Chapter

Chemistry with Schiff Bases of Pyridine Derivatives: Their Potential as Bioactive Ligands and Chemosensors

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Abstract

Pyridine is a valuable nitrogen based heterocyclic compound which is present not only in large number of naturally occurring bioactive compounds, but widely used in drug designing and development in pharmaceuticals as well as a precursor to agrochemicals and chemical-based industries. Pyridine derivatives bearing either formyl or amino group undergo Schiff base condensation reaction with appropriate substrate and under optimum conditions resulting in Schiff base as product which behave as a flexible and multidentate bioactive ligand. These Schiff bases are of great interest in medicinal chemistry as they can exhibit physiological effects similar to pyridoxal-amino acid systems which are considered to be very important in numerous metabolic reactions. They possess an interesting range of bioactivities including antibacterial, antiviral, antitubercular, antifungal, antioxidant, anticonvulsants, antidepressant, anti-inflammatory, antihypertensive, anticancer activity etc. and considered as a versatile pharmacophore group. Further, several pyridine-based Schiff bases show very strong binding abilities towards the various cations and anions with unique photophysical properties which can be used in ion recognition and they are extensively used in development of chemosensors for qualitative and quantitative detection of selective or specific ions in various kinds of environmental and biological media. These chapter insights the bioactivity and ion recognition ability of Schiff bases derived from pyridine derivatives.

Keywords: pyridine derivatives, Schiff bases, bioactive ligands, pharmacophore, chemosensors, ion recognition

1. Introduction

Nitrogen based heterocyclic compounds are well dispersed in nature and present in large number of alkaloids, vitamins, essential oils, amino acids, metabolites etc. all of them are essential for various biochemical processes and cellular life. Pyridine is considered among the most important nitrogen based heterocyclic compounds which is present in numerous bioactive compounds. Pyridine acts as a versatile solvent and gives different types of reactions including nucleophilic substitution, electrophilic substitution, N-protonation easily. It also possesses some unique optical properties. Due to its important physical, chemical and biological properties, pyridine forms large number of derivatives which are found to be less toxic, but possess much enhanced chemical and biological activities as compared to parent compound. These pyridine derivatives are frequently used in various chemical-based industries like paints and adhesives, dyes and textiles, flavors and perfumes, disinfectants and explosives and so on. They are also used in large scale as a precursor for production of various agro-chemicals like herbicides, insecticides, fungicides etc. Pyridine moieties or scaffold are also present in large number of lifesaving drugs and dietary supplements. Pyridine has capability to bind with number of transition metal ions and form innumerable metal complexes. Some of them are widely used as organometallic catalysts in chemical reactions whereas some others possess unique photophysical and luminescence properties and can be used as electrochemical or colorimetric sensors. The most important applications of pyridine and its derivatives are found in pharmaceutical field due to their significant biological activities. Pyridine nucleus is found to be basic skeleton of large number of bioactive molecules which ranges from Antitubercular, Antibacterial, Antiviral, Antianginal, Antihistaminic, Antiulcer, Antitumor drugs etc. Such bioactive pyridine derivatives bearing excellent coordination and strong binding ability can act as important bioactive ligand and can effectively bind with important biomolecules such as proteins, DNA, coenzymes, amino acids and other metabolites by reflecting their pharmacological potential. Thus, pyridine derivatives or scaffolds form the basis of a potent pharmacophore group having biological significance with important therapeutic applications.

Pyridine derivatives bearing either formyl or amino group readily undergo Schiff base condensation reaction with appropriate substrate and optimum conditions. Schiff bases are the condensation products of primary amines and carbonyl compounds and considered as sub-class of imines. They act as an effective organic ligand due to the presence of imine nitrogen which is basic in nature and exhibits π-acceptor properties. Further, if some other hetero atoms like nitrogen, oxygen or sulfur of a specific functional group is present in vicinity of azomethine group, the schiff base act as multidentate ligands with flexibility in structure. Thus, Schiff bases of pyridine can be regarded as much better ligand as compared to pyridine itself in terms of strong binding ability, flexibility in structure and greater bioactivity. Schiff bases derived from pyridine derivatives are of great interest in medicinal chemistry due to their role of bioactive ligand as these can exhibit physiological effects similar to pyridoxal-amino acid systems which are considered to be very important in numerous metabolic reactions. They possess a wide variety of biological activities that include antibacterial, antiviral, antitubercular, antifungal, antioxidant, anti-inflammatory, anticonvulsants, antidepressant, antihypertensive, anticancer activity and so on. Due to their vast pharmacological activities, they are considered as a versatile pharmacophore. Further, pyridine-based Schiff bases also play important role in analytical chemistry. As Schiff bases show very strong binding abilities towards the various cations and anions, flexibility in their structure and unique photophysical properties, they can be used in ion recognition and therefore they are extensively used in development of different types of chemosensors for selective detection of specific ions in various kinds of environmental and biological media as well as in industrial and agricultural fields.

In the view of the versatile pharmacological properties as possessed by Schiff bases derived from pyridine derivatives, it is expected that they have high potential in the field of various biological activities that are still unexplored and can be used effectively in drug discovery. Further, the designing of specific sensor for the recognition of various ions is one of the most demanding areas of chemical research due to their significant contribution in analytical, industrial, agricultural, environmental and biological fields and there is an urgent need to explore the chemistry of pyridine-based Schiff bases to find out their applications as chemosensors for ions recognition studies. This chapter throws some light on chemistry and biological significance of pyridine derivatives, reviews the recent work done on Schiff bases derived from pyridine derivatives and their potential as effective bioactive ligands as well as efficient chemosensors.

2. Pyridine derivatives: chemistry and biological significance

2.1 Pyridine

2.1.1 A valuable N-based heterocyclic compound

Heterocyclic compounds are widely distributed in nature and they are found to be essential for various biochemical processes. They also play a vital role in the metabolism of all living cells as well as in the composition of genetic material of the cells. Many of them are pharmacologically active and are in clinical usage. Among these heterocyclic compounds, those based on nitrogen are of great importance as they are widely spread in nature, possess more therapeutic values and less toxicity as compared to other heterocycles based on oxygen or sulfur. Moreover, their structure can be subtly manipulated to achieve a required modification in function. Such nitrogen based heterocyclic compounds represent important building blocks in both natural and synthetic bioactive compounds. Among these, pyridine is the simplest monoazine compound but considered as one of the most valuable N-based heterocyclic. An important property of pyridine is that it's a polar solvent but aprotic in nature. Thus, it can be easily mixed with polar as well as with many non-polar organic solvents which makes it a versatile solvent. Further, the derivatives of pyridine are found to be less toxic, but possess much more important chemical and biological properties as compared to parent pyridine and therefore, they are frequently used as precursors for many important chemicals, agrochemicals and pharmaceuticals. Owing to their important chemical properties and biological significance, pyridine derivatives find applications in variety of fields as shown in **Figure 1**. These properties of

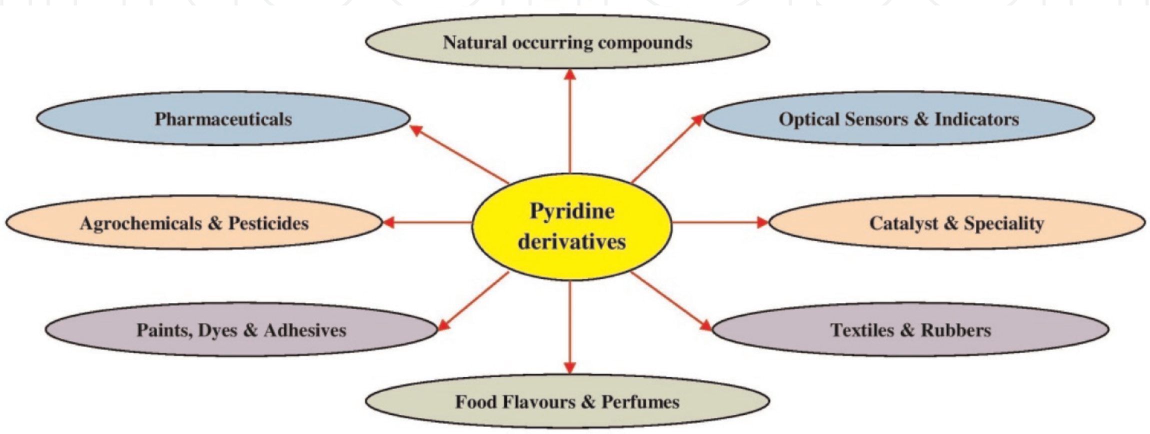

Figure 1.
Applications of pyridine derivatives in variety of fields.

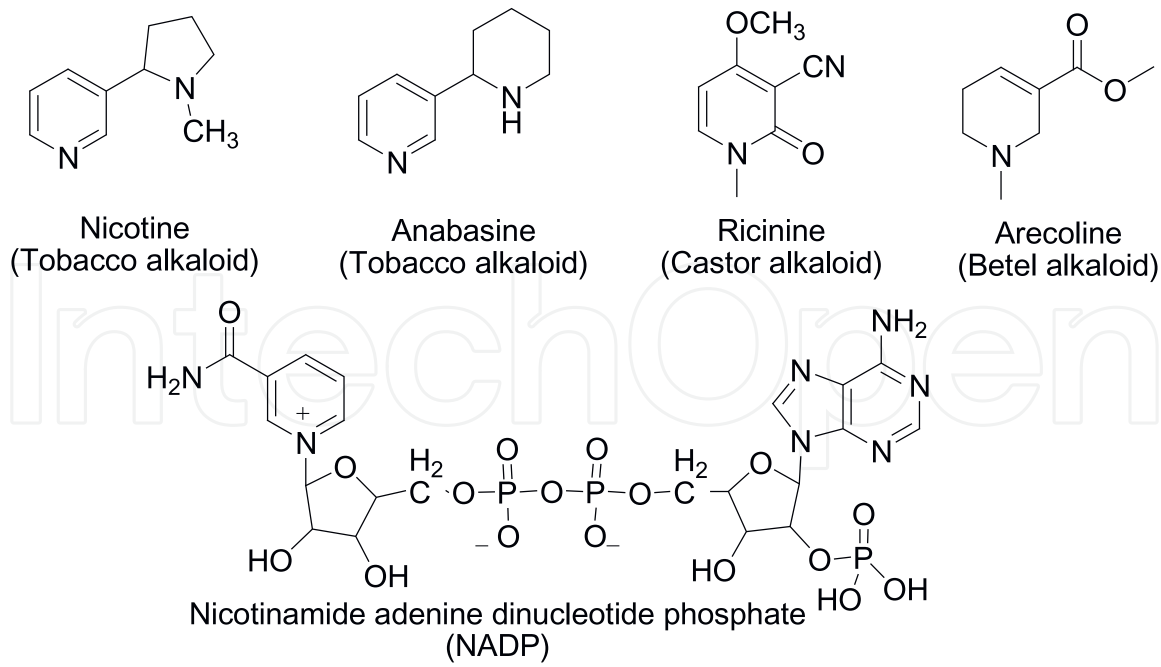

Figure 2.
Naturally occurring compounds containing pyridine ring.

pyridine and its derivatives make them useful in synthesis of innumerable products such as medicines, agrochemicals, catalysts, optical sensors, food flavorings, perfumes, dyestuffs, paints, adhesives, rubber products, textile fabrics etc. [1–5].

2.1.2 Naturally occurring compounds

Pyridine derivatives are the fundamentally important nitrogen-based heterocycles which are present in large number of naturally occurring compounds. They are often present as a partial structure in many plant-based alkaloids. For example: Nicotine and Anabasine are found in tobacco whereas Ricinine is present in castor oil and Arecoline is present in betelnut. Nicotinamide adenine dinucleotide phosphate is a cofactor used in anabolic reactions and nucleic acid syntheses which is used by all forms of cellular life (**Figure 2**) [6].

2.1.3 Vitamins and dietary supplements

Some essential B group vitamins such as Niacin (Vitamin B_3) and Pyridoxine (Vitamin B_6) are simply the derivatives of pyridine. Chromium picolinate and Zinc picolinate are used as dietary supplements (**Figure 3**) [6, 7].

2.1.4 Pharmaceutical compounds

Pyridine moieties are present in large number of bioactive compounds and form the basis of pharmacophore group. They can be used as prodrugs or drug molecules themselves which possess wide range of medicinal applications including Antitubercular, Antibacterial, Anticholinesterase, Antihistamine, Antiulcer, Antianginal etc. (**Figure 4**). Further detailed studies on bioactivity of pyridine derivatives are given in Section 2.2 [8, 9].

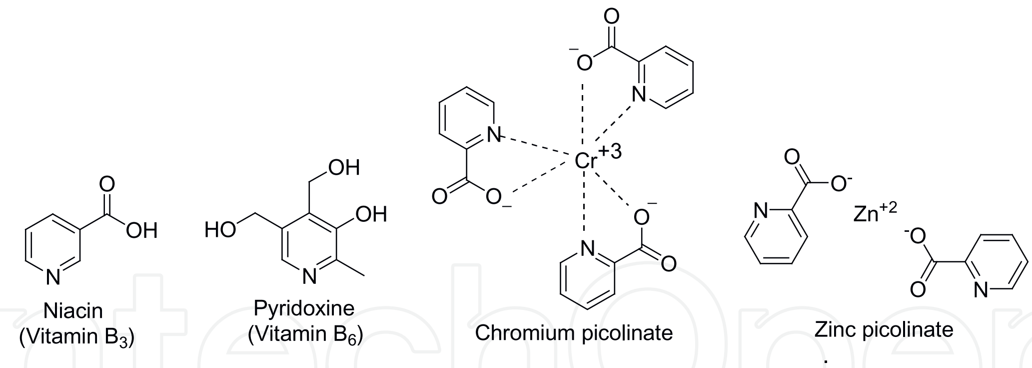

Figure 3.
Vitamins and dietary supplements based on pyridine derivatives.

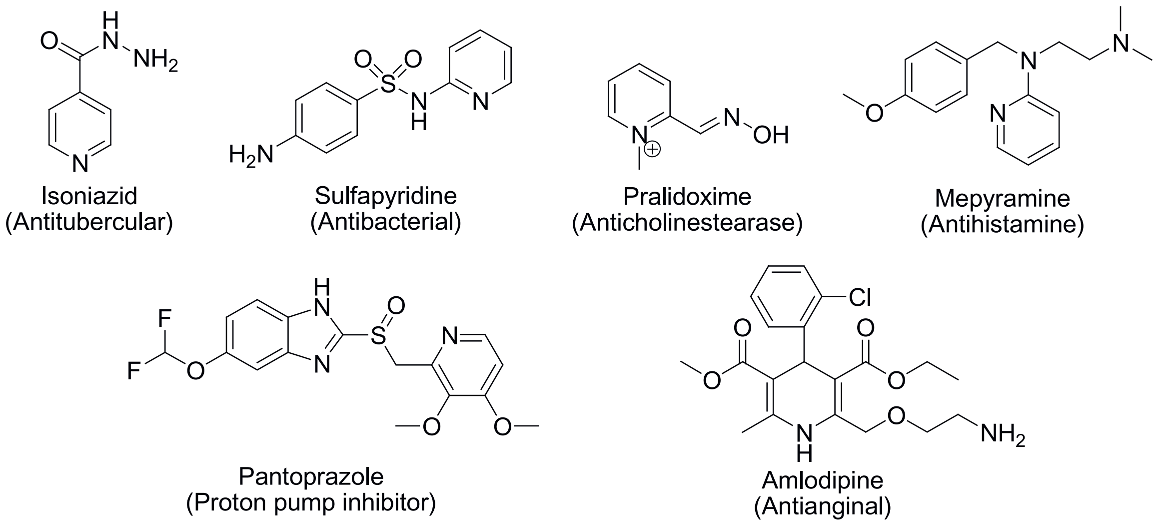

Figure 4.
Pharmaceutical compounds having pyridine moiety.

2.1.5 Agrochemicals

Pyridine or its derivatives are used as starting materials for synthesis of many agrochemicals or pesticides. They act as the precursor or intermediates for many important herbicides, fungicides and insecticides (**Figure 5**) [10, 11].

2.1.6 Catalysts

Several pyridinium salts are used as catalyst in many organic reactions. For example: Collins reagent is used to convert primary alcohols into aldehydes; Cornforth reagent is used for oxidation of primary and secondary alcohols into carbonyls whereas PCC is used primarily for selective oxidation of alcohols into carbonyls. Pyridineborane is used as a reducing agent with improved stability and solubility over $NaBH_4$ (**Figure 6**). Crabtree catalyst and Milstein catalyst are well known organometallic catalyst used for hydrogenation and dehydrocoupling of alcohols respectively [12, 13].

2.1.7 Optical sensors

Several bipyridine or terpyridine based metal complexes exhibit intense luminescence and can be used as fluorescent chemosensors. For example: $[Ru(bipy)_3]^{+2}$ is used as a luminophore whereas $[Fe(bipy)_3]^{+2}$ is used in redox titrations and colorimetric analysis. The complex $[Fe(phen)_3]^{2+}$ is widely used as Ferroin indicator in redox titrations and for the photometric determination of Fe (II) (**Figure 7**) [14, 15].

2.1.8 Chemical based industries

Pyridine derivatives are also used on large scale in many chemical-based industries. Pyridone based azo disperse dyes are widely used for making dyestuffs. Pyridine derivative ADP is applied to improve network capacity of cotton in textile industries. Polyvinyl pyridines are used as copolymer with styrene for making adhesives and install water proofing properties in paint industries. Several alkyl or acyl derivatives of pyridines are the main source of flavors and essential oils which are widely used in food industries and cosmetic industries (**Figure 8**) [16–19].

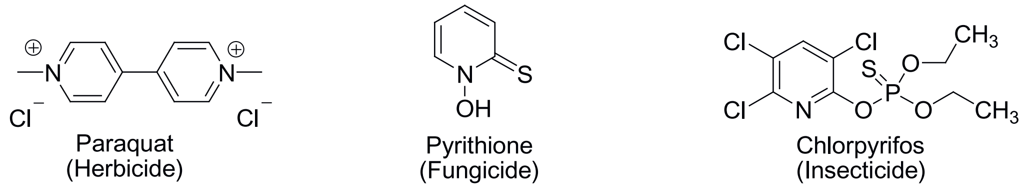

Figure 5.
Agrochemicals based on pyridine derivatives.

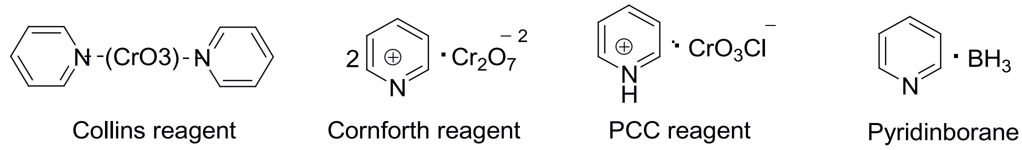

Figure 6.
Catalysts based on pyridinium salts.

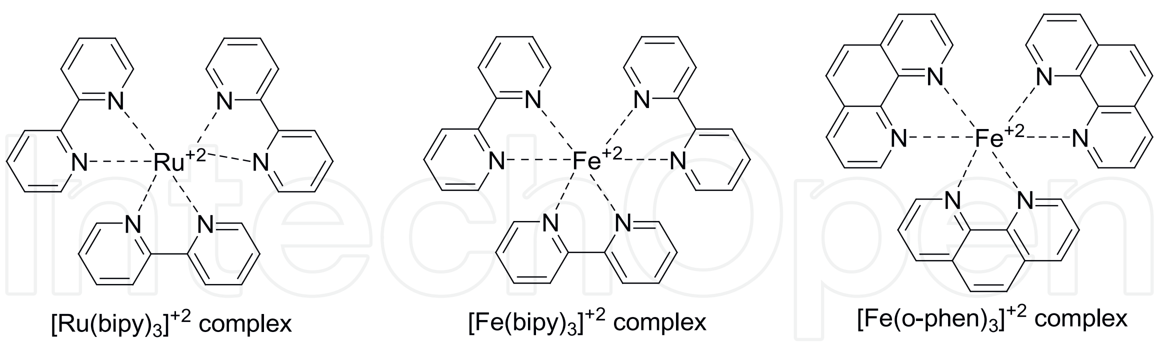

Figure 7.
Optical sensors based on bipyridine and o-phenanthroline metal complex.

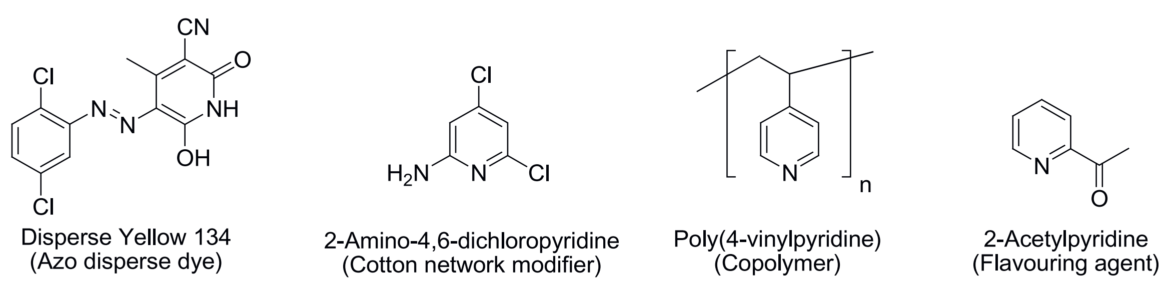

Figure 8.
Pyridine derivatives used in chemical-based industries.

2.1.9 Speciality reagents

Many specialty reagents used in chemical lab are based on pyridine. Pyridine is often used as a reaction solvent for many organic reactions because of its polar nature, low reactivity and miscibility with wide range of solvents. For example: pyridine is an important constitutes of Karl Fischer reagent for determining traces of water in pharmaceuticals, deuterated pyridine is used as common solvent in ^{1}H-NMR spectroscopy, and pyridine is also used as denaturant for making anti freezing mixtures of ethyl alcohol.

Hence, pyridine and its derivatives have significant applications in various fields, especially in the medicinal and agrochemicals. Due to such wide range of applications and extremely usage in industries, pyridine and its derivatives are considered among the most important and valuable N-based heterocyclic compounds which is also evident from the current annual worldwide production of pyridine which is approximately 20,000 ton per year.

2.2 Biological importance of pyridine derivatives

Pyridine is one of the most important nitrogen-based heterocyclic compounds which is present in large number of naturally occurring compounds. It is widely used as a precursor to agrochemicals and pharmaceuticals. Pyridine moieties are present in large number of drug molecules as well as in essential dietary supplements. This indicates that pyridine compounds can be used as precursor of drugs and with their proper structural modification or derivatization they can be led to important prodrugs or drugs itself of therapeutic value. Pyridine is an important heterocyclic organic compound. Pyridine and their heterocyclic annulated derivatives are of great interest due to the wide variety of biological activities as observed in these compounds. Pyridine nucleus is found to be basic skeleton of large number of bioactive molecules which ranges from Antitubercular, Antibacterial, Antiviral, Antiseptic, Antihistaminic, Antianginal, Anticholinesterase, Anti-inflammatory, Antiulcer, Anticancer etc.

2.2.1 B-group vitamins

Pyridine ring is present as basic nucleus in various B group vitamins such as Nicotinamide, Nicotinic Acid and Pyridoxine which are used as essential dietary supplements and for therapeutic effect (**Figure 9**).

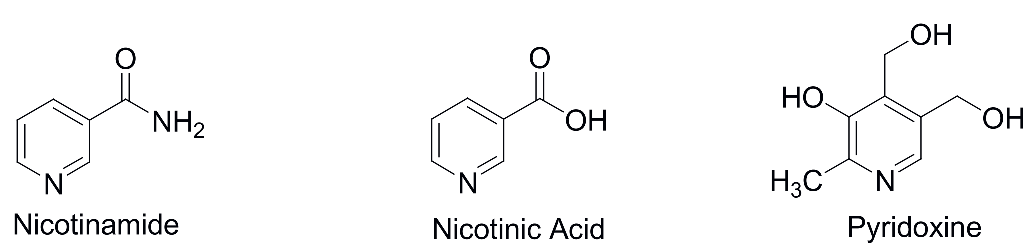

Figure 9.
B-group vitamins based on pyridine derivatives.

2.2.2 Antituberculars

These drugs are medications used to treat bacterial infection caused by *Mycobacterium tuberculosis*. Pyridine nucleus is found to be basic skeleton of major antitubercular drugs such as Isoniazid, Ethionamide and Prothionamide which are used in treatment of tuberculosis (**Figure 10**).

2.2.3 Antibacterials

These drugs are a principal type of antimicrobial agent or antibiotic which are used to either kill or inhibit the growth of certain bacteria. Sulfapyridine and Sulfasalazine are sulpha drugs containing pyridine nuclei which act as antibacterial agents used to inhibit bacterial infection (**Figure 11**).

2.2.4 Antihistamines

These drugs are used to oppose the activity of histamine receptors in human body so that to treat different allergic conditions like allergic rhinitis, common cold, influenza etc. Betahistine, Chlorpheniramine, Dexchlorpheniramine, Mepyramine, Pheniramine and Triprolidine are Histamine H1-receptor antagonist and used as antihistaminic drugs for allergic disorders. All of them contain the pyridine ring as an important part of their structure (**Figure 12**).

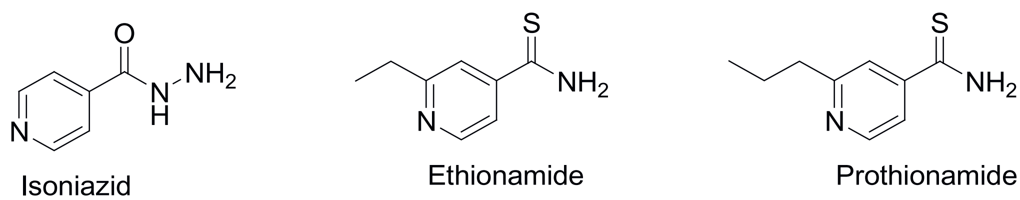

Figure 10.
Antitubercular drugs containing pyridine as basic skeleton.

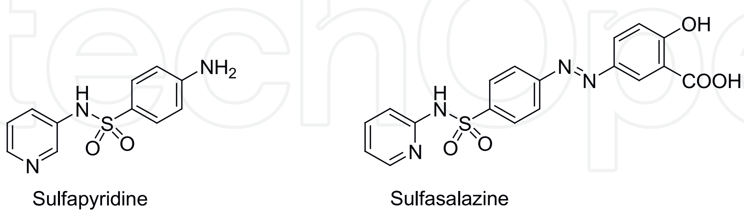

Figure 11.
Antibacterial drugs containing pyridine nuclei.

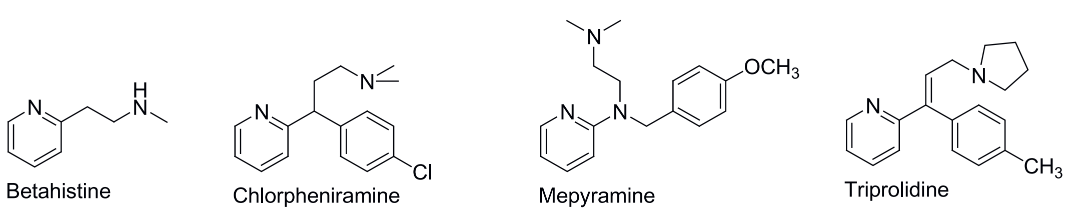

Figure 12.
Antihistamine drugs having pyridine nucleus.

2.2.5 Antianginals & antihypertensive drugs

Antianginal drugs are used in treatment of angina pectoris, a type of heart disease. They are also classified as calcium channel blockers or beta blockers. Antihypertensive drugs are used to prevent conditions of high blood pressure, stroke and myocardial infarction. Amlodipine, Azelnidipine, Clinidipine, Felodipine, Lacidipine, Nicardipine and Nifedipine are some Antianginal/Antihypertensive drugs which contain the pyridine as core structure (**Figure 13**).

2.2.6 Anticholinesterase drugs

These drugs act as antidote for cholinesterase inhibitors and prevent the breakdown of neurotransmitter acetylcholine. Examples are Pralidoxime and Pyridostigmine which are simply the pyridinium salt derivatives (**Figure 14**).

2.2.7 Analgesic and anti-inflammatory drugs

These drugs are used to reduce pain, decreases inflammation and also reduce fever. Etoricoxib, Phenyramidol, and Piroxicam are used as analgesic and ant-inflammatory drugs that contain the pyridine scaffold (**Figure 15**).

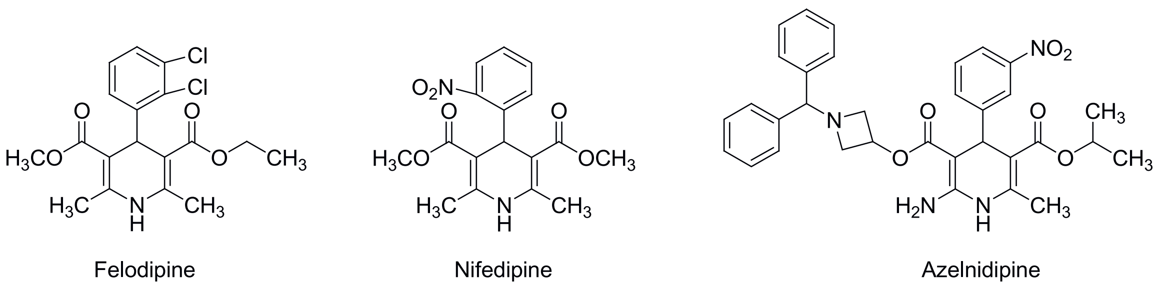

Figure 13.
Antianginal drugs bearing pyridine as core structure.

Figure 14.
Anticholinestearase drugs based on pyridinium salts.

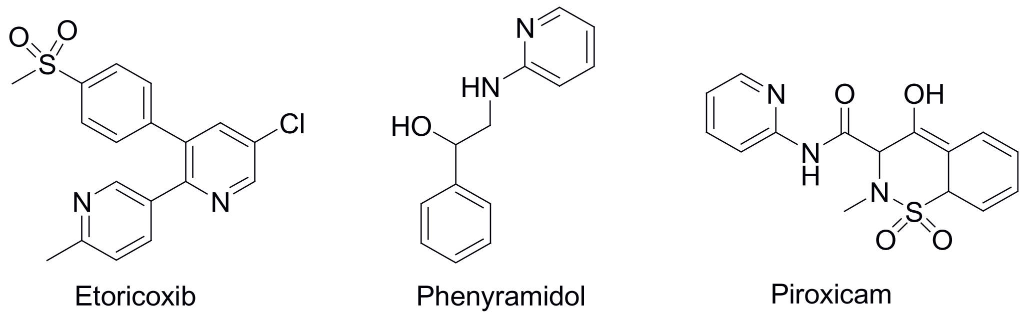

Figure 15.
Analgesic/anti-inflammatory drugs having pyridine scaffold.

2.2.8 Antiulcer drugs

These are class of drugs used to treat peptic ulcer or gastrointestinal tract infections. They also include the class proton pump inhibitor that is used in reduction of gastric acid production. Lansoprazole, Omeprazole, Pantoprazole and Rabeprazole are proton pump inhibitor and used as antiulcer drugs. All of them contain pyridine nucleus as an important part of their structure (**Figure 16**).

2.2.9 Anticancer drugs

These drugs are effective in the treatment of malignant or cancerous disease by inhibiting the cell division and proliferation. Abiraterone, Imatinib and Sorafenib are used as anticancer drugs that consist of pyridine ring (**Figure 17**).

2.2.10 Antivirals

These drugs are used in treatment of viral infections. They do not destroy the target pathogen but inhibit its growth. Atazanavir and Indinavir are antiretroviral drugs that are used in treatment of HIV/AIDS. Both of them have pyridine nuclei as a part of their structure (**Figure 18**).

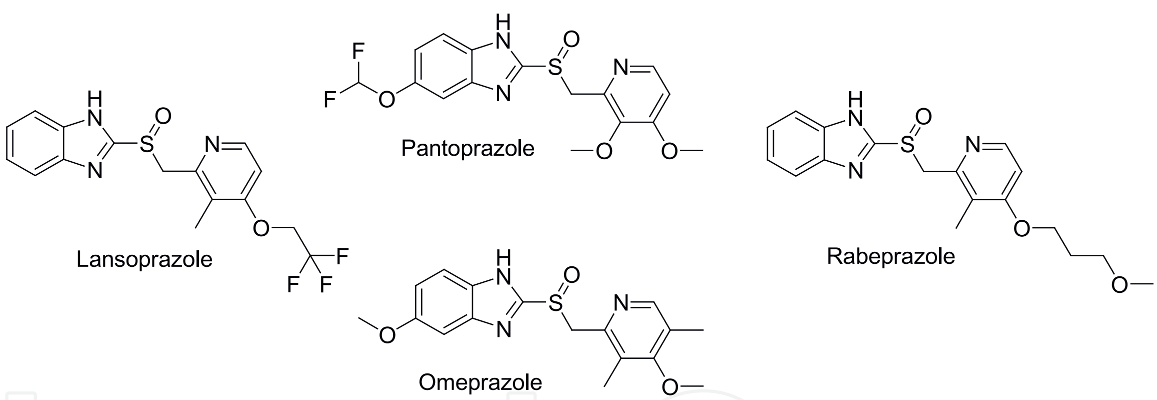

Figure 16.
Antiulcer drugs containing pyridine nuclei.

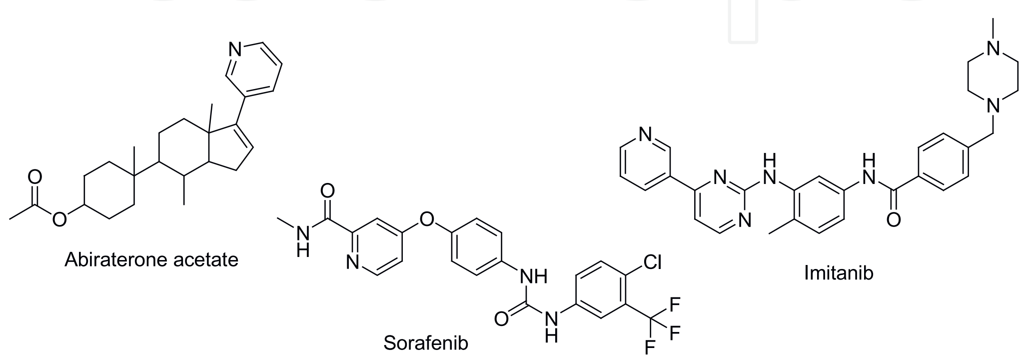

Figure 17.
Anticancer drugs bearing pyridine ring as part of their structure.

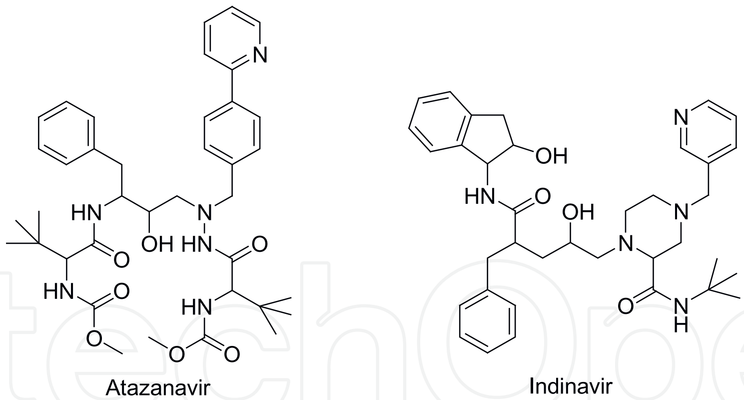

Figure 18.
Antiviral drugs containing pyridine moiety as part of their structure.

2.2.11 Antiseptics

These are antimicrobial agents that can be applied on living tissues or skin in order to reduce the possibility of infection or putrefaction. Cetylpyridinium chloride and Laurylpyridinium chloride are used as antiseptic in oral and dental care products. Both of these are simply the derivatives of pyridinium chloride salt (**Figure 19**).

Additionally, there are many other important pyridine-based drugs like Bisacodyl as laxative, Disopyramide as antiarrhythmic, Nikhetamide as respiratory stimulant, Pioglitazone as antidiabetic, and Torsemide as diuretic and so on (**Figure 20**) [20–22].

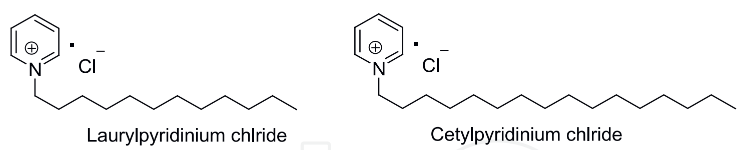

Figure 19.
Antiseptics based on pyridinium salts.

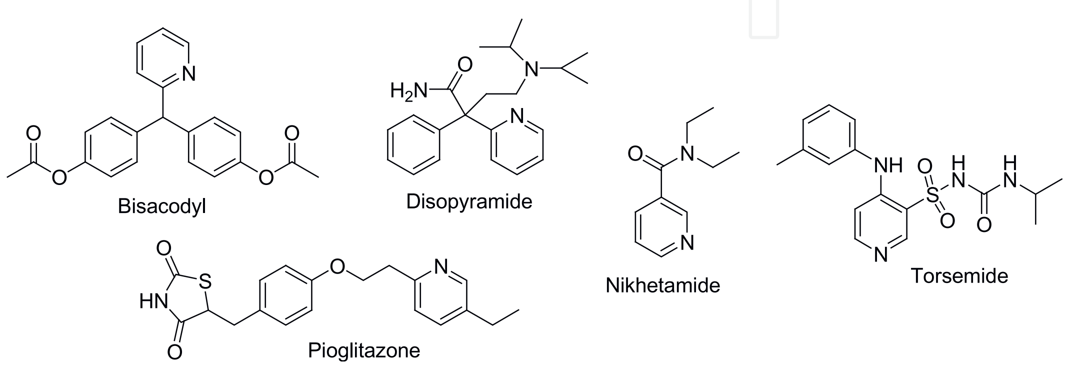

Figure 20.
Miscellaneous drugs having pyridine ring as part of their structure.

3. Schiff bases of pyridine: the excellent bioactive ligands and efficient chemosensors

3.1 Schiff bases and their metal complexes

3.1.1 Schiff base

Schiff bases are generally the condensation products of primary amines and carbonyl compounds. They are considered as a sub-class of imines which are the organic compounds containing carbon-nitrogen double bond. Structurally, Schiff base is an analogue of an aldehyde or ketone in which the carbonyl (C═O) group has been replaced by an imine or azomethine (>C═N—) group. Schiff bases are generally synthesized by the condensation reaction between primary amines and aldehydes or less commonly ketones (**Figure 21**). Schiff bases are more readily formed with aldehydes as compared to ketones. Schiff bases derived from aliphatic aldehydes are unstable in nature and readily get polymerized whereas those derived from aromatic aldehydes are more stable especially due to their effective conjugation systems.

Schiff bases have an interesting range of applications in various field of science ranging from synthesis to catalysis, analysis and medicine to modern technologies. For example, they are widely used in organic synthesis especially as the precursor of heterocyclic compounds and as the catalysts in many catalytic reactions. Several Schiff bases can be used for the qualitative and quantitative detection of metal ions. Some Schiff bases can be used as optical, fluorescent as well as electrochemical sensors. The most important application of Schiff bases is in the field of medicinal chemistry. Some important drugs consist azomethine group of Schiff base in their structure e.g., Thiocetazone, Nitrofurazone, Nitrofurantoin etc. (**Figure 22**).

In recent years, various Schiff base containing derivatives have been synthesized and evaluated for their biological activities including antimicrobial, antitubercular, antifungal, antioxidant, anti-inflammatory, anticonvulsants, antidepressant, antihypertensive and anticancer activity. As they possess a wide variety of biological activities, they are considered as a versatile pharmacophore and emerged as a potent class of pharmaceuticals. Several studies showed that the presence of a lone pair of electrons in sp^2 hybridized orbital of nitrogen atom of the azomethine group is of considerable chemical and biological importance as it interferes in normal cell processes by the formation of hydrogen bond between the active centers of cell constituents and

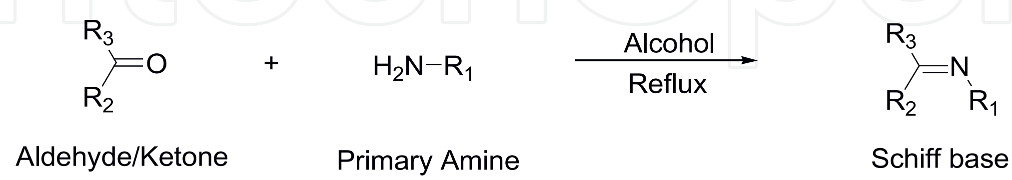

Figure 21.
Reaction scheme for Schiff base condensation.

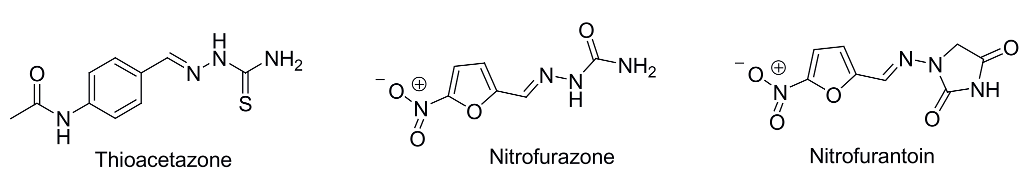

Figure 22.
Important drugs containing azomethine (—CH═N—) group.

sp^2 hybridized nitrogen atom. Thus, Schiff bases have key role in design and development of novel compounds which are more potent and have interested biological activities. Due to the vast pharmacological activities, they constitute a significant class of compounds for new drug development and continue to be an active area of research in medicinal chemistry [23–27].

3.1.2 Schiff base metal complexes

Schiff bases are widely used as ligands in coordination chemistry due to the presence of imine nitrogen which is basic in nature and exhibits π-acceptor properties. These act as Flexi-dentate ligands due to presence of nitrogen of azomethine group and other hetero atoms like nitrogen, oxygen or sulfur of specific functional group if present. The metal complexes of Schiff bases are also known as metallo-imines and they play a central role in coordination chemistry. Jacobsen's catalyst is a well-known example of Schiff base metal complex which is derived from chiral tetradentate Salen ligand (**Figure 23**).

Some metal complexes play a vital role in the bioactivity of life saving drugs especially anticancer drugs. Cisplatin, Carboplatin and Oxiplatin are anticancer drugs designed from binding of organic ligands with platinum metal ion (**Figure 24**).

In organic synthesis the Schiff base reactions are very useful in making carbon-nitrogen bonds. Schiff base are considered as a very important class of organic ligands which can be used as building blocks and find extensive applications in organic synthesis as well as in organocatalysis. Thus, Schiff base appears to be an important intermediate in a number of enzymatic reactions that involves interaction of an enzyme with an amino or a carbonyl group of the substrate. It is a well-known fact that the binding of bioorganic molecules or drugs to the metal ions drastically change their biomimetic properties, therapeutic effects and pharmacological activities. Thus, both the Schiff base ligands and their metal complexes have further extensive applications ranging from material sciences to biological sciences. Due to their biological activities and clinical usage, they are of worth attention. Their successful application

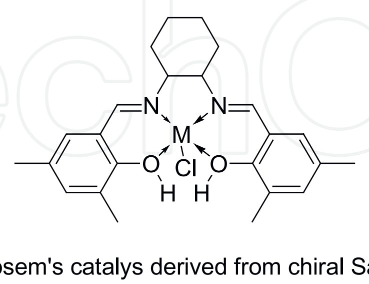

Figure 23.
Jacobsen's catalyst.

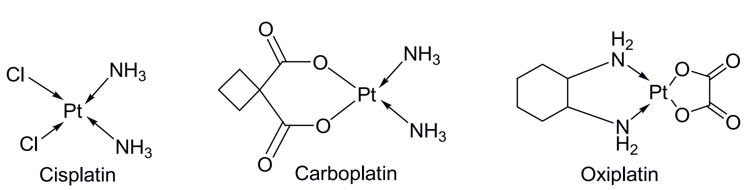

Figure 24.
Metal complexes of platinum used as anticancer drugs.

can lead to the formation of series of novel compounds with wide range of physical, chemical and biological activities [28–33].

3.2 Schiff bases of pyridine as bioactive ligands and versatile pharmacophore

3.2.1 Protein-ligand interactions

Protein-ligand interactions are essential for all processes happening in living organisms as proteins are the fundamental units of all living cells that play a vital role in various cellular functions. It is a reversible non-covalent interaction comprises biological recognition at molecular level in which the molecules i.e. protein and ligand recognize each other by stereo specificity. The evolution of the protein functions depends on the development of specific sites which are designed to bind ligand molecules. Ligand binding capacity is important for the regulation of biological functions which occur through the molecular mechanics involving the conformational changes in proteins. This change initiates a sequence of events leading to different cellular functions. A detailed understanding of the protein–ligand interactions is therefore central to understand biology at the molecular level. Moreover, knowledge of the mechanisms responsible for the protein-ligand recognition and binding helps to understand the drug-receptor interaction in detail and facilitate the discovery, design, and development of drug molecules. A modern computational technique based on protein-ligand interactions is Molecular docking which is now routinely used for drug designing and development processes [34, 35].

3.2.2 DNA-Metal complex interactions

Many transition metal complexes are known to bind with DNA via both covalent and non-covalent interactions. Formation of a protein-ligand complex is based on molecular recognition between biological macromolecules and ligands which depends on affinity and specificity. The interaction between transition metal complexes and DNA has aroused the widespread interest because it helps not only to understand the life processes at the molecular level but also to promote the development of chemistry discipline itself. The interest in preparation of new metal complexes gained the tendency of studying on the interaction of metal complexes with DNA for their applications in biotechnology and medicine. Cisplatin, Carboplatin, Oxiplatin and their derivatives are widely used as anticancer drugs which are based on DNA-Metal complex interactions but they create several side effects such as anemia, diarrhea, alopecia, petechia, nephrotoxicity, emetogenesis, ototoxicity, neurotoxicity etc. Efforts are continuously made to prepare the chemotherapeutic drugs without side effects or fewer side effects. In recent times, the treatment of cancer with a chemotherapeutic approach is based on DNA-Metal complex interactions [36–38].

3.2.3 Role of Schiff bases as bioactive ligand

The Schiff bases display significant biological activities due to presence of imine (>C=N—) functional group. Thus, Schiff base derived from aromatic aldehyde and aromatic amines have enormous applications in biological fields. Pyridine carboxaldehyde derivatives of Schiff bases are of great interest due to their role in natural and synthetic organic chemistry as these can exhibit physiological effects similar to pyridoxal-amino acid systems which are considered to be very important in numerous metabolic reactions (**Figure 25**).

They show diverse biological activities in terms of antibacterial, antiviral, antitubercular, antipyretic, anti-inflammatory, antiulcer, antihistaminic, antitumor etc. (**Figure 26**). The bonding interaction between aromatic ring of Schiff base ligand and aromatic amino acid side chains of receptor has also been revealed in most of the X-ray crystal structures of protein complexes. This protein ligand interaction involves some non-covalent interactions and the evaluation of the structure-activity relationship of Schiff bases also demonstrates their desired biological activity. This ensures the application of Schiff bases in drug designing process and they are widely used as prodrugs as well as the drug molecules itself [39–41].

A series of Schiff bases have been synthesized using 2-vinylaniline and various aldehydes including pyridine-2-aldehyde (**Figure 27**). These Schiff bases were then complexed to transition metal ions like Mn^{+2}, Co^{+2}, Ni^{+2} and Cu^{+2}. All of these compounds were evaluated for their antibacterial activity against bacterial species like *E. coli*, *Staphylococcus aureus* and *Pseudomonas aeruginosa* as well as for their antifungal activity against fungal species like *Candida albicans* and *Candida krusei*. It was concluded that different Schiff bases and their metal complexes had varying degree of antibacterial and antifungal activities. However, all the metal complexes had enhanced antimicrobial activity as compared to their ligand [42].

A combination of pyridine-2-aldehyde with S-methyl and S-benzyl dithiocarbazate resulted in synthesis of Schiff bases (**Figure 28**) which were allowed to form

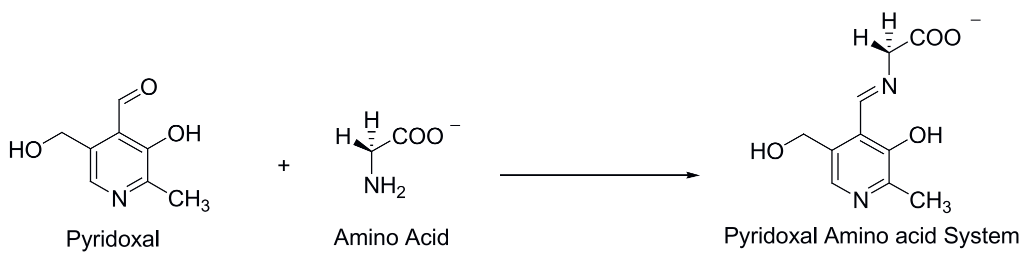

Figure 25.
Pyridoxal amino acid system.

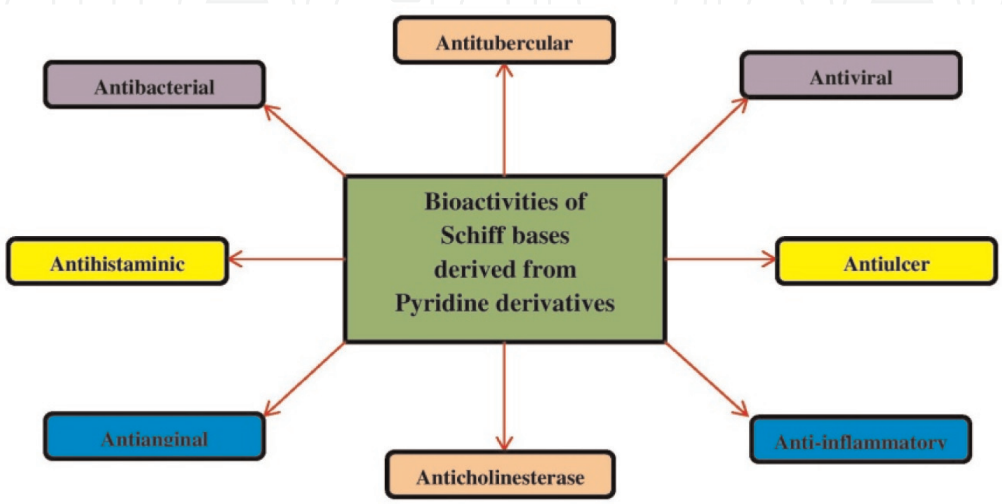

Figure 26.
Bioactivities of Schiff bases derived from pyridine derivatives.

complexes with Mn^{+2} and Zn^{+2} ions. These Schiff bases and metal complexes were evaluated for their biological activities against bacteria, fungi and K562 leukemia cell line. It was observed that Schiff base with S-methyl dithiocarbazate and its complex with Zn^{+2} had broad antimicrobial activity as compared to the Schiff base with S-benzyl dithiocarbazate and its complex with Mn^{+2}. Further only S-methyl dithiocarbazate and its complex with Mn^{+2} showed significant antitumor activity against K562 leukemia cell line [43].

Schiff bases have been derived from pyridine-4-carbaldehyde and various aromatic amino compounds such as 2, 3 and 4-aminobenzoic acids, 4-aminoantipyrene, 2-aminophenol, 2-aminothiophenol etc. (**Figure 29**). The synthesized compounds were evaluated for their antioxidant activities and DNA binding interaction studies. It was found that the Schiff base of pyridine-4-carboxaldehyde and aminophenol was an efficient antioxidant with 74% inhibition of free radicals generated by DPPH. Further most of the synthesized Schiff bases showed efficient binding with DNA which was in good agreement with molecular docking studies [44].

A Schiff base was derived from 2,6-diaminopyridine and salicylaldehyde by microwave irradiation (**Figure 30**) which form complexes with transition metal ions such as Co^{+2}, Ni^{+2}, Cu^{+2}, Zn^{+2} and Cd^{+2}. It was found that all the complexes were non electrolyte and possessed an octahedral geometry in which N donor sites of imine and O donor site of phenolic groups were coordinated to the metal ions [45].

A series of Schiff bases was derived from Isoniazid and various aromatic aldehydes like 2-benzyloxybenzaldehyde and its derivatives as well as with various ketones like n-hexanophenone, cyclohexanone etc. (**Figure 31**). All these novel Schiff bases were then evaluated for their antitubercular activities. It was found that these compounds

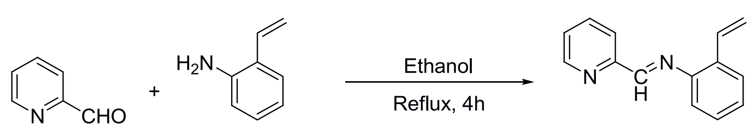

Figure 27.
Schiff base derived from pyridine-2-aldehyde and 2-vinylaniline.

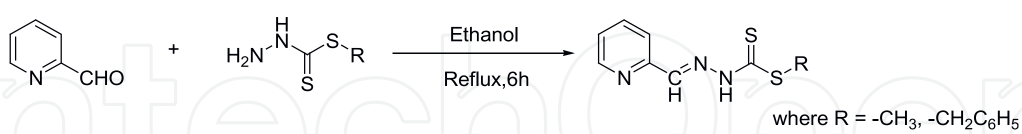

Figure 28.
Schiff bases derived from pyridine-2-aldehyde with dithiocarbazate derivatives.

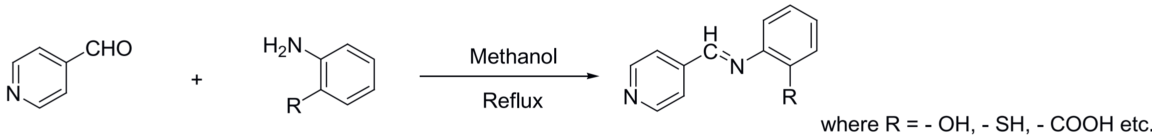

Figure 29.
Schiff bases derived from pyridine-4-aldehyde with different aromatic amino compounds.

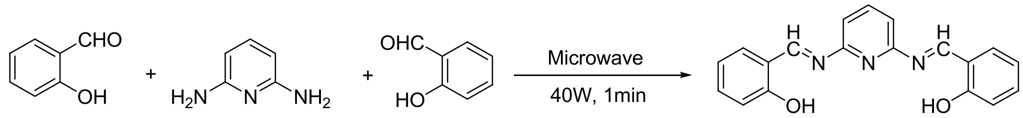

Figure 30.
Schiff base derived from salicylaldehyde and 2,6-diaminopyridine.

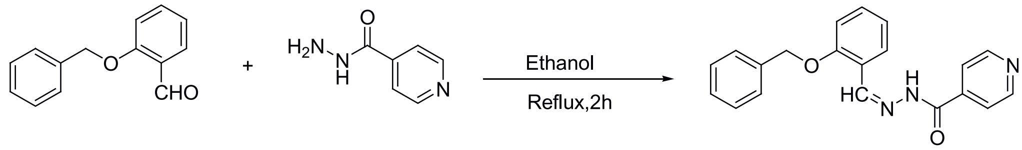

Figure 31.
Schiff base derived from 2-bezyloxybenzaldehyde and isoniazid.

showed high level of activity against Mycobacterium tuberculosis in vitro and in vivo and they had also low toxicity [46].

Schiff bases were derived by the reaction of Isoniazid with 2-acetylfuran and 2-acetyl-5-methylfuran (**Figure 32**). Antibacterial and antifungal activity of the Schiff bases and their complexes were evaluated. It was observed that all these compounds were active against all the microbial strains and their metal complexes with Pd^{+2} and Pt^{+2} were far more active as compared to their parent Schiff base [47].

A Schiff base was derived from Isoniazid and 2-hydroxy-5-methoxybenzaldehyde (**Figure 33**). The metal complexes of this Schiff base were prepared using transition metal ions Mn^{+2}, Ni^{+2}, Cu^{+2} and Zn^{+2}. It was observed that Mn^{+2}, Ni^{+2} and Cu^{+2} complexes had moderate activity against gram positive *Staphylococcus aureus* and gram-negative *E. coli*. It was found that Zn^{+2} complexes showed the highest antifungal activity against the fungal species *Aspergillusflavus* [48].

A Schiff base synthesized from Isoniazid and 2-hydroxynaphthaldehyde (**Figure 34**) was complexed with various transition metal ions like Co^{+2}, Ni^{+2}, Cu^{+2} and Zn^{+2}. The biological activity of Schiff base as ligand and its metal complexes were tested on gram-positive bacteria *E. coli* and gram-negative bacteria *Staphylococccus Aurous* as well as two fungi *Aspergillusflavus* and *Candida albicans*. It was observed that all the metal complexes possessed biological activity and some of them were more potent than their parent Schiff base [49].

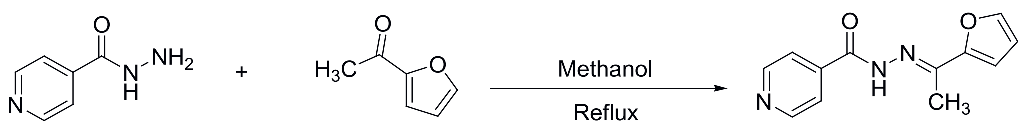

Figure 32.
Schiff base derived from isoniazid and 2-acetylfuran.

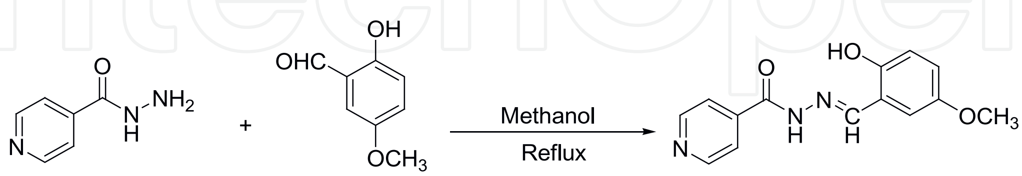

Figure 33.
Schiff base derived from isoniazid and 2-hydroxy-5-methoxybenzaldehyde.

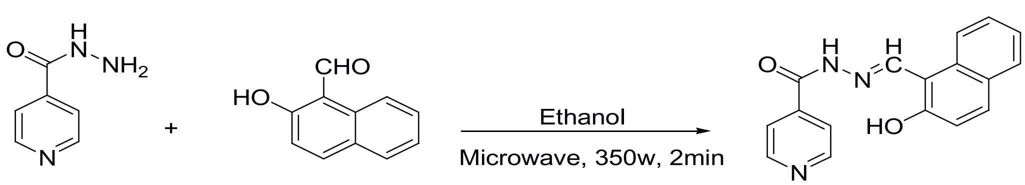

Figure 34.
Schiff base derived from isoniazid and 2-hydroxynaphthaldehyde.

Schiff base derived from Nicotinic acid hydrazide and 2,5-dimethoxybenzaldehyde (**Figure 35**) were complexed with various transition metal ions. In-vitro antimycobacterial activities of these complexes were evaluated against *Mycobacterium tuberculosis* and *H37Rv*. It was found that some of the metal complexes showed higher activity than the Isoniazid and the Schiff base whereas some others showed moderate activity. However, all these metal complexes were found to be more toxic as compared to Isoniazid [50].

Schiff base synthesized from the reaction of Isoniazid and Ketoprofen (**Figure 36**) was found to be a bioactive compound due to large energy gap between HOMO and LUMO as observed from Frontier orbital theory analysis. It was also found to be a more potent against *Mycobacterium tuberculosis* infection as compared to Isoniazid with the help of Molecular docking studies [51].

Two schiff bases were developed by the condensation of 3,4-diaminopyridine with 3,5-difluorine-2-hydroxybenzaldehyde and 5-fluorine-2-hydroxybenzaldehyde (**Figure 37**). The antifungal activity of both the schiff bases were assessed against yeast among which the schiff base obtained from 3,5-difluorine-2-hydroxybenzaldehyde was found to give good results [52].

A schiff base was synthesized by the reaction between 2-benzoylpyridine and 2-aminopyrimidine (**Figure 38**). The binuclear complexes of the schiff base with transition metal ions V(IV), Co (II) and Cu (II) were obtained and examined for their antibacterial properties against three bacterial strains *Escherichia coli*, *Klebseilla pneumonia* and *Staphylococcus aureus*. The antifungal activity was also determined against three fungal strains *Candida albicans*, *Candida glabrata* and *Candida parapsilosis*. It

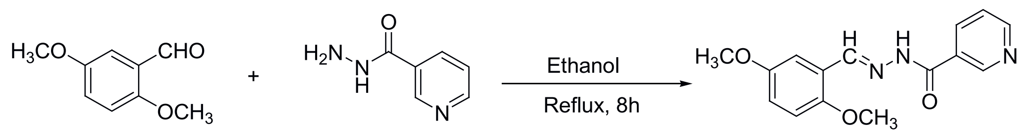

Figure 35.
Schiff base derived from 2,5-dimethoxybenzaldehyde and nicotinic acid hydrazide.

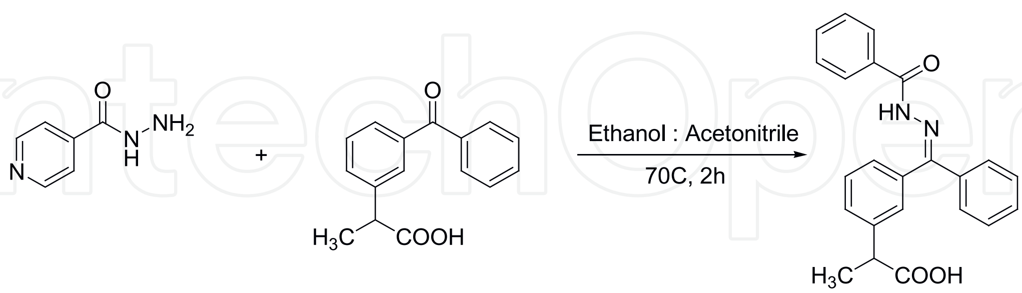

Figure 36.
Schiff base derived from isoniazid and ketoprofen.

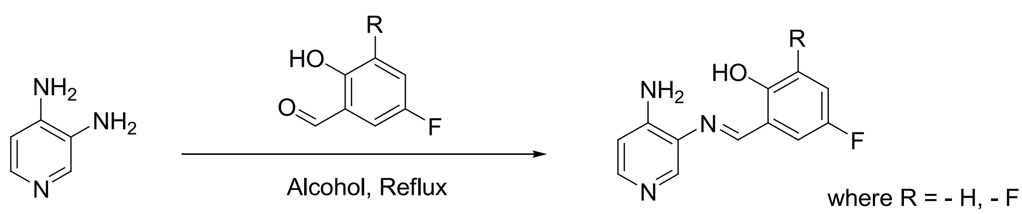

Figure 37.
Schiff bases derived from 3,4-diaminopyridine with 5-fluoro-2-hydroxy benzaldehyde derivatives.

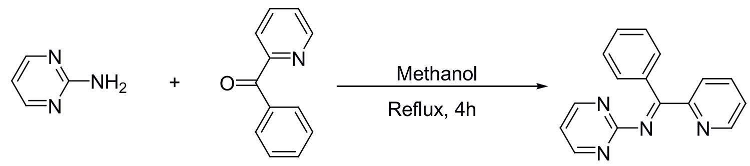

Figure 38.
Schiff base derived from 2-aminopyrimidine and 2-benzoylpyridine.

was revealed that the schiff base showed good to moderate antibacterial and antifungal activities [53].

A novel methyl substituted pyridine Schiff base was obtained by reacting 2,4-dihydroxybenzaldehyde and 2-amino-4-methylpyridine (**Figure 39**). Its metal complexes were also designed with transition metal ions Fe(III), Co(III), Cu(II) and Ni (II). The schiff base and all of its metal complexes were examined for their antimicrobial and antioxidant properties which were found to be moderate to good against reference standards [54].

A series of schiff bases were synthesized from syringaldehyde by reaction with different aminopyridines (**Figure 40**) and their antibacterial properties were evaluated for different gram-positive and gram-negative bacteria. It was observed that compound3 was more effective against gram negative bacteria *P. aeruginosa* in comparison to standard ampicillin drug. The antioxidant potential was also determined and predicted [55].

A pyridine-based Schiff base (S)-N-benzylidene-2-(benzyloxy)-1-(5-(pyridine-2-yl)-1,3,4-thiadiazol-2-yl) ethanamine was synthesized (**Figure 41**). Its antioxidant and antimitotic activities were correlated with standards Ascorbic acid and Methotrexate respectively and both of these activities were found in good agreements to standards [56].

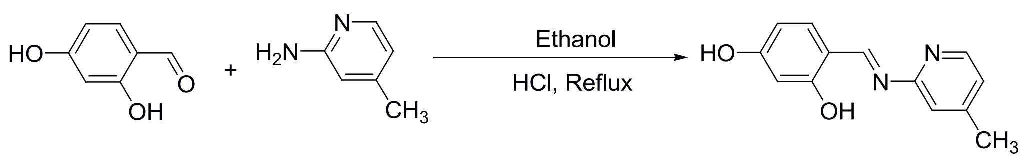

Figure 39.
Schiff base derived from 2,4-dihydroxybenzaldehyde and 2-amino-4-methylpyridine.

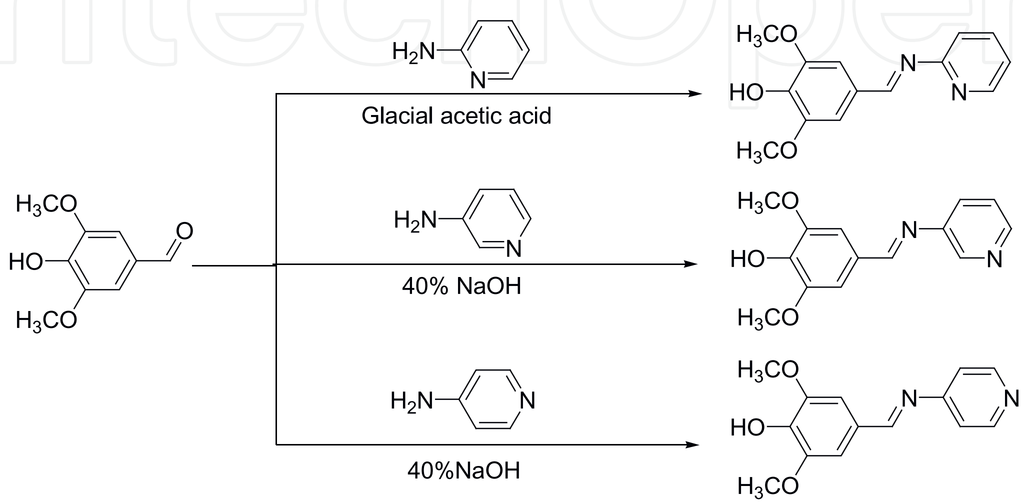

Figure 40.
Schiff bases derived from syringaldehyde with different aminopyridines.

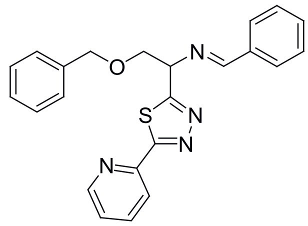

Figure 41.
Schiff base derived from pyridine-thiadiazol based compound and benzaldehyde.

3.3 Schiff bases of pyridine as chemosensors for ion recognition studies

3.3.1 Chemosensors

A chemosensor is a molecular structure i.e. an organic or inorganic complex that can be used for sensing of an analyte to produce a detectable change or a signal. In general, chemosensors are the chemical molecules that bind selectively with the guest moiety and produce a detectable or measurable change in physical, chemical or spectral properties of the system. As shown in **Figure 42**, the designing of a chemosensor is simply based on Host-Guest recognition.

These changes may be the color development or masking, modulation of emission intensity or redox potential which can be detected with the help of UV–visible absorption spectroscopy, fluorescence spectroscopy and voltammetry respectively. Thus, chemosensors are designed to contain a signaling moiety and a recognition moiety that gives rise to change in either UV–visible absorption or the emission properties. The color change or spectral change observed in either case is due to the formation of host-guest complex i.e., the complex formed between the receptor and ion. The visualization of color is based on the coordination between organic molecules having lone pair of electrons which act as donors and the metal ion or a specific anion which act as receptor [57–60].

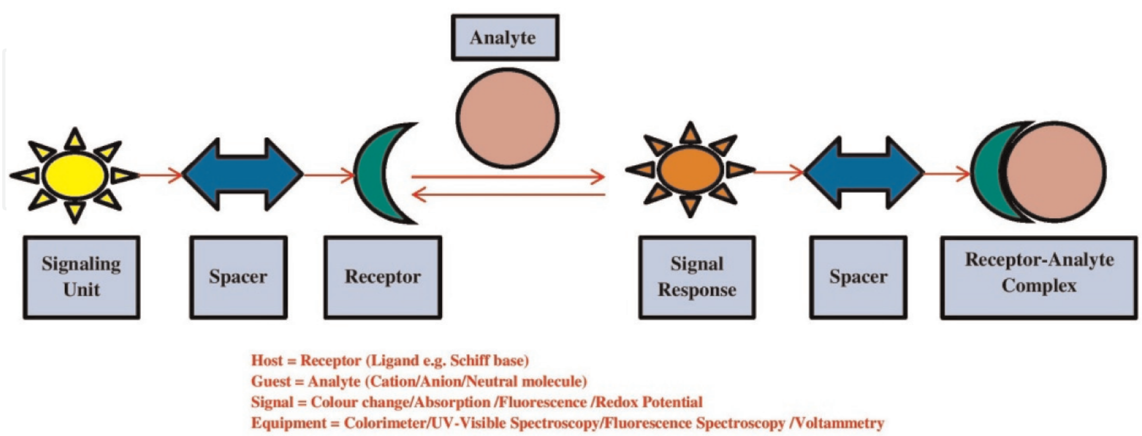

Figure 42.
Designing of chemosensor based on host-guest recognition.

3.3.2 Need for cation recognition

There are several transition metal ions which are very crucial for the life of living organisms. Some of them are required in trace quantity but if their concentration exceeds than the trace amount, they become toxic for the biological systems and may lead to various diseases and disorders. There are certain non-essential elements for living system which are widely used in industries and daily life. Their frequent and larger use can lead to overloading of such elements in the human body which may cause a large number of diseases like bone disorder, neurodegenerative diseases, sclerosis, dialysis encephalopathy etc. Their high concentration in water is harmful to growing plants and aquatic life. Transition metal ions as pollutants have some toxic impact on human health as well as on environment. The detection of these ions has gained extreme importance in recent years in the field of chemical, biological and environmental sciences. There is an urgent need to develop some efficient approaches to detect such metal ions with high selectivity and sensitivity so that to control the harmful effect on human health and environment [61, 62].

3.3.3 Need for anion recognition

Anion recognition plays a vital role in aqueous medium due to analysis of various anions in biological and environmental systems. Anion sensing continues to be a developing field in supramolecular chemistry because of its significance in industrial chemistry, environmental sciences as well as in biological fields. However, anion sensing in pure water is challenging job because they have large variation in size as compared to metal cations. Moreover, they have large solvation energy in aqueous medium and there is a strong competition occurs between solvent and anions for binding with the receptor. These problems can be overcome to certain extent by the use of chemosensors. A large number of chemosensors have also been reported for anion recognition and sensing with high selectivity as well as sensitivity. Literature review revealed that most of these sensors have complicated structure and hard synthetic routes. Moreover, some of them have poor yields and troublesome purification process. It can be expected that chemosensors derived from Schiff bases may solve these issues up to certain extent as they do not have much complex structure and can be synthesized easily with good yield and purity [63–65].

3.3.4 Role of Schiff bases in ion recognition

Schiff bases are organic molecules that contain azomethine group and are capable of donating lone pair of electrons, so that they can coordinate with large number of metal ions especially transition metal ions. Schiff bases of nitrogen-based heterocycles such as pyridine or their derivatives can act as excellent ligands due to presence of ring nitrogen atom with a localized pair of electrons leading to the formation of very stable complexes with transition metal ions. It has been demonstrated that the presence of nitrogen atom of azomethine group and oxygen atom of phenolic or carbonyl group in Schiff base has strong affinity towards metal ions which results in metal-oxygen-nitrogen cycle i.e. chelatogenic cycle. Due to this, the intramolecular charge transfer is improved between the π-conjugated rings which displays unique emission enhancement. Schiff bases have the strong binding abilities to the various ions and also have individual photophysical properties. This property of Schiff base can be used in ion recognition and their derivatives are extensively used in development of chemosensors for detection of metallic cations and anions in various kinds of environmental and biological media. **Figure 43** represents the different kind of chemosensors based on Schiff bases that can be derived from pyridine derivatives [66–70].

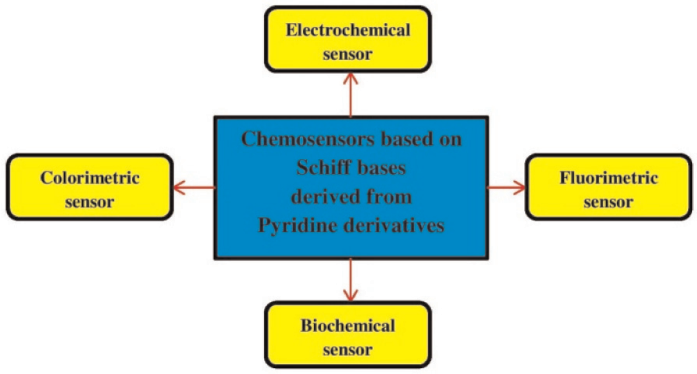

Figure 43.
Chemosensors based on Schiff bases derived from pyridine derivatives.

A pyridylazo compound (**Figure 44**) was designed which showed a very high affinity towards Al^{+3} ions. The turn on fluorescence behavior showed that the synthesized compound could be used for detection of Al^{+3} ions with high selectivity in qualitative as well as quantitative estimations [71].

A condensation reaction between 4′-amine-2,2′6′2″-terpyridine with benzaldehyde derivatives resulted in the synthesis of Schiff bases (**Figure 45**) which were studied for its cation recognition properties for various ions. It was observed that the synthesized Schiff bases selectively recognized Al^{+3} ions due to enhancement in fluorescence [72].

A reversible fluorescent colorimetric imino-pyridyl bis Schiff base receptor was developed (**Figure 46**) for the detection of $Al^{+3}$and HSO_3^- in aqueous medium.

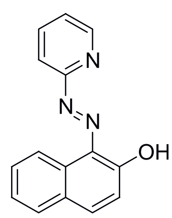

Figure 44.
Fluorescent chemosensor based on pyridylazo compound.

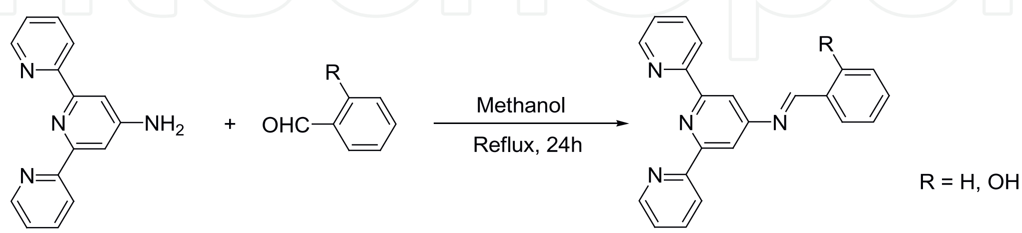

Figure 45.
Schiff base derived from 4′-amine-2,2′,6′,2 -terpyridine with benzaldehyde derivatives.

Figure 46.
Schiff base derived from pyridine-4-aldehyde and 4-aminoaniline.

The receptor exhibited excellent fluorescent colorimetric response towards Al^{+3} ions with high selectivity and also selective colorimetric response towards HSO_3^- ions [73].

A fluorescent chemosensor based on 2-(7,10-diphenylfluoranthen-8-yl)-pyridine (**Figure 47**) was designed and examined for its cation recognition ability. It was found to show excellent selectivity towards Fe^{+3} ions by exhibiting a great decrease in emission intensity [74].

A series of donor-acceptor systems was synthesized in which pyridine moiety acted as acceptor unit and carbazole moiety acted as donor unit (**Figure 48**). The synthesized compounds were then investigated for their sensing properties towards various metal cations. The compound showed a remarkable enhancement in fluorescence in presence of Cu^{+2} ions and could be used as sensor for Cu^{+2} ions with high selectivity over various other metal ions [75].

A chemosensor based on naphthalimide and pyridine moiety was designed (**Figure 49**) and found to show good response towards Cu^{+2} ions with high selectivity and sensitivity in the presence of wide range of metal ions in aqueous media [76].

A fluorescent chemosensor based on BODIPY with two pyridine ligands was synthesized (**Figure 50**) and examined for detection of various cations and anions. It was found to display very high selectivity and sensitivity towards Cu^{+2} ions by giving a visible color change from pink to blue and quenching of fluorescence emission. Further, it was noted that on addition of S^{-2} anions to the Cu^{+2} complex the color could be restored [77].

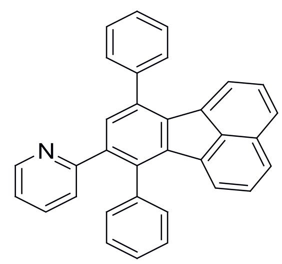

Figure 47.
Fluorescent chemosensor based on 2-(7,10-diphenylfluoranthen-8-yl)-pyridine.

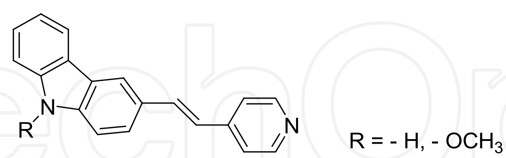

Figure 48.
Fluorescent chemosensor based on pyridine-carbazole based compound.

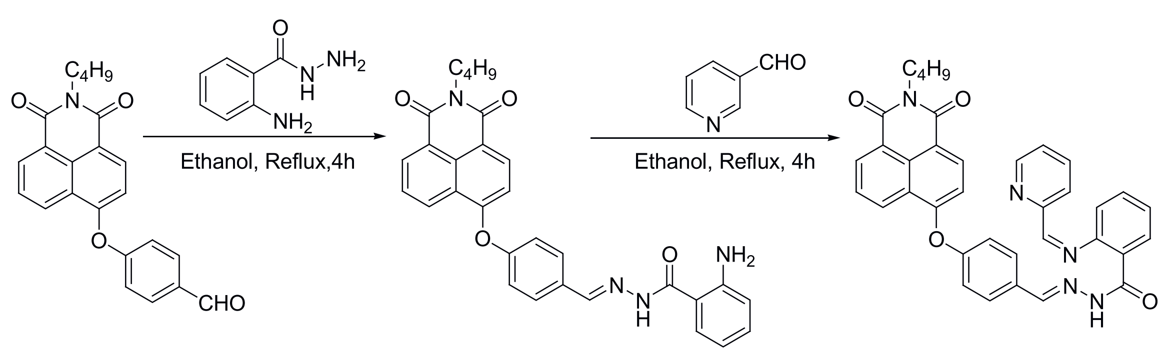

Figure 49.
Schiff base derived from naphthalimide based compound and pyridine-3-aldehyde.

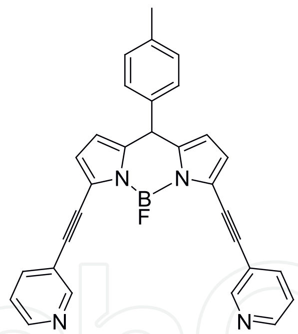

Figure 50.
Fluorescent chemosensor based on BODIPY with two pyridine ligands.

A schiff base ligand was synthesized from 4-hydroxy-3,5-dimethoxybenzaldehyde and pyridine dicarbohydrazide (**Figure 51**) which was then examined for its ion sensing ability and it was found to recognize Cu^{+2} ions over the other metal ions. Further the Schiff base complex with Cu^{+2} ions was able to detect CN^{-} ion over different anions [78].

A Schiff base was synthesized from 2,6-diaminopyridine and salicylaldehyde whereas another schiff base was synthesized from pyridine-3-carbohydrazide and 2,5-dimethoxybenzaldehyde (**Figure 52**). Both of them were evaluated for their cation sensing properties and were found to form complexes with transition metal ions such as Co^{+2}, Ni^{+2}, Cu^{+2}, Zn^{+2} and Cd^{+2}, thus had potential to act as chemosensors for detection of these ions over other competing ions in aqueous media [45].

A chemosensor derived from pyridine-dicarbohydrazide and benzothiazole aldehyde (**Figure 53**) for the detection of various cations and anions. The sensor allowed the naked eye recognition of toxic Cu^{+2} ions in presence of many other cations as well as the recognition of some biologically relevant anions like F^{-}, AcO^{-} and AMP^{-2} ions with great sensitivity [79].

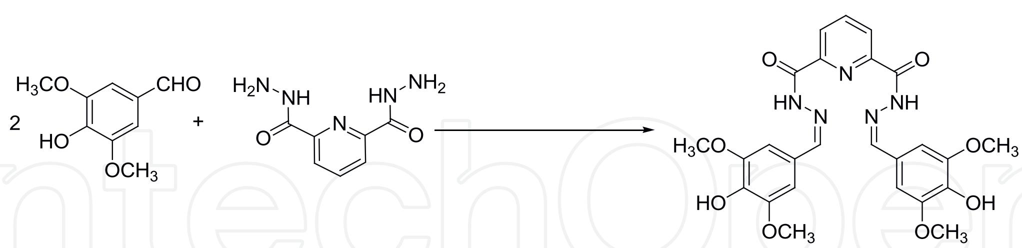

Figure 51.
Schiff base derived from 4-hydroxy-3,5-dimethoxybenzaldehyde and pyridine dicarbohydrazide.

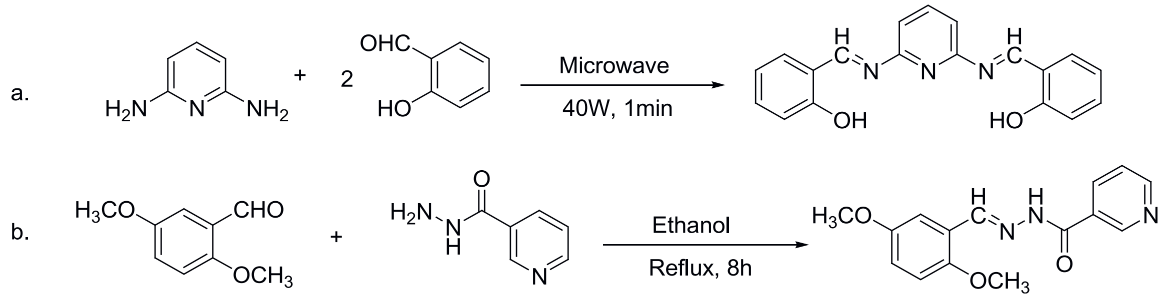

Figure 52.
a. Schiff base derived from 2,6-diaminopyridine and salicylaldehyde. b. Schiff base derived from 2,5-dimethoxybenzaldehyde and pyridine-3-carbohydrazide.

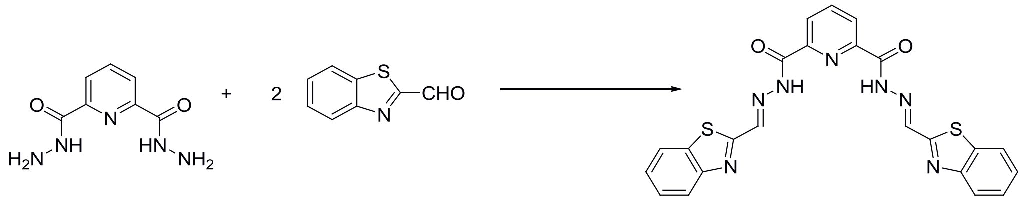

Figure 53.
Schiff base derived from pyridine dicarbohydrazide and benzothiazole aldehyde.

A chemosensor was designed from schiff base based on the condensation reaction between pyridoxal and 2-aminoethanol (**Figure 54**). The chemosensor produced a selective chromogenic behavior towards Ag^+ ions by changing the color of solution from light yellow to red observable by naked eye and also have excellent specificity and sensitivity towards Ag^+ ions over various other interfering cations in aqueous solution [80].

A Schiff base was derived from 4-E-2-phenyldiazenylaniline and pyridine-2-carboxaldehyde (**Figure 55**) and investigated for its cation recognition ability. The schiff base was found to be highly sensitive and selective for sensing of Ag^+ ions and Cd^{+2} ions and could act as chemosensor for the detection of Ag^+ and Cd^{+2} in presence of other interfering ions [81].

A porphyrin appended terpyridine compound was synthesized (**Figure 56**) and designed as chemosensor for its cation recognition ability. It was observed that the synthesized compound exhibited enhanced fluorescence in the presence of Cd^{+2} ions

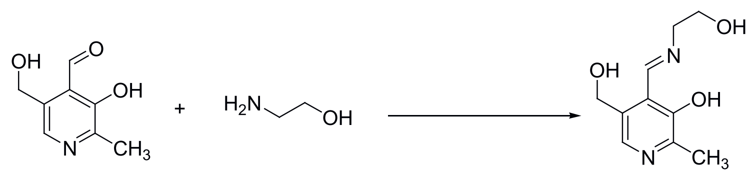

Figure 54.
Schiff base derived from pyridoxal and 2-aminoethanol.

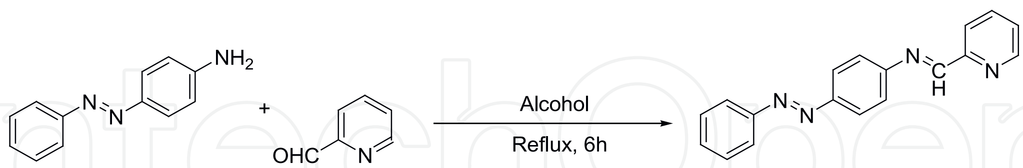

Figure 55.
Schiff base derived from 4-E-2-phenyldiazenylaniline and pyridine-2-aldehyde.

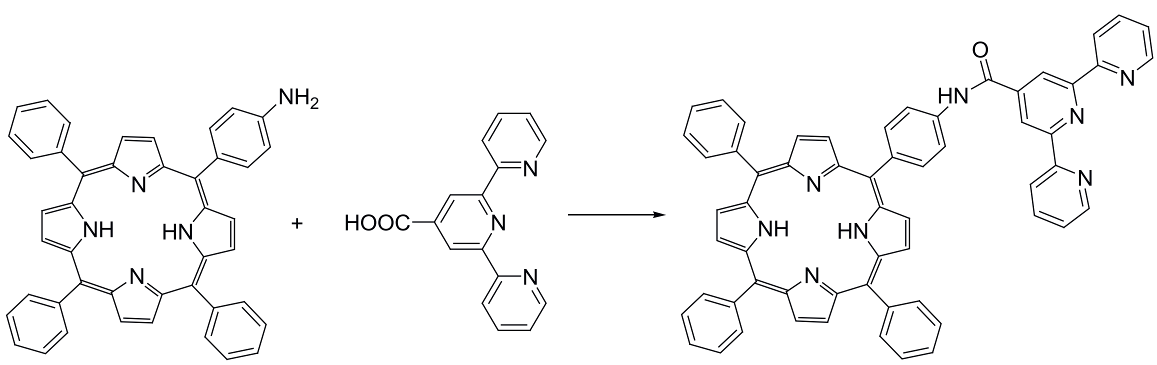

Figure 56.
Fluorescent chemosensor based on porphyrin appended terpyridine compound.

with high selectivity and sensitivity and could act as fluorescent chemosensor for Cd^{+2} ions in the presence of various other metal ions [82].

A schiff base based on 2,6-diaminopyridine was synthesized (**Figure 57**) and evaluated for its binding affinity with various metal ions. It was observed that the synthesized compound has prominent selectivity towards Pb^{+2}ions among various other metal ions and therefore could act as chemosensor for detection of Pb^{+2} ions [83].

A new bipyridine based ruthenium complex was synthesized (**Figure 58**) and investigated for its cation recognition ability. It was found that the synthesized compound was able to recognize Hg^{+2} ions in aqueous solution with high selectivity and could be used as chemosensor for the selective and sensitive detection of Hg^{+2} ions over various other cations [84].

A pyridine-based derivative of (Z)-2-(4-amino-phenyl)-3-(pyridine-4-yl) acrylonitrile was designed (**Figure 59**) and evaluated for its cation recognition properties. It was observed that the compound could selectively recognize Hg^{+2} ions by exhibiting a visible color change from light yellow to orange and could be used as a naked-eye sensor for detection of Hg^{+2} ions in presence of various other cations [85].

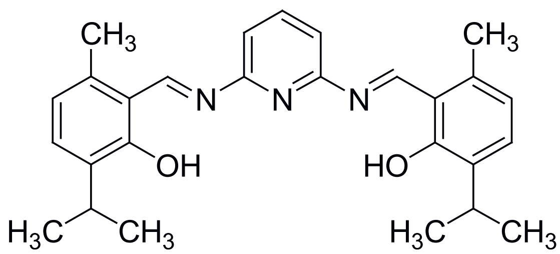

Figure 57.
Schiff base derived from 2,6-diaminopyridine and salicylaldehyde derivative.

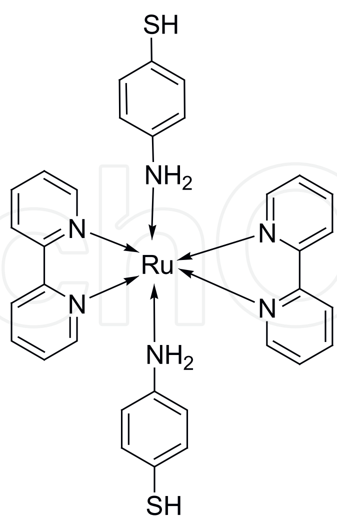

Figure 58.
Chemosensor based on bipyridine based ruthenium complex.

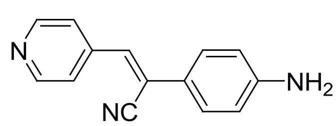

Figure 59.
Colorimetric sensor based on (Z)-2-(4-amino-phenyl)-3-(pyridine-4-yl) acrylonitrile.

Isoniazid functionalized silver nanoparticles were synthesized by wet chemical method (**Figure 60**) and it was observed to exhibit good absorbance and emission peaks with visible color change in the presence of Hg^{+2} ions. Therefore, these isoniazid capped silver nanoparticles could act as a selective chemosensor for the detection of Hg^{+2} ions in aqueous media [86].

Two schiff bases derived from fluorescein by condensation with 3-aminopyridine and 4-aminopyridine respectively (**Figure 61**) were evaluated for their ion recognition properties for various cations and anions. The compound 1 was able to detect Ce^{+3} cation in presence of various other metal ions and also F^{-} anion over other interfering anions and therefore could act as chemosensor for Ce^{+3} and F^{-} ions [87].

A simple, colorimetric and fluorimetric chemosensor was designed from an acylhydrazone based schiff base synthesized from Isoniazid and 2-hydroxynaphthaldehyde (**Figure 62**). The sensor was found to produce an immediate

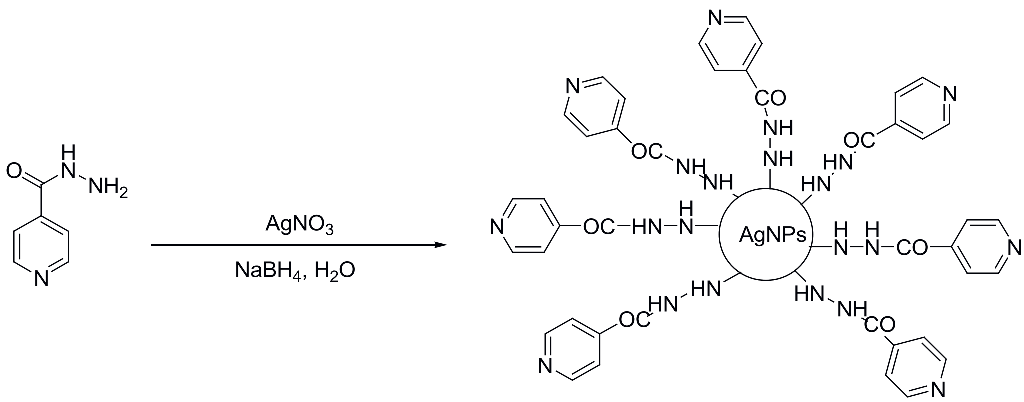

Figure 60.
Chemosensor based on isoniazid functionalized silver nanoparticles.

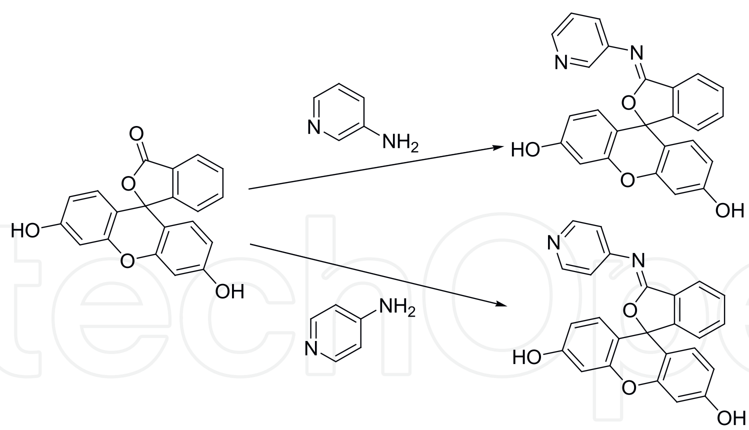

Figure 61.
Schiff bases derived from fluorescein with 3-aminopyridine and 4-aminopyridine.

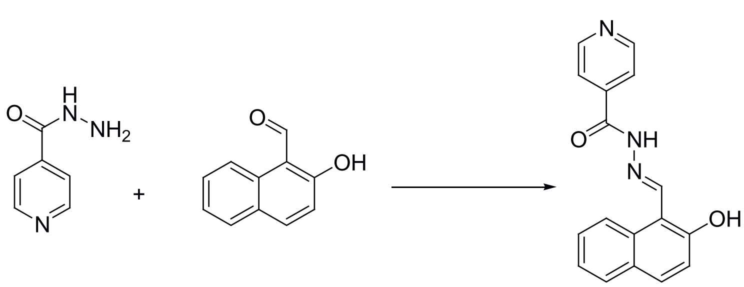

Figure 62.
Schiff base derived from Isoniazid and 2-hydroxynaphthaldehyde.

visible color change from colorless to yellow in the presence of CN^- ions in aqueous media with high selectivity and sensitivity [88].

Two schiff bases were prepared from pyridine-2-hydrazide with 5-nitrofuran-2-carboxaldehyde and 5-nitrothiophene-2-carboxaldehyde respectively (**Figure 63**) and tested for their anion sensing properties. The compound could selectively detect F^- and CO_3^{-2} ions over other interfering anions whereas compound could detect CO_3^{-2} ion with high selectivity and sensitivity. Finally, the compound was able to distinguish between F^- and CO_3^{-2} due to difference in their bathochromic shift [89].

A Hantzsch ester fluorescent probe based on thienyl-pyridine appended to dihydropyridine ring was synthesized (**Figure 64**) and applied for fluorescent sensing of nitric oxide in aqueous solution. The sensor showed extremely strong blue fluorescent which was switched off in the presence of NO and also possessed high selectivity and sensitivity towards NO [90].

A chemosensor based on 3,3′-(4-(2-amino-4,5-dimethoxyphenyl) pyridine-2,6-diyl) dianiline was synthesized (**Figure 65**) and found that it could detect formaldehyde through fluorescence enhancement and show the visible color change from yellow to blue. The compound could act as chemosensor for detection of formaldehyde qualitatively as well as quantitatively [91].

A simple Schiff base chemosensor was developed by the condensation reaction between 8-hydroxyjulolidine-9-carboxaldehyde and 2-hydrazinylpyridine (**Figure 66**). The ion recognition ability was determined for four transition metal ions

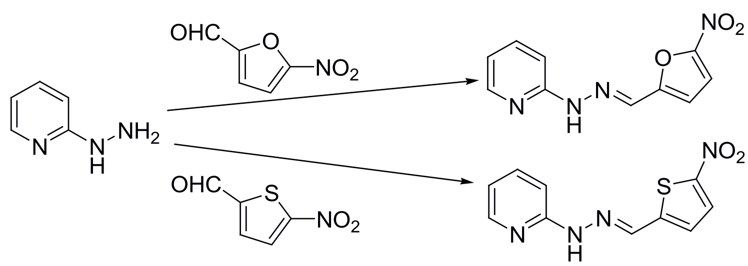

Figure 63.
Schiff bases derived from pyridine-2-carbohydrazide with 5-nitrofuran-2-aldehyde & 5-nitrothiophene-2-aldehyde.

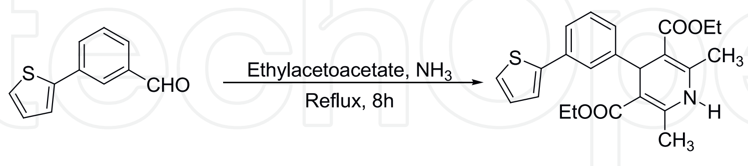

Figure 64.
Fluorescent probe based on thienyl-pyridine appended to dihydropyridine.

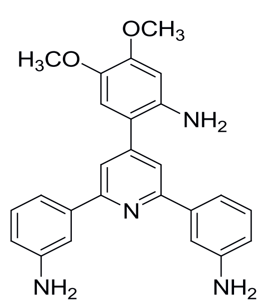

Figure 65.
Chemosensor based on 3,3′-(4-(2-amino-4,5-dimethoxyphenyl) pyridine-2,6-diyl) dianiline.

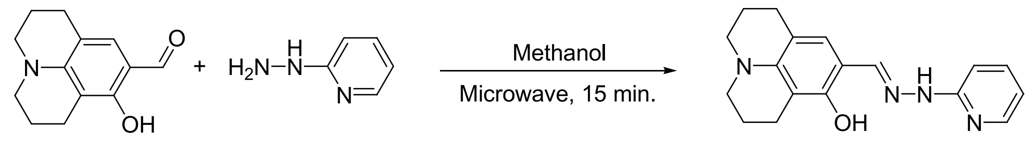

Figure 66.
Schiff base derived from 8-hydroxyjulolidine-9-carboxaldehyde and 2-hydrazinylpyridine.

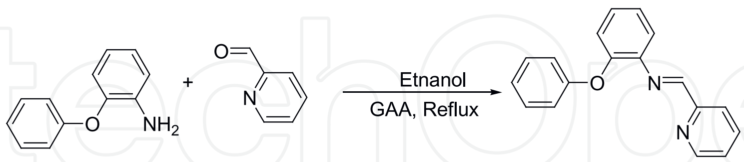

Figure 67.
Schiff base derived from 2-phenoxyaniline and pyridine-2-aldehyde.

Co^{+2}, Ni^{+2}, Cu^{+2} and Zn^{+2} using colorimetric and fluorescent analysis. It was revealed that the chemosensor can serve as an effective tool for the detection of all the four ions in environment as well as in biological applications [92].

A new fluorescent probe was designed from Schiff base 2-(pyridine-2-ylmethylene)-phenoxyaniline (**Figure 67**) and used for selective detection of Cd^{+2} ion. A significant fluorescence enhancement was observed and it gave satisfactory results for detection of Cd^{+2} ions in tap water and river water samples [93].

4. Conclusion

Pyridine is among the most valuable nitrogen-based heterocyclic compounds known for its important chemical and biological properties. The pyridine moieties are widely distributed in nature as in many naturally occurring compounds, vitamins, essential oils and metabolites which are required for various cellular functions. Additionally, pyridine derivative is used on large scale as precursor or intermediates in chemical and agrochemical products. Further, these derivatives possess therapeutic potentials due to their important bioactivities and with their proper structural modification or derivatization they can be led to important prodrugs or drugs. Literature review reveals that when pyridine-based nucleus is modified to some extent by introducing new functional group or even new molecule at appropriate positions, the bioactivity may be enhanced significantly. Thus, Schiff bases are continuously designed from amino or carboxaldehyde derivatives of pyridine since last few years and evaluated for their biological potential. As they possess a wide variety of biological activities, they are considered as a versatile pharmacophore and emerged as a potent class of pharmaceuticals for new drug development and continue to be an active area of research in medicinal chemistry. Development of novel drugs as a pharmacophore group is a constantly growing need that concerns researchers throughout the world as increasing number of diseases continue to be an emerging problem. The chemistry of pyridine-based Schiff bases is less extensive and not much work has been done in this field. In the view of the stated pharmacological properties of pyridine compounds, it is expected that they have high potential in the field of various biological activities that are still unexplored. Further, owing to their strong binding abilities towards various ions and unique photophysical properties, Schiff bases find applications in ion recognition and widely used as chemosensors for selective detection of ions. The ion recognition studies have gained extreme importance in recent years in the field of chemical, biological and environmental sciences. There is an urgent need to develop some efficient approaches to detect metal ions with high selectivity and sensitivity so that to control their harmful effect on human health and environment. It can be expected that the chemosensors derived from Schiff bases of pyridine derivatives do not have much complex structure and can be synthesized easily with good yield and purity as compared to most of other chemosensors. Thus, designing of specific chemosensor for the recognition of various ions is one of the most demanding areas of present chemical research due to their significant contribution in analytical, industrial, agricultural, environmental and biological fields. Keeping all these facts in the mind, it is of extreme importance to synthesize some Schiff bases derived from pyridine derivatives and to evaluate their potential as bioactive ligands and chemosensors. This chapter covers not solely the chemistry and biological significance of pyridine derivatives, but also reflects the light on Schiff bases derived from them with their pharmacological importance and ion recognition properties. It is worthwhile to have a full overview about pyridine, its derivatives and Schiff bases derived from them, all at one place with recent researches that will provide a single platform for potential researchers of these fields. Thus, the main objective of this chapter is to promote the research and development of some new pyridine-based Schiff bases and to evaluate their various biological activities for their effective use in drug designing process as well as their applications in ion recognition studies to develop more efficient chemosensors.

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Conflict of interest

The author declares no conflict of interest.

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