International Journal for Multidisciplinary Research (IJFMR)
E-ISSN: 2582-2160 ● Website: www.ijfmr.com ● Email: editor@ijfmr.com

A Review on Hetero Cyclic Compounds & Schiff Base

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ABSTRACT
The Azetidinone is well known as the (Beta-lactams) rings of a four-membered cyclic amine it is named due to N atom which is linked to Beta-carbonyl with carbonyl. Pyrazine ring plays an important role as a basic scaffold in drug designing. These compounds containing N-heterocyclic moieties are a class of privileged compounds that have found numerous application as pharmaceuticals. Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Schiff in 1864. Pyrazines is used to treat anti-diabetic, anti-tubercular and anti-cancer activities.These compounds containing N-heterocyclic moieties are a class of privileged compounds that have found numerous application as pharmaceuticals. All these above heterocyclic compounds have so many pharmacological activities such as anti microbial, anti bacterial, anti-cancer activities.

KEYWORDS: Azetidinenone, Metal complexes, Pyrazine, Schiff base.

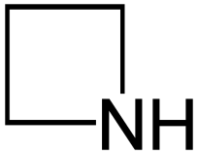
INTRODUCTION

Heterocyclic chemistry is one of the most important branch in chemistry that encompass the synthesis characteristics and applications of the hetero compounds they may be either cyclic or noncyclic in nature heterocyclic compounds play a vital role in the metabolism of living cells. They are used as vehicles in the synthesis of other compounds[1-3] some of these chemicals has been associated with therapeutic property[4]·The ring contain at least one atom of an element other than carbon large number of them five and six membered heterocyclic compound the hetero atom may be oxygen, nitrogen, Sulphur[5]·The some of common hetero-cyclic compounds used in the medicines are amino acids like praline histidine and crypto-phan vitamins co-enzyme precursors such as thiamine, riboflavin, folic acid, B_{12} and E families of the vitamins[6].Heterocyclic chemistry with nitrogen as heterocyclic atom is considered as significant and special class of organic chemistry, nitrogen containing heterocyclic compounds-unlike pyrimidine, quinolone, pyrrole, indole, imidazole, triaxle and pyrazine have prominent place in medicinal chemistry among these pyrazine indole and triaxle are considered the moieties because of their biological and pharmacological activities[7-12].

INTRODUCTION OF AZETIDINE

The Azetidine is well known as the (Beta-lactams) rings of a four-membered cyclic amine it is named due to n atom which is linked to Beta-carbonyl with carbonyl. chemistry of this has[13-15]wide spectrum and essential part in organic synthetic chemistry[16]and some of biological activities such as antibacterial, anti-inflammatory,[17]CNS activity and anticancer activity The molecular action of the Beta-lactam

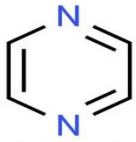
derivative antibiotic is power selective and irreversible inhabitation. When it is use for processing enzymes of developing peptidoglycan layer [18].It is also used for different type of micro activity by bacteria or virus which affected the vital cell in human[19].



1.1 AZETIDINE MOEITY

INTRODUCTION OF PYRAZINE MOEITY

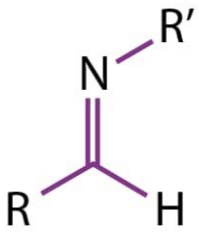
Pyrazine ring plays an important role as a basic scaffold in drug designing [20] such as glipizide, pyrazinamide and bortezomib to treat anti-diabetic, anti-tubercular and anti-cancer activities[21]. These compounds containing N-heterocyclic moieties are a class of privileged compounds that have found numerous application as pharmaceuticals[22]. The derivatives of pyrazine have their applications in food, medicines, dyes, semiconductors and act like ligands in co-ordination chemistry[23]. The pyrazine derivatives are found to show anti-microbial, anti-allergic, biological activities. when combined with metal complexes, the nitrogen-containing organic compound exhibits various biological activities and DNA binding activity. Pyrazine compounds are synthesized by the reaction of diamines with diols in a vapour phase. These are also obtained by condensation reaction [24].



1.2 PYRAZINE MOEITY

INTRODUCTION TO SCHIFF BASE

Schiff bases are condensation products of primary amines with carbonyl compounds and they were first reported by Schiff in 1864[25].The common structural feature of these compounds is the azomethiene group with a general formula RHC=N-R1, where R and R1 are alkyl, aryl, cyclic alkyl or heterocyclic groups which may be variously substituted. These compounds are also known as anils, imines or azomethines[26].Schiff bases are derived from indole-3-carboxaldehyde and m-amino benzoic acid were synthesized[27].Schiff base ,it is the most widely used organic compounds, have been widely used in synthesis of intermediates ,biological actions, polymers, and so forth and obtained a lot of progress. Schiff bases have been shown to exhibit a broad range of biological activities .Schiff bases form a significant class of compounds in medicinal and pharmaceutical chemistry with several biological applications that includes antibacterial, antifungal, anticancer, antioxidant, neurological disorders and diuretic activities[28].



1.3 SCHIFF BASES MOEITY

PHYSICAL PROPERTIES OF AZETIDINE

Azetidin-2-ones are hydrolytically sensitive colourless solid. They have a melting point of 73 - 74°c. Other simple azetidin-2-ones are low melting solids or oils. A number of monocyclic azetidinones were subjected to x-ray crystallographic studies and came into a conclusion that the ring is essentially planar with N2 atom slightly out of the mean plane of its substituent's except where steric factors enforce greater deviations from planarity. In normal amides C=O shows a distance of 1.32Å, but azetidinones shows a distance of 1.38. The increased distance is the reason for angle strain[29].

PHYSICAL PROPERTIES OF PYRAZINE

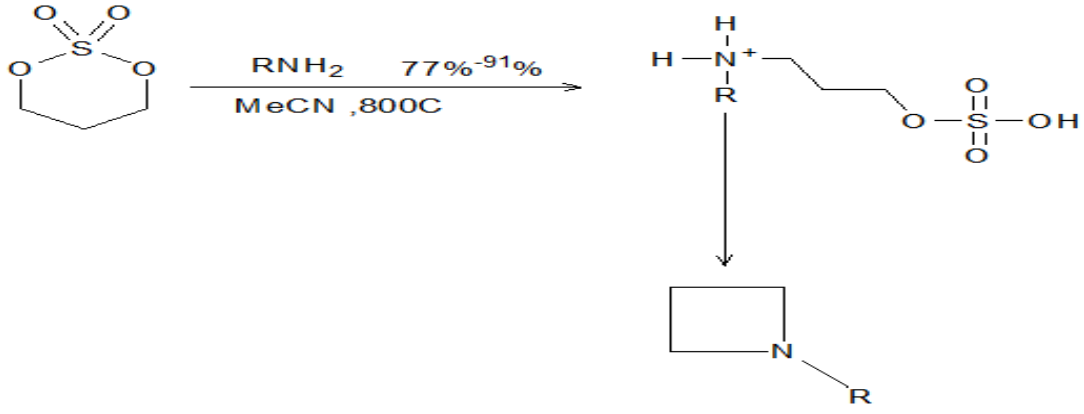
Pyrazine are water soluble colourless solids. They have a low melting point 52c and boiling point is 115c.Pyrazine has spectral characterisation using different spectral techniques including IR, NMR together with elemental analysis[30,31].

PHYSICAL PROPERTIES OF SCHIFF BASES

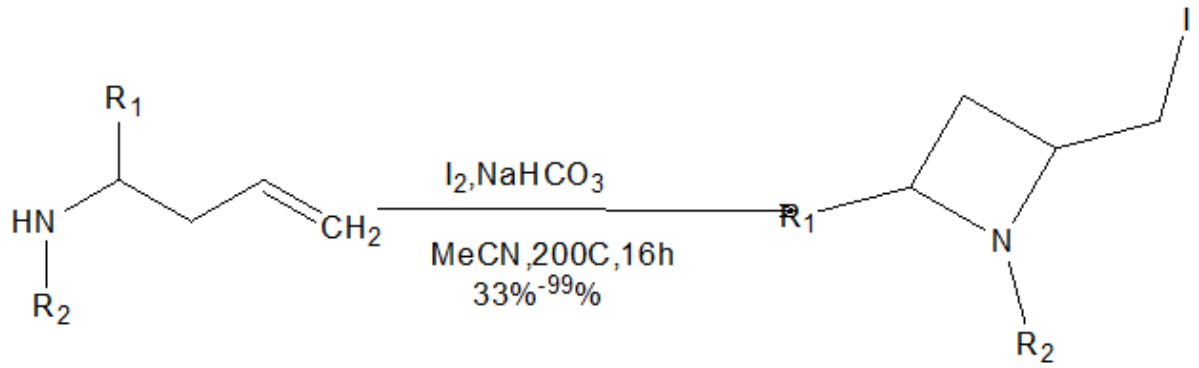
Schiff bases are usually coloured and transparent solids.They have used in the determination of metal amounts and in the identification carbonyl compounds due to their precise melting points. The carbon-nitrogen double bond in Schiff bases rotates more easily than the carbon-carbon double bond which allows stereoisomer to transform into each other. The reason for this polarisation occurs in the azomethine bond due to the fact that nitrogen is more electronegative than carbon[32].

SYNTHESIS OF AZETIDINE

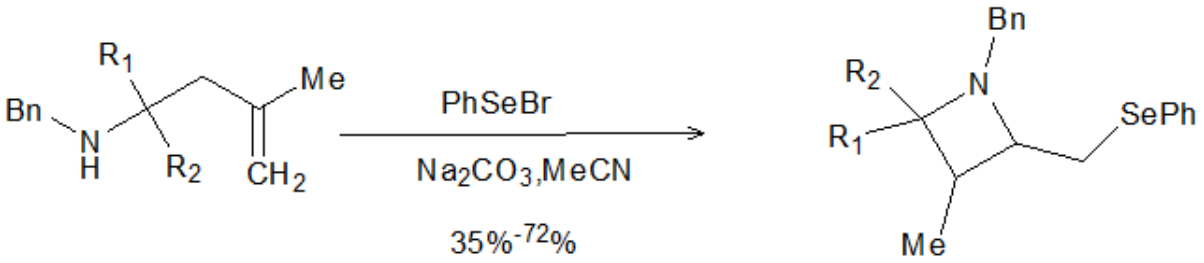
1. Cyclization of these sulphates on microwave irradiation in aqueous potassium hydroxide leads to the formation of N-substituted azetidines in moderate to good yields.



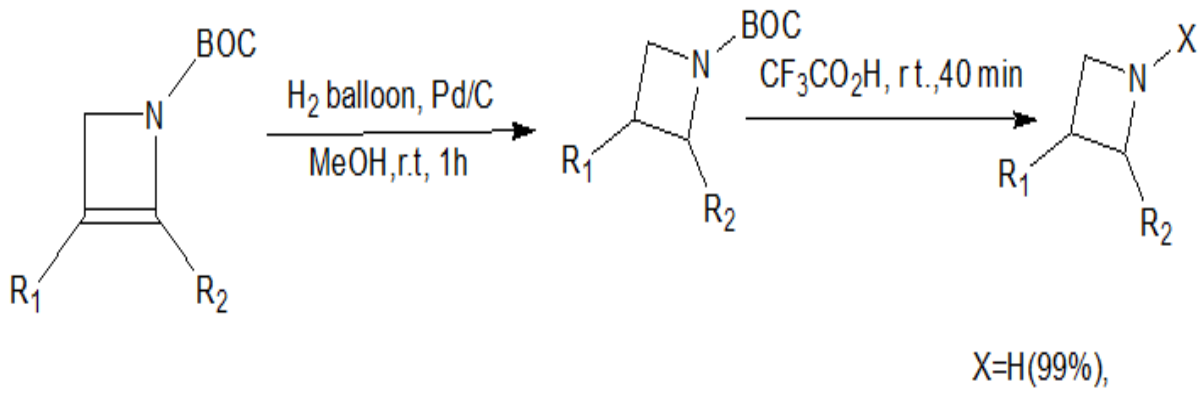
2. In the presence of sodium hydrogen carbonate, the reaction between homoallylic amines and three equivalents of iodine in acetonitrile at room temperature results in iodocyclization forming 2-(iodomethyl) azetidine derivative with cis-diastereo selectivity.



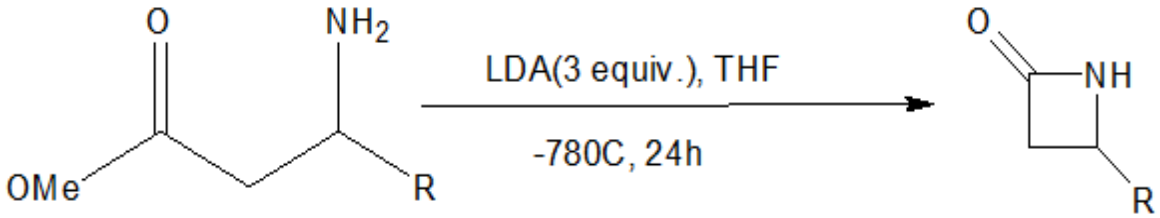
3. The 4-exo trig cyclization of a homoallylic amine, N-benzyl-1-(1-pyridin-3-yl)but-3-ene-1-amine, in the presence of iodine at room temperature forming cis-1-benzyl-4-iodomethyl-2-(pyridine-3-yl)-azetidine. Then the functionalization was iodine was reached by nucleophilic displacement. The formation of pyrolidines from iodomethyl azetidines was achieved by heating, with complete stereo control. A regioselective synthesis of N-benzyl-2,4-disubstituted azetidines is reported by the activation of homoallylic amines with phenylselenium bromide.



4. Reduction of 3,4-disubstituted N-azetidines in the presence of catalyst hydrogen and palladium leads to the formation of syn-2,3-disubstituted N-Boc azetidines in quantitative yields. Subsequent amine de protection with tri fluoroacetic acid leads to NH-azetidines in good yields.



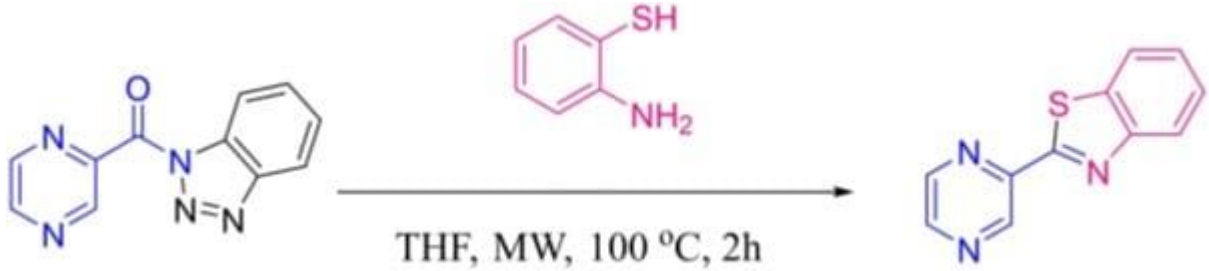
5. Cyclization of chiral β-amino esters in the presence of lithium di-isopropyl amide (LDA) results in the formation of 2-azetidinones in quantitative yields[33].



R=Me$(CH_2)_7$, $C_6H_5(CH_2)_2$,

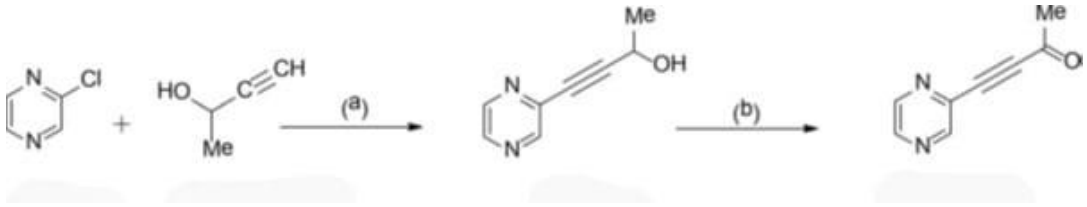
SYNTHESIS OF PYRAZINE

1. To understand the role of amino acids in the conjugates, we have synthesized the conjugate containing pyrazine and benzothiazole without amino acid linker following a similar reaction condition



2. Synthesis of Taraxerone derivative fused to a pyrazine ring via Willgerodt Kindler reaction. Reagents: Morpholine, Sulphur.[34]

3. Synthesis of tetra-aryl and tetra-alkenylpyazines via Suzuki-Miyaura coupling reaction[35].



SYNTHESIS OF SCHIFF BASES[36]

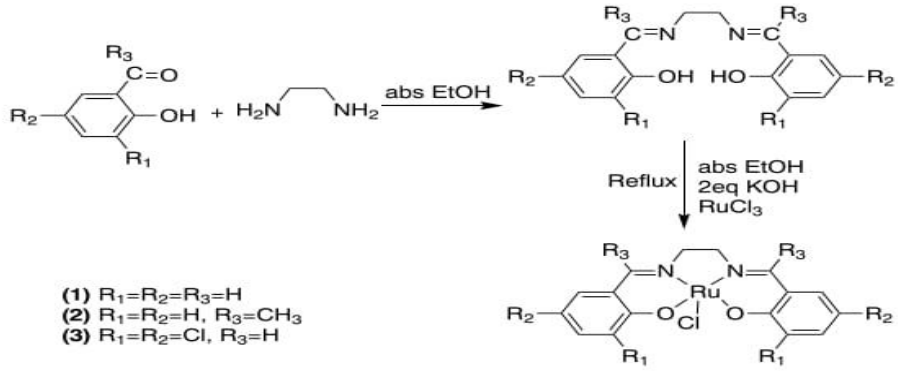


Figure 5. Suggested structures of Schiff base ligand and its metal complexes with Ru(III).

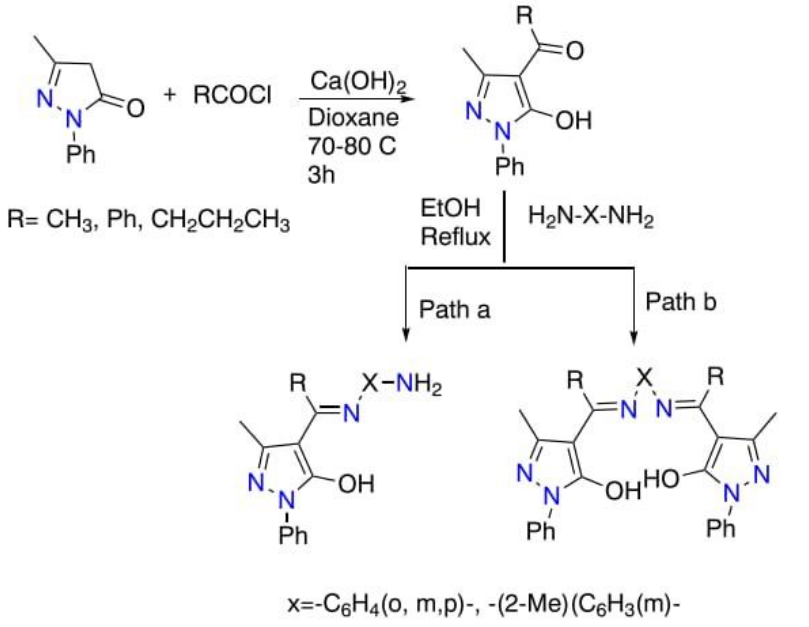
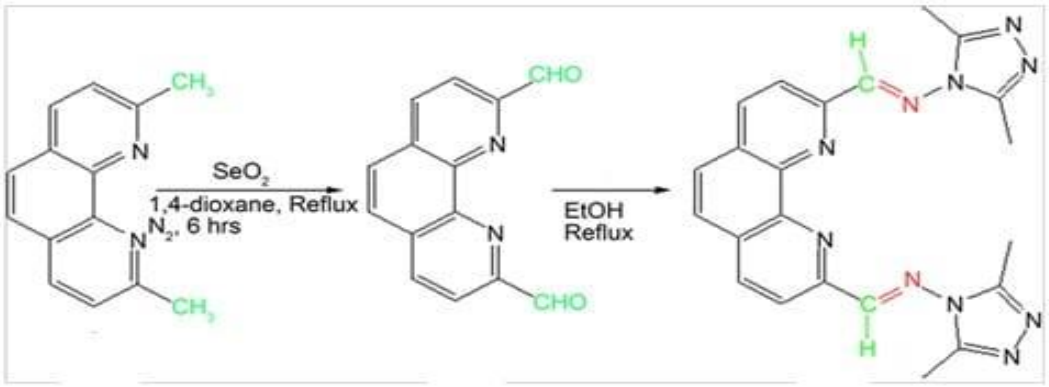


Figure 15. Synthetic scheme of Schiff bases from 4-acyl-5-pyrazolones with aromatic diamines.

1,10-phenanthroline-2,9-dicarboxaldehyde was synthesized form 2,9-dimethyl-1,10- phenanthroline hemihydrate following previously reported procedure . Neocuproine hemihydraes (3.0 g, 0.0144 mol) was dissolved in 200 ml 1,4-dioxane containing 4% water and SeO_2 (6.0 g, 0.054 mol) was added and the reaction mixture was refluxed for 6 h (Scheme . Then the reaction mixture was filtered through thick celite pad. Light yellow product was precipitated on slow cooling to room temperature. The product was isolated and dried under vacuum. The crude product was purified by recrystallization in chloroform to get pure compound.



IMPORTANCE OF AZETIDINE

Azetidines are used to synthesize dyes and coordination polymers. These are used in pharmaceutical industries and to synthesize organic compounds. Azetidine compounds and this metal complexes have antimicrobial,anti-cancer properties[37].

IMPORTANCE OF PYRAZINE

1. Pyrazine derivatives comprise a variety of pharmacological actions including antipyuretic,anti-inflammatory,analgesic,anti-cancer,anti-bacterial anti-oxidant activity.
2. Pyrazine find various applications as ingredients in pesticides insecticides dyes and pharmaceutical compounds[37].

IMPORTANCE OF SCHIFF BASES

1. Hydrazide–hydrazones are synthesized in search of effective antibacterial and antifungal agents—especially due to the growing problem of antibiotic resistance.
2. In many cases, it is the presence of electron-withdrawing aromatic ring substituents that is essential for the antimicrobial activity of hydrazide–hydrazones.
3. The lowest MIC values (μg/mL) are shown for the chlorine substituent in position 2, against E. coli, S. aureus and B. subtilis, 0.31, 0.62 and 0.31, respectively.
4. They were compared with the MIC values of ciprofloxacin an organic antimicrobial compound inhibiting bacterial DNA topoisomer[38].

ACTIVITIES OF AZETIDINE

ANTIBACTERIAL ACTIVITY

Synthesis of 2-{2-[3-chloro-2-(aryl)-4-oxoazetidin-1-ylamino]-acetylamino}benzothiazole-6 carboxylicacid,2- aminoaminobenzothiazole-6-carboxylicacid on condensation with chloroacetyl chloride gave 2-(2-chloroacetyl amino) benzothiazole-6-carboxylic acid which on further amination with hydrazine hydrate gave 2-(2-hydrazinoacetyl amino) benzothiazole-6-carboxylic acid 2-(2-hydrazinoacetylamino) benzothiazole-6-carboxylic acid. The Schiff bases thus obtained were treated with various aromatic aldehydes in presence of glacial acetic acid and further dehydrative annulory action a was carried out with chloroacetyl chloride and triethylamine to yield 2-{2-[3-chloro-2-(aryl)-4-oxoazetidin-1-ylamino] acetylaminoactivity against S. aureus, B. subtilus, P. aeruginosa and Ecoli.

ANTI-INFLAMMATORY ACTIVITY

Synthesis of N-Substituted-3-chloro-2-azetidinones and screened it for anti-inflammatory action. It was synthesized by treating chloroflouro aniline with KSCN in presence of bromine in glacial acetic acid and ammonia to get 2-AMINO-6-FLOURO-7-CHLORO-1,3 BEZOTHIAZOLE which was treated with anthranilic acid in presence of dry pyridine to get 2-amino-N[6-FLOURO-7-[1,3]benzothiazole-2-yl]benzamide.This was then reflexed with vanillin and alcohol in presence of conc.HCL.2[3-hydroxy-4-methoxy-bezilidine amido]6-flouro-7-chloro[1,3]benzothiazole or Schiff base. Solution of Schiff base in1,4-dioxane was added to well stirred mixture of chloro acetyl chloride and tri ethyl amine to get azetidone[39]

BIOLOGICAL ACTIVITY OF PYRAZINE

ANTIMICROBIAL ACTIVITY

3,5-dichloro-pyrazine-2(1H)-one shows fungicidal activity. against the human fungal pathogen Candida albicus.Phevalin (a),Tyrvalin(b), Leuvalin(c) its antibacterial activity Methicillin against staphylococcus aureus.&Arglecin(e),Argvallin(d), against Streptomyces. Hemecanthin shows antibacterial activity against C.albican 3,6-diisobutyl Pyrazin-2(1H)one compound and
3- isobutyl-6-
hydroxy2- methylpropyl) Pyrazine2(1H)one shows antifungal activity against asAspergillus sp.
Sorazinone show antibacterial activity against Norcardip sp.

ACTIVITIES OF SCHIFF BASES

ANTIMALARIAL ACTIVITY

Malaria is an under-appreciated disease that continues to pose major public health issues. Malaria is now present in over 100 countries in Africa, Latin America, Asia, and Oceania. Plasmodium malaria is caused by four different types of Plasmodium (P. falciparum, P. vivax,P. ovale, and P. malaria). Plasmodium is transmitted by female mosquitos of the Anopheles genus. Schiff bases have been found to be useful moieties in the development of antimalarial drugs.

Ancistrocladidine is a secondary metabolite produced by Ancistrocladaceas and Dioncophyllaceae plants with an imine group in their molecular scaffold. The activity of compound ‘2a' against P. falciparum K1 and has been demonstrated. The ancistro-cladidineminimum inhibitory concentrations (MIC values) required to totally stop P. falciparum K1 and 3D7 growth were 0.3 and 1.9 µg/mL, respectively. Compound 1 was 90- and 10-fold more selective. falciparum K1 and 3D7 than rat skeletal myoblast L-6 cells, respectively. In vitro activity of Schiff base-functionalised 5-nitroisoquinolines against an

ACC Niger chloroquine resistant P-falciparum strain.Among the5-nitroisoquinoline derivatives, Schiff base was the most effective antimalarial drug[40].

ANTI-FUNGAL ACTIVITY

Fungal infections are not normally limited to the surface tissues; it has been a major rise in life threatening systemic fungal infections . The primary reason for this is the growing number of patients who are at risk, including those who are elderly, have undergone major surgery, are on immunosuppressive therapy, have AIDS, are undergoing cancer treatment, and have had solid organ and hematopoietic stem cell transplantation. Antifungal agents that are more effective must be researched and antifungal agents[41].

CONCLUSION

In this review, reviewed the various synthetic proceuders for the three compounds. The heterocyclic rings has various pharmacological activities & uses biological activities activities .such as anti-microbial activity, anti-cancer activities. Pyrazine was evaluated as a good catalyst. Some Schiff bases are going to act as a intermediates for the synthesis of new nucleus and derivatives shows anti-bacterial and anti-fungal activities. Azitidinine persists the anti bacterial activity.

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