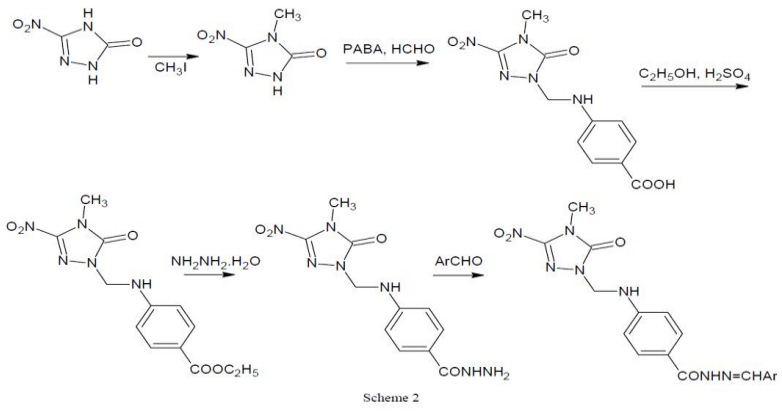
Thirty-nine Schiff bases were synthesized by Cleiton M. da Silva and its co-workers using microwave-assisted condensation of the corresponding aldehydes and aromatic amines. Their reactive nitrogen species (RNS) scavenging activity and inhibitory effects against cancer cell growth were then subsequently investigated. Additionally, the interaction between the calf thymus DNA (ctDNA) and selected Schiff bases was evaluated using fluorescence spectroscopy, and their binding parameters were determined.[24]

R.A. Vasudeva et al. gave in vitro biological evaluation of some novel 1,3,5-triazine– Schiff base conjugates as potential antimyco bacterial agents have been reported with a variety of aromatic/hetero-aromatic aldehydes and ketones in ethanol shown in scheme 3.[25]



Scheme-3: 1,3,5-triazine– Schiff base.

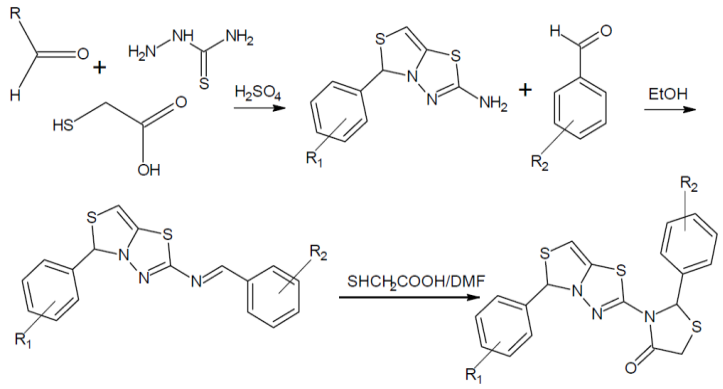
B.P. Pramod and coworkers have reported the synthesis and antitubercular activity of some novel N-methyl triazolone derivatives. The methylation of triazole-5-one gives N-methyl triazolone initially, which then reacted with p-amino benzoic acid and converted to acids, and then to ester and to hydrazide shown in scheme-4.[26]



Scheme. 4: N-methyl triazolone derivatives.

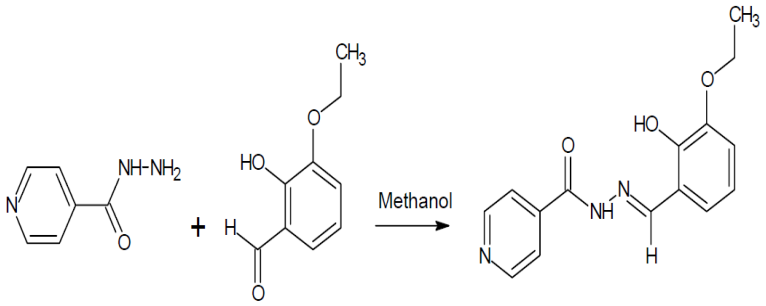
M. Himaja et al. have reported the synthesis and antitubercular activity of some novel thiazolidinone derivatives. Intially 2-amino-5-aryl- 5H-thiazolo[4,3-b]-l,3,4-thiadiazole were

synthesized by mixing of aromatic aldehyde, thioglycolic acid and thiosemicarbazide shown in scheme5.[27]



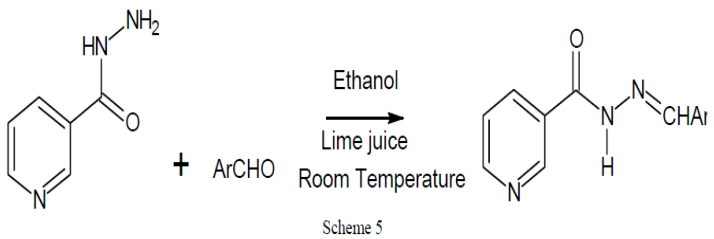
Scheme-5: Synthesis of 2-amino-5-aryl- 5H-thiazolo[4,3-b]-l,3,4-thiadiazole.

P. Elham, K. Hadi and S.R. Nahid, Zahedan synthesised N-(3-methoxyhydroxybenzylidene) isonicotinohydrazide, an isoniazid derivative and studied its antitubercular and antimicrobial activity shown in scheme-6.[28]



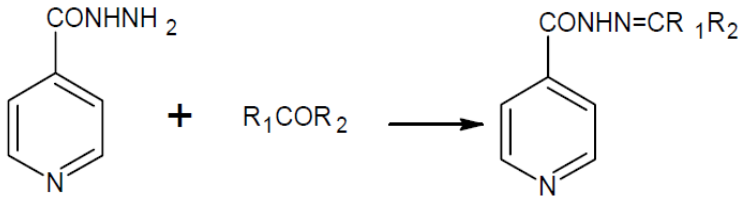
Scheme-6: Synthesis N-(3-methoxyhydroxybenzylidene) isonicotinohydrazide.

D. Vidya and S. Rachana have reported green synthesis of nicotinic acid hydrazide Schiff bases and its biological evaluation. The synthesis was carried out by dissolving nicotinic acid hydrazide in ethanol followed by addition of lemon juice with swirling and then aldehyde at room temperature shown in scheme 7.[29]



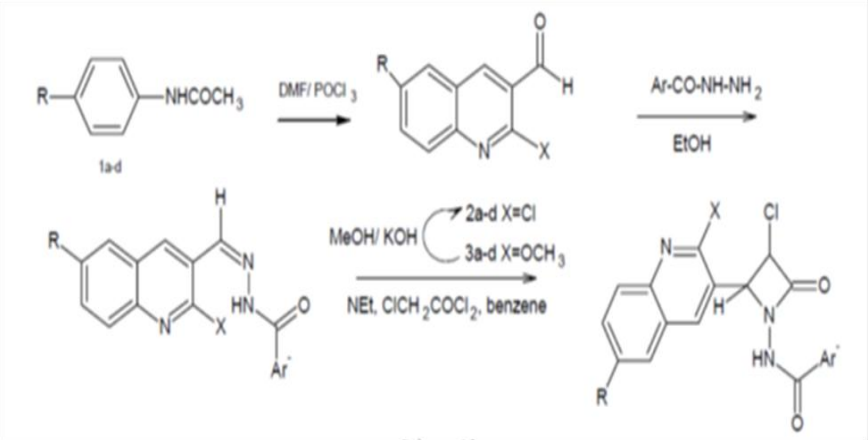
Scheme. 7: Synthesis of nicotinic acid hydrazide Schiff base.

J. H. Michael et al have reported the preparation and antitubercular activities in vitro and in vivo of novel Schiff bases of isoniazid. Schiff bases are readily prepared in good yields, by condensation of isoniazid with the appropriate ketone or aldehyde in boiling alcohol shown in scheme 8.[30]



Scheme-8: Synthesis of Novel Schiff bases of isoniazid.

D.J. Shrinivas et al have reported design, synthesis of quinolinyl Schiff bases and azetidinones as enoyl ACP-reductase inhibitors. Initially 6- substituted-2-chloroquinoline-3-carbaldehydes was chosen as starting material to design Schiff bases. Various 4-substituted acetanilides were treated with Vilsmeier-Haack reagent to obtain 6-substituted-2-chloroquinoline-3-carbaldehydes which was then treated with methanol in the presence of potassium hydroxide furnished 6-substituted-2- methoxyquinoline-3-carbaldehydes. The Schiff bases were prepared by reacting 6-substituted-2- methoxyquinoline-3-carbaldehydes with isoniazid and 4-(1H-pyrrol-1-yl)benzohydrazide in the presence of glacial acetic acid. The 6-substituted-2- chloroquinoline-3-carbaldehydes was reacted with isoniazid in the presence of glacial acetic acid to get N-[(6-substituted-2-chloroquinolin-3-yl) methylene] isonicotinohydrazides shown in scheme 9.[31]



Scheme 9: Synthesis of N-[(6-substituted-2-chloroquinolin-3-yl) methylene] isonicotinohydrazides.

Sunnapu Prasad And Krishnamoorthy Susila were studied and review on the importance of Schiff bases as potent scaffold for antitubercular activity.[32]

CONCLUSION

This review, an informative attempt were made to present a current scenario of the bioactive compounds from schiffs base and its derivatives, moieties possessing diverse electron-donating and -withdrawing groups were prepared that have been investigated for their pancreatic lipase inhibition. The purpose of this review is to provide an overview of the inhibitory activity of naturally occurring and synthetic chalcones.

ACKNOWLEDGEMENTS

We acknowledge The Principal and Head, Department of Chemistry S.S.V.P.S's L.K. Dr. P. R. Ghogrey Science College, Dhule for providing the lab facilities and their constant encouragement.

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