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REVIEW ARTICLE ON IMIDAZOLE

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ABSTRACT

Imidazole has a special role in heterocyclic chemistry and its derivatives have piqued interest in recent years due to its diverse chemistry and pharmacology properties. Imidazole is a nitrogen-containing heterocyclic ring that is essential in biology and pharmaceuticals. Anti-bacterial, anti-cancer, anti-tubercular, anti-fungal, analgesic, and anti-HIV, etc are some of the biological activities of imidazole and its derivatives. The high therapeutic properties of imidazole-related drugs have encouraged medicinal chemists to synthesize a large number of novel chemotherapeutic agents. This article aims to review the synthesis and some of the important reactions and various pharmacological activities of imidazole and its derivatives.

KEYWORDS: Imidazole, anti-bacterial, anti-fungal, anti-HIV, analgesic, anti-cancer, anti-histamine, anti-helminthics, anti-tubercular, anti-deppresent.

INTRODUCTION

The name "imidazole" was derived in 1887 by the German chemist Arthur Rudolf Hantzsch (1857–1935). It is a five membered aromatic heterocyclic compound, having molecular formula of $C_3N_2H_4$. It is classified as diazole having non-adjacent nitrogen atom.

IMIDAZOLE can serve as a weak acid and weak base.

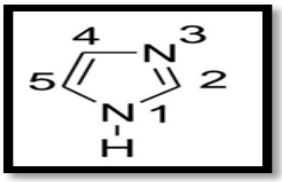

Fig. 1: Structure of imidazole.

Imidazole is a highly polar compound, as evidenced by its electric dipole moment of 3.67D.[1] Imidazole is an amphoteric. As it can function as both an acid and a base. As an acid, the pKa of imidazole is 14.5. The acidic proton is located on N-1. As a base, the pKa of the conjugate acid is approximately 7. In the medicinal field, imidazole has many biological/ pharmacological properties.

Reactivity of imidazole

The electrophilic reagent would attack the unshared electron pair on N-3, but not that on the 'pyrrole' nitrogen since it is the part of the aromatic sextet. While the imidazole ring is rather susceptible to electrophilic attack on an annular carbon, it is much less likely to become involved in nucleophilic substitution reaction unless there is a strongly electron withdrawing substituents elsewhere in the ring. In the absence of such activation the position most prone to nucleophilic attack is C-2. The fused benzene ring in benzimidazoles provides sufficient electron withdrawal to allow a variety of nucleophilic substitution reaction at C-2.

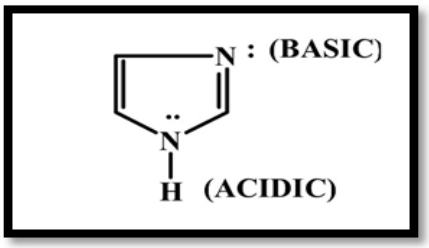

Fig. 2: Reactivity of imidazole.

The overall reactivity of imidazole is referred from sets of resonance structure in which the dipolar contributors have finite importance. These predict electrophilic attack in imidazole at N-3 or any ring carbon atom, nucleophilic attack at C-2 or C-1and also the amphoteric nature of the molecule.

Physicalproperties

- It is colourless liquid having a high B.P of 256^0C than all other 5- membered heterocyclic compounds.
- Imidazole's shows a large value of dipole moment of 4.8 D in dioxane.
- Imidazole show amphoteric properties and has pKa of 7.2 more than pyrazole and pyridine.
- Imidazoles are an aromatic compound possessing a resonance value of 14.2 K cal1/ mol, which is almost half the value for pyrazole.

- The electrophillic substitution occurs frequently in imidazole and nucleophillic substitution happens in the presence of electron withdrawing group in its nucleus.
- Imidazoles have Melting point 90^0C, it is a weakbase and tautomeric substance, since position 4 and 5 are equivalent.
- It's spectroscopic parameters are λ_{max} of 207 nm, I.R.=1550, 1492, 1451(cm^{-1}), τ = 2.30, 2.86, mass spectroscopy is studied for heterocyclic compounds containing one hetero-atom, in detail, not in case containing two or more heteroatom.

Chemical properties

1. Aromaticity

- Imidazole have 3C and 2N, all are sp2 hybridize.
- Sp2 hybridization is planar, it makes a planar imidazole ring structure.
- Each ring atoms also contains unhybridized p-orbital that is perpendicular to the plane of sigma bond (plane of ring).
- Here p orbitals are parallel to each other, so overlapping b/w p-orbitals is possible.
- The total no. of non bonding e- are 6 (3 of three C, 1 from 1 N and 2 of other N). The resonance of $6e^-$ follows the Huckel's rule.

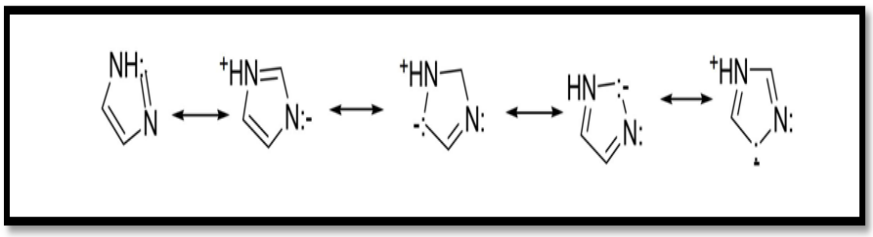

Fig. no. 3: Aromaticity of imidazole.

2. Tautomerism

Imidazole with ring N-hydrogen are subject to tautomerism.

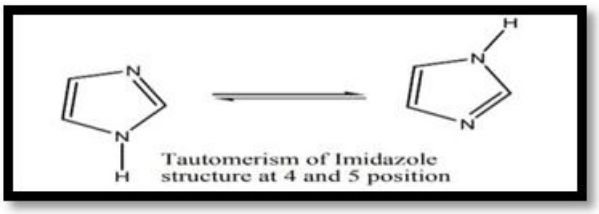

Fig. no. 4: Tautomerism of imidazole.

3. Hydrogen bonding: The intermolecular H-bonding, where there is linear association of molecule.

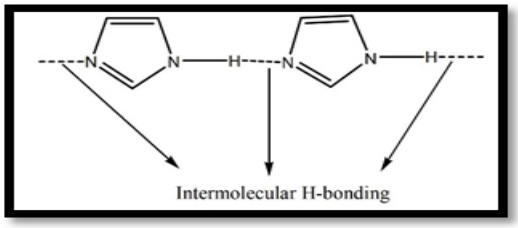

Fig. no. 5: Hydrogen bonding of imidazole.

4. **Acid – Base reaction:** Imidazoles are moderately strong base (weak acidic properties or pseudoacidic) but more acidic than many other hetero cyclic compounds. They form salts with many acids.

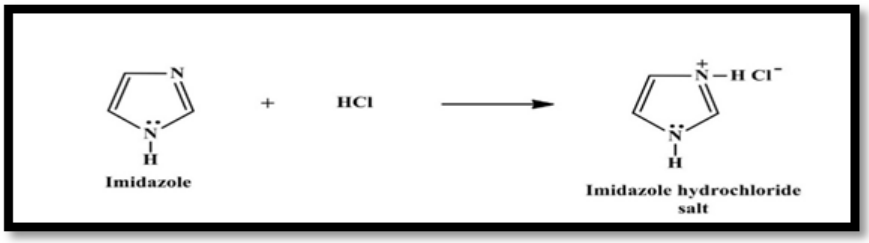

Fig. no. 6: Acid-base reaction of imidazole.

Some important reactions of imidazole

1. Halogenation of Imidazole is very complex and depending on the substrate, reagents and reactions concentration. Direct chlorination gives undefined product. Bromination (Br2+CHCl3, -10ºC) yields 2, 4, 5-tribromo derivative. Iodination of Imidazole takes place in alkaline condition to give 2, 4, 5-triiodoimidazole.

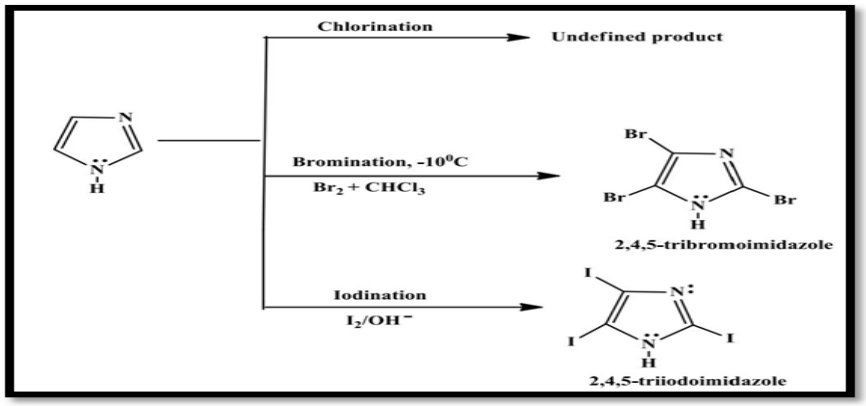

Fig. no. 7: Halogenation of the imidazole.

2. On diazotization, coupling occurs at position 2nd, if position 2nd is occupied or blocked, then it occurs at 4/5 position.

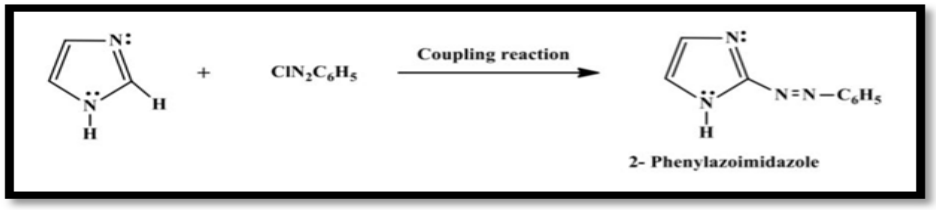

Fig. no. 8: Diazotization reaction of the imidazole.

3. Mercuration takes place at 4 and 5 positions.

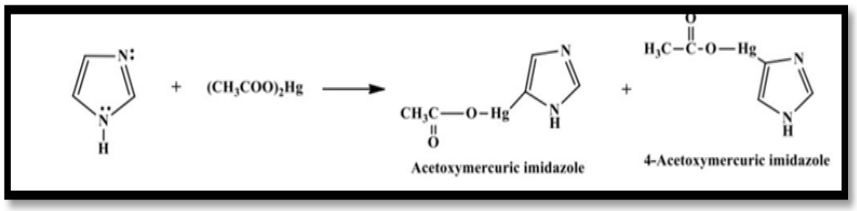

Fig. no. 9: Mercuration reaction of the imidazole.

4. Nucleophilic substitution reaction

Attack of nucleophile occurs at 2nd position.

Ex.- 1-methyl 4,5- diphenyl imidazole reacts with KOH at 300ºC to give imidazole -2 [3H] one.

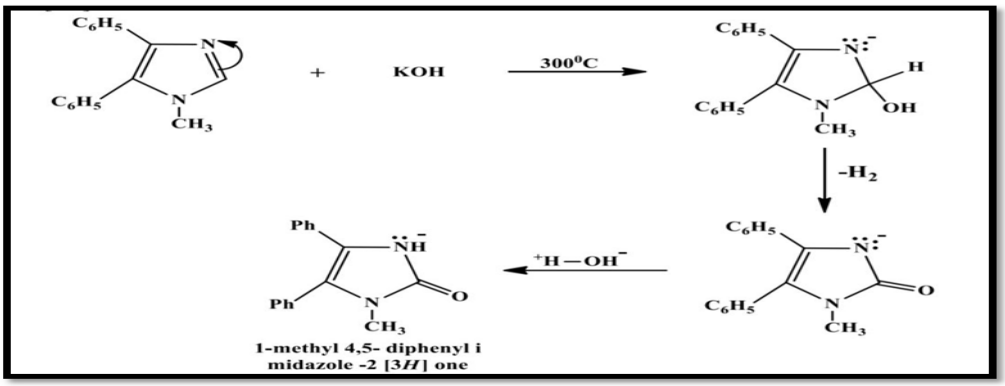

Fig. no. 10: Nucleophilic substitution reaction of imidazole.

Synthesis of imidazole

1. Radziszewski synthesis

Radiszewski reported the condensation of a dicarbonyl compound, benzil and α- keto aldehyde, benzaldehyde or α-diketones in the presence of ammonia, yield 2, 4, 5-triphenyl-imidazole.[2]

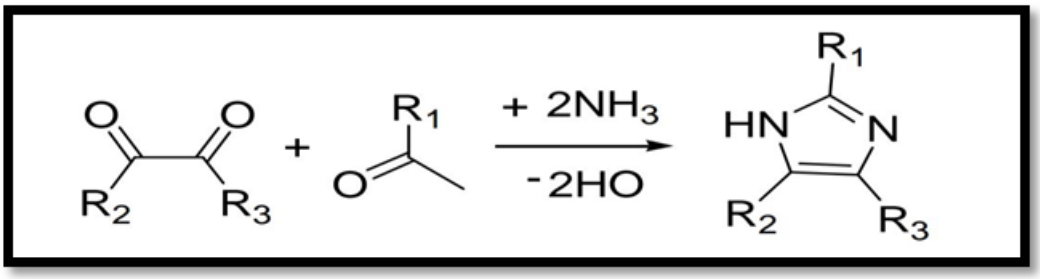

Fig. no. 11: Radziszewski synthesis.

2. Debus synthesis

Debus Synthesised imidazole by using glyoxal and formaldehyde in ammonia. This synthesis, while producing relatively low yields, is still used for creating Carbon-substituted imidazoles.[3]

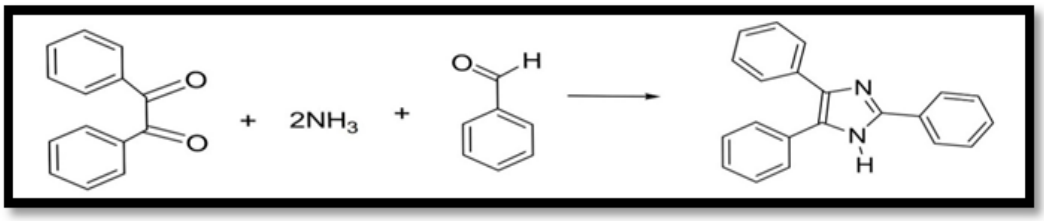

Fig. no. 12: Debus synthesis of imidazole.

3. Wallach synthesis

Wallach reported that when N, N- dimethyloxamide is treated with phosphorus pentachloride, a chlorine containing compound is obtained which on reduction with hydroiodic acid give N-methyl imidazole. Under the same condition N, N-diethyloxamide is converted to a chlorine compound, which on reduction gives 1- ethyl –2- methyl imidazole.[4]

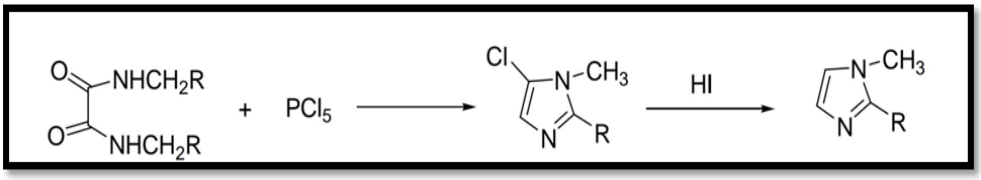

Fig. no. 13: Wallach synthesis of imidazole.

4. Markwald synthesis

The preparation of 2- mercaptoimidazoles from α-amino ketones or aldehyde and potassium thiocyanate are used for the synthesis of 2-thiol substituted imidazoles. The sulphur can readily be removed by a variety of oxidative method to give the desired imidazoles.[5]

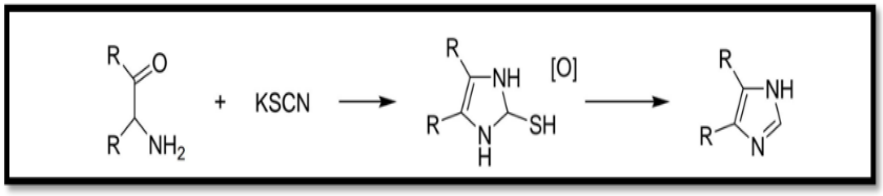

Fig. no. 14: Markwald Synthesis of imidazole.

5. Dehydrogenation of imidazoline

A milder reagent barium manganate to convert imidazolines to imidazoles in the presence of sulphur. Imidazolines obtained from 1, 2 ethanediamine and alkyl nitriles on reaction with BaMnO4 yield 2-substituted imidazoles.[6]

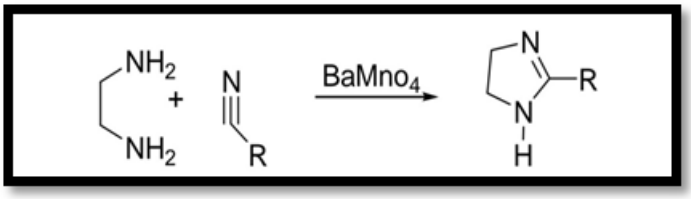

Fig. no. 15: Dehydrogenation reaction of imidazole.

6. From α- Halo ketone

The interaction between alpha halo ketone acyloin reacts with amidine to yield imidazole derivatives.[7]

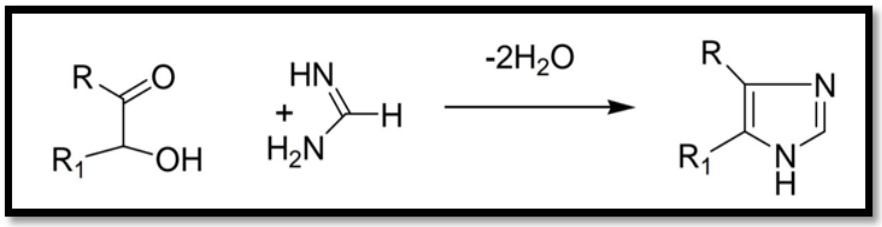

Fig. no. 16: Synthesis of imidazole from α-Halo ketone.

7. From Aminonitrile and Aldehyde

Mixture of an aldehyde and aminonitrile both condensed under suitable reaction condition to give substituted imidazole.[8]

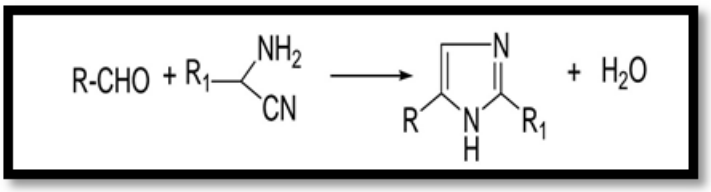

Fig. no. 17: Synthesis of imidazole from Aldehyde and Amino nitrile.

Biological /Pharmacological activities of imidazole derivatives

It is found that imidazole and their derivatives they possess potent activities against fatal diseases and playing a significant role in a fight against many diseases.

1. Anti-hiv activity

1. Acquired immune deficiency syndrome (AIDS) is a viral disease caused due to the special virus Human Immunodeficiency Virus.[9]

2. In this regard imidazole and their derivatives are playing a significant role in the treatment of disease. During the course of drugs for the treatment of HIV-AIDS, the activity is mainly focused on the interaction of the compound with the active site of the viral enzyme to inhibit its growth.[10]

3. Derivatives of 2-(1-aryl-1H-imidazol-2-ylthio)acetamide[imidazole thioacetanilide (ITA)] was evaluated against Human Immunodeficiency Virus type-1 (HIV-1).[11]

4. Some 5-carbonyl-1H-imidazole-4-carboxamides were developed which were the potent inhibitor for HIV-1 integrase, because of the presence of the imidazole moiety.[12]

5. Some butterfly-like inhibitors of N-benzyl-imidazole derivatives were synthesized and subjected to HIV-1 inhibition activities and were found potent inhibitor due to the specific shape.[13]

6. 5-(5-furan-2-ylpyrazol-1-yl)-1H-benzimidazole were synthesized and showed excellent inhibition against the formation of HIV capsid. Modifications of the compounds at many positions of carbon and nitrogen enhanced the antiviral activities and compounds after modification showed maximum inhibition.[14]

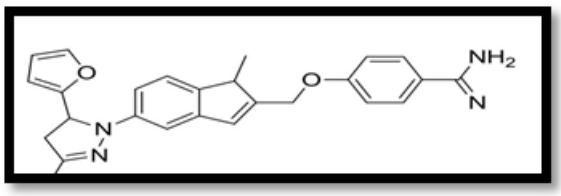

Fig. 18: 5-(5-furan-2-ylpyrazol-1-yl)-1H-benzimidazole.

Caparavarin is a non-nucleoside drug having imidazole moiety and is under the process of drug development for the treatment of AIDS but its use is being restricted due to some side

effect like inflammation etc. It was found that the compounds similar to the caparavarine structure showed maximum activity against the virus.[15]

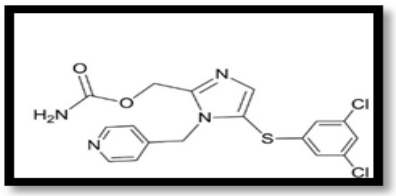

Fig. 19: Caparavarin.

2. Anti-cancer activity

Cancer is a disease which accompanied by the mortality causes due to the malfunctioning of the cells. The need of time is to develop some new drugs which can bind to the proteins of the infected cells and help to destroy their regeneration. Nitrogenous compounds are found to be very good anti-cancerous agents. In this regard a natural product with the imidazole moiety(-)-dibromophakellstatin isolated from the marine sponges, was tested against 36 different cancerous cell line.[16]

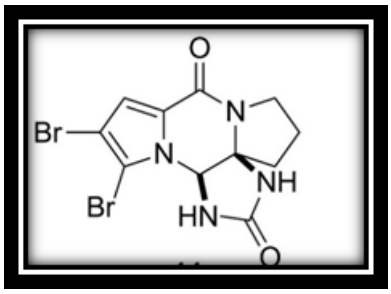

Fig. 20: Dibromophakellstatin.

Compound with the 5-fluoro-2-hydroxyphenyl substituent was found to be the most active derivative of the series with many GI50 values against many breast cancer cell lines.[17]

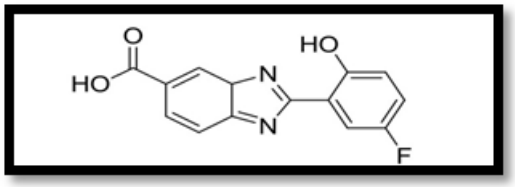

Fig. 21: 5-fluoro-2-hydroxyphenyl.

Some amino substituted xantheno [1,2-d]imidazole derivatives were synthesized and tested against the breast cancer cell lines.[18]

The compound with substituted at the 2 and 5 position of the imidazole showed maximum inhibition and it was found that with the increase of the N-alkyl basicity increase in activity was observed metal complex of chlorido-[1, 3-dimethyl-4,5-diarylimidazol-2-ylidene] were synthesized and tested for their cytotoxic activity against four human cancer cell lines and found active candidate for the treatment of cancer.[19]

Some derivatives of the acetyl hydrazole containing 2-(phenylthiomethyl)-1H-benzo-[d]-imidazole were synthesized and tested against five cancerous cell lines. Activity was determined by using MTT analysis. It was found that among them the two compounds N-(5-bromo-2-hydroxybenzylidene)-2-(2-(phenylthiomethyl)-1H-benzo[d]-imidazol-1-yl) acetohydrazide and N-(2,4-dihydroxybenzylidene)-2-(2-(phenylthiomethyl)-1H-benzo[d]-imidazol-1-yl)acetohydrazide showed excellent activities against all the five cancer cell lines.[20]

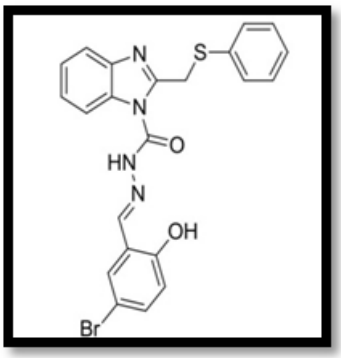

Fig. 22

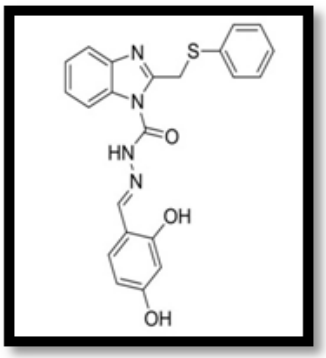

Fig.23

Sulfa drugs are famous for the broad spectrum of activities. Amidosulfonamidomethane linked bis-imidazoles were synthesized and found potent against the colon, prostate and lungs cancer cell lines.[21] Anthra[1,2-d]imidazole-6,11-dione derivatives were synthesized and tested for their cytotoxic activities. Maximum derivatives were found active against different cancerous cell lines.

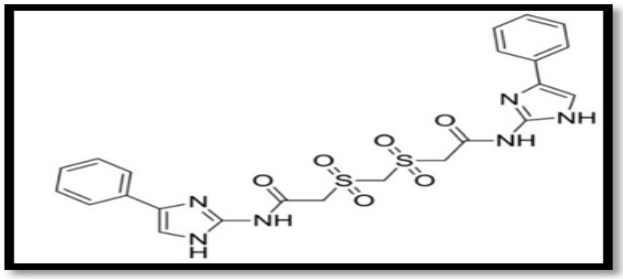

Fig. 24: Amidosulfonamidomethane linked bis-imidazoles.

3. Anti-histamine activity

Histamine is an important chemical mediator and neurotransmitter that influences a variety of physiological and patho physiological processes in the body via stimulation ofa class of G protein-coupled histamine receptor subtypes, i.e., H1, H2, H3, and H4. The biogenicamine, histamine, is known to participate in allergic and inflammatory reactions, gastric acid secretion, and immunomodulation, as well as in neuro transmission. Antihistaminic drugs or histamine receptor antagonists that were the first to be introduced are ones that bind at H1-receptor sites and block the action of histamine.

1. Cimetidine is a prototypical H2-receptorantagonist, developed at GlaxoSmithKline by Black and co-workers, and has established new visuals for the effective treatment of gastric ulcers, heartburn, and gastriti.[22]

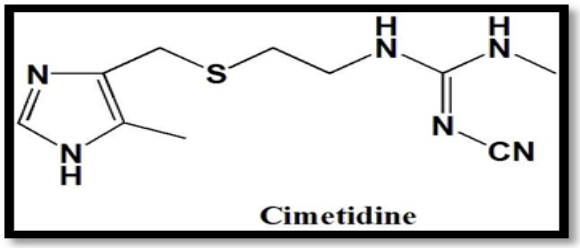

Fig. 25: Cimetidine structure.

2. H3-receptor antagonists have received a major boost for the treatment of dementia, Alzheimer's disease, narcolepsy, hyperactivity disorder orallergic rhinitis, and many more compounds from different companies have been under clinical investigation.[23] Early potent H3-receptor antagonists, like cipralisant, thioperamide, and clobenpropit, iodophenpropit.[24] proxifan.[25] and ciproxifan[26] have been reported.

3. Histamine has been shown to act through at least three different classes of receptor, designated HI, H2 and H3. Histamine is a mediator which is released from mast cells during the allergic response and can cause undesirable effects on bronchial smooth muscle and blood vessels. These effects of histamine occur at the HI receptor and are blocked by the classical antihistamines (e.g. diphenhydramine, chlorpheniramine) and the newer non-sedating antihistamines (e.g. terfenadine, astemazole, loratidine). In addition to being a powerful mediator of the allergic response, histamine is also a powerful inducer of gastric acid secretion which is not blocked by HI antagonists.

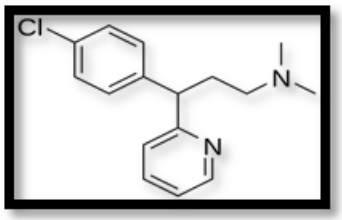

Fig. 26: Chlorpheniramine.

4. Anti-Bacterial Activity

Jain et al. synthesized 2-(4-substituted phenyl)-1-substituted-4, 5-diphenyl-1H-imidazole and evaluated their antimicrobial activity against Staphylococcus aureus, Escherichia coli, and Bacillus subtilis by cylinder wells diffusion method using Norfoxacin as a reference drug.[27]

Yadav et al. synthesized 2-((1H-benzo[d]imidazol-2-yl)thio)-N-(4-oxo-2-(2,3,4,5,6-Penta substituted phenyl)thiazolidin-3-yl)acetamide and 2-((1H-benzo[d]imidazol-2-yl)thio)-N-(2-substituted-4-oxothiazolidin-3-yl) acetamide, by using the antibacterial activity of these derivatives was evaluated against different bacterial strains (Staphylococcus aureus, Escherichia coli, and Bacillus subtilis) using Norfoxacin as a reference drug. The antimycotic activity of these derivatives was evaluated against diferent fungal (Candida albicans and Aspergillus niger) strains using Fluconazole as a reference drug.[28]

Methods as the paper disk diffusion were commonly used for in vitro antibacterial activity study, and the quantitative antibacterial activity was determined by the minimum inhibitory concentration method. Imidazoles were described by their biological activity against various microorganisms. But the physiological action rate is largely determined by the substituent nature. On the one hand, antibacterial activity depends on various hydrophobic substituents on nitrogen atoms.

This review contains the examples of combination of Imidazole with metalions and compounds with antibacterial effect. There are Imidazole-based complexes with different metals that show the various pharmacological effects, including antibacterial activity.[29] For example, antibacterial activity of Imidazole compounds with bactericidal effect in complex with Ag was studied.[30]

In 2013, John McGinley et al. (National University of Ireland) synthesized 1-(3-aminopropyl)imidazole and obtained the Schiff base ligands easily coordinated with Ag(I) centers. Studies were carried out against Staphylococcus. aureus, Eschericia coli and P.

aeruginosa strains. As a result, the most complexes with Ag (I) had the moderate antibacterial activity.[31]

Copper ions (II) and cobalt ions (II) were combined with Imidazoles to study the antibacterial activity against gram-positive and gram-negative bacteria.

Ana Maria Atria et al. (University of Chile, Chemistry and Pharmacy Department) synthesized the copper and cobalt complex with Imidazole derivatives: Diaqua-bis(5-nitroimidazole)-copper(II)-dinitrate; Tetrakis(4-phenylimidazole)-copper(II)-dinitrate, solvate ethanol; bis(4-phenylimidazole)-bis(acetate)-copper(II); Hexakis(4-phenylimidazole)-cobalt(II)-acetate and bis(2-phenylimidazole)-bis(acetate)-cobalt(11). The antimicrobial activity of these complexes against Staphylococcus. typhi, staphylococcus. enteritidis, Staphylococcus. enterica, Staphylococcus. aureus, and Listeria monocytogenes was studied in vitro.[32]

A mixture of bromophenyl, imidazole and pyrazole had the most potent antibacterial effect on staphylococcus, and a mixture of bromine, fluorophenyl, chlorophenyl, imidazole and pyrazole was active against P.Aeruginosa.[33]

The synthesized imidazole-triazole compounds were screened in vitro to study the antimicrobial activity. Activity against S.epidermis and E. Coli was confirmed.[34]

The results of synthesis and antimicrobial evaluation of triazole containing triaryl-1H-imidazole implemented by Chauhan Sunil et al. were reported. Efficiently synthesized triazoles containing triaryl-1H-imidazole had the significant antimicrobial activity against fungal and bacterial strains. Triazolyl imidazole was significantly effective against Pseudomonas. aeruginosa, Aspergillus. niger, Bacillus. subtilis, Staphylococcus. epidermidis and Candida. Albicans.[35]

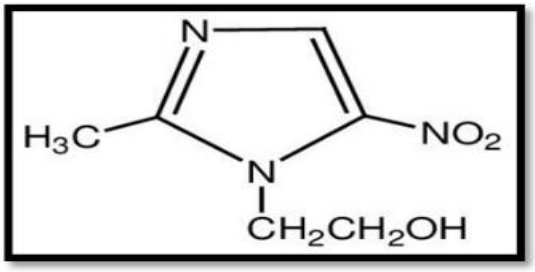

Fig. 27: Metronidazole.

5. Anti-fungal activity

In clinical application, azoles are more commonly used to treat yeast and fungal infections, while Imidazole-based anti-fungals (for example, Miconazole, Econazole, Ketoconazole, and Clotrimazole) and Triazole-based anti-fungals (for example, Fluconazole and Itraconazole) are the basis for fungal infection treatment. The critical need for new compounds is defined by the development of resistance to the existing antifungal drugs and the high toxicity of some anti-fungals. The literature review has shown that many anti-fungals, containing Imidazole compounds, have two carbons between Imidazole and aromatic moiety.

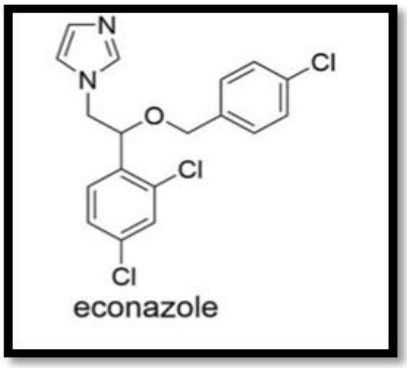

Fig. 28: Econazole structure.

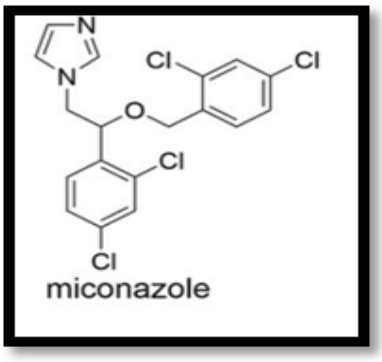

Fig. 29: Miconazole.

In 2018, N.D. Yakovychuk et al. (Bukovinian State Medical University, Chernivtsi, Ukraine) synthesized new nitro-containing Imidazole derivatives studied in vitro for antifungal activity. Method of double serial dilution in Sabouraud's liquid medium was used; antifungal effects on Candida. albicans, Candida. guillermondii, Candida. krusei, Candida. glabrata, Candida. kefyr, Candida. tropicalis, Candida. unscripicua and Candida. zeylanoides were studied. As a result, 3-methyl-4-[1-(1-naphthyl-4-chloro-1H-imidazol-5-yl)-2-nitroethyl-]-1H-pyrazol-5-ole and 2, 4-dichloro-5-(2-nitrovynil)-1-(4-fluorophenyl)-1H-imidazole were the most active substances. 4-chloro-1-imidazole has the lower anti-candidiasis activity, 5-(2-nitrovinyl) Imidazoles and their derivatives had the highest antifungal activity against Candids. krusei, Candida. kefyr and Candida. Unscripicua strains. Nitro-containing Imidazole derivatives had a low antifungal activity against Candida. tropicalis, Candida. Guilliermondii, Candida. albicans, and Candida. glabrata strains.[36]

It was concluded that Imidazole derivatives have the high specificity and activity, a broad spectrum of action and a fungistatic effect. Imidazole compounds with other complexes had the antifungal effect mainly on Candida. albicans, Aspergillus. niger and Candida. krusei.

Nitrogen containing Imidazole derivatives and Imidazoles with a thiazolidinone ring were the most active compounds among the studied compounds.

6. Anti-tubercular activity

Xiaoyun Lu et al. tested the 4-(2,6-dichlorobenzyloxy) phenyl imidazoles and their derivatives against the Mycobacterium tuberculosis using the microplate alamar blue assay (MABA) for anti tuberculosis activities compounds were found to possess good activities.[37]

Moura et al (2012) synthesized the naphtho-imidazoles starting from the beta-lapachone. These compounds were tested for tuberculosis analysis against the mycobacterium. tuberculosis H37Rv (pansusceptible), rifampicin-resistant (RIFr, ATCC 35338) and isoniazid-resistant (INHr, ATCC 35822) strains of bacteria among them the compounds with imidazole units showed good to moderate activity against these strains.[38]

A series of N-(4-(4-chloro-1H-imidazol-1-yl)-3-methoxyphenyl) amide and N-(4-(4-chloro-1H-imidazol-1-yl)-3-methoxyphenyl) sulfonamide derivatives showed potent antitubercular activities activity against Mycobacterium. tuberculosis H37Rv, Mycobacterium. smegmatis, Mycobacterium. fortuitum strains.[39]

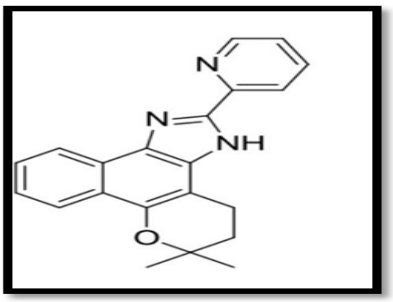

Fig. 30: Naphtho-imidazole.

Ramya V et al synthesized series of novel 5-(nitro/bromo)-styryl-2-benzimidazoles derivatives and screened for in vitro anti-tubercular activity against Mycobacterium tuberculosis, and these compounds showed good anti-tubercular activities. Streptomycin was used as reference drug.[40]

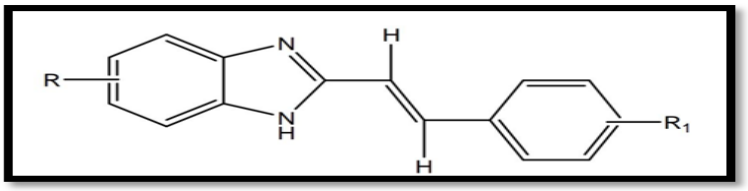

Fig. 31: Imidazole derivative.

Preeti Gupta et al. synthesized substituted -1H-imidazole-4-carboxylic acid derivatives and 3-(2-alkyl-1H-imidazole-4-yl)-propionic acid derivatives against durg-sensitive and drug-resistent Mycobacterium. tuberculosis strains. The title compound was found to be most potent compound when compared to standard.[41]

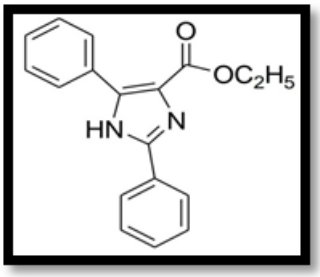

Fig. 32: Imidazole derivative.

Jyoti Pandey et al synthesized a series of imidazole derivatives and compounds were screened against M.tuberculosis where this compound showed good antitubercular activity.[42]

7. Anti-depressant activity

Farzin Hadizadeh et al synthesized moclobemide analogues by replacing moclobemide phenyl ring with substituted imidazole and studied for the antidepressant activity using forced swimming test. It was found to be more potent than moclobemide.[43]

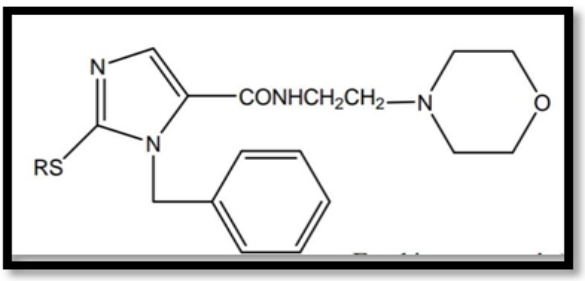

Fig. 33: Imidazole derivative.

8. Anti-inflammatory, analgesic activity

Puratchikody A. et al studies on 2-substituted-4, 5-diphenyl-1H-imidazoles and checked the anti inflammatory activity based on Carrageenan-induced paw edema method. This compound shows maximum activity and indomethacin used as reference drug.[44]

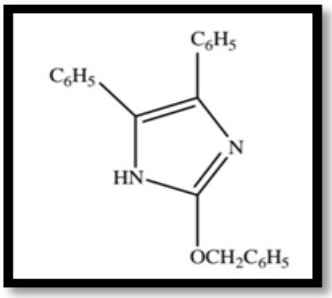

Fig. 34: 2-(benzyloxy)-4, 5-diphenyl-1H-imidazole.

Kavitha C.S. et al has synthesized a series of 2-methylaminibenzimidazole derivatives and newly synthesized compounds were screened for analgesic and anti-inflammatory activities. This compound shows analgesic activity and compared with standard nimesulide drug.[45]

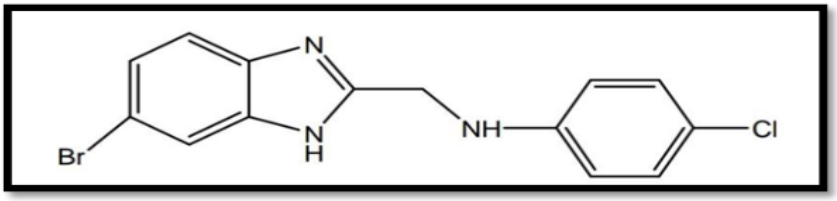

Fig. 35: N-((6-bromo-1H-benzo[d]imidazol-2-yl) methyl)-4-chlorobenzenamine.

This compound shows potent anti inflammatory activity and also compared with nimesulide.

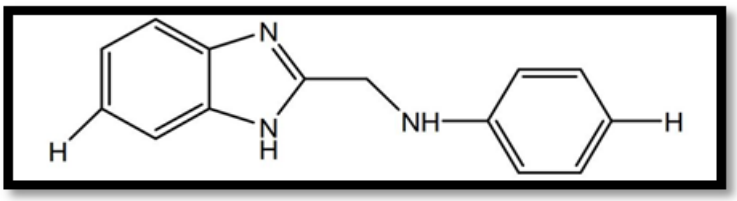

Fig. 36: N-((1H-benzo[d]imidazol-2-yl) methyl)benzenamine.

9. Anti-leishmanial activity

Kalpanabhandari et al reported a novel series of substituted aryloxy arylalkyl and aryloxy alkyl imidazole and evaluated for their anti-leishmanialactivity against Leshmaniadonovani in vitro process. Most of the compounds showed 94–100% inhibition.[46]

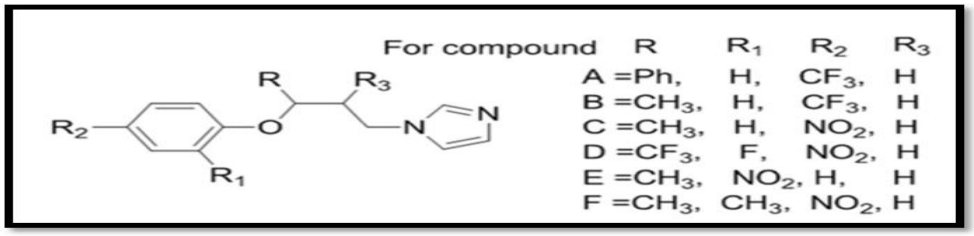

Fig. 37: Substituted aryloxy aryl alkyl and aryloxy alkyl imidazole.

10. Anti-helmintics activity

It was found that imidazole is less sensitive in extra intestinal parasites particularly intravascular and intestinal dwelling parasites than gastrointestinal parasites. The activity against developing stages is superior to that against arrested or adult stages in comparable habitats. The hatching and larval development are inhibited at doses which are sub-efficacious against adult in vivo. They required to achieve efficacy against nematodes are lower than those used for cestode and trematode control.

For cestode or trematode control higher dose of drug or multiple treatments is needed. The member of class (2-alkyl benzimidazole) has been found to remove various species of nematodes and trematodes from different hosts. 4, 5, 6, 7-tetra chloro-2-trifluoromethylbenzimidazole show high activity against the nematodes Ancylostoma caninum, Haemonchuscontrtus, ascarissuum and trimatodes Fasciola hepatica and several 2-5 di substituted benzimidazole,- with proven potentials to kill various species of intestinal nematodes have also been found to- posses activity against cestodiasis of man and animal. Mebendazole at the dose of 100 mg/kg cure patient suffering with Taenia. Solium and Taenia. Saginata.

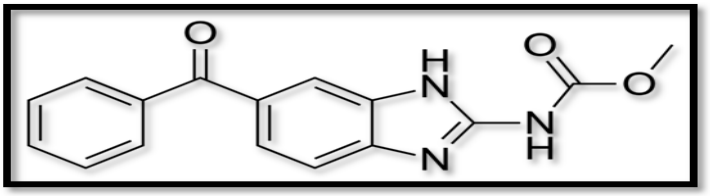

Fig. 38: Mebendazole.

11. Anti-oxidative activity

Naureen et al. synthesized 3-(4, 5-diphenyl-1-(substituted phenyl)-1H-imidazol-2-yl)-substituted-2-(substituted phenyl)-1H-indole and evaluated for antioxidant potential by using Quercetin as reference drug.[47]

Rajasekaran et al synthesized (E)-(1H-benzo[d]imidazol-1-yl)(4-((substituted benzylidene) amino) phenyl) methanone, 2-(1H-benzo[d] imidazol-1-yl)-N-(5-phenyl-1,3,4-oxadiazol-2-yl)aceta-mide and 1-(1H-benzo[d]imidazol-1-yl)-2-((substituted-1,3,4-oxadiazol-2-yl)thio)ethanone and evaluated for antioxidant potential by using DPPH [2,2-diphenyl-1-picryl-hydrazyl-hydrate] assay. All the synthesized derivatives showed good scavenging potential as compared to ascorbic acid.[48]

Subramaniam et al. synthesized (Z)-3-(2-(5-(3-methyl benzylidene)-4-oxo-2-phenyl-4, 5-dihydro-1H-imidazol-1-yl) ethyl)-2-phenyl quinazolin-4(3H)-one derivatives (Scheme 23) and evaluated for antioxidant potential by using DPPH assay. These compounds showed good scavenging potential as compared to ascorbic acid.[49]

Applications of imidazole

1. One of the applications of imidazole is used in the purification of Histone tagged proteins in immobilized metal affinity chromatography (IMAC).
2. Imidazole is used to elute tagged proteins bound to Ni[nickel] ions attached to the surface of beads in the chromatography column. An excess of imidazole is passed through the column, displaces the Histone-tagged from nickel coordination and free the Histone-tagged proteins are formed.
3. Imidazole can be used to prepare buffers in the pH range of 6.2-7.8 at room temperature. It is recommended as a component of a buffer for assay of horseradish peroxides.
4. It is also used as a chelator for the binding of different divalent cations.[50]
5. The oral administration of imidazole shows beneficial effects on psoriasis and seborrheic dermatitis.
6. In psoriasis the improvement begins after a period of one and a half to three months.
7. In seborrheic dermatitis the patients begin from less redness, itchiness, and scaling within a period of four to six weeks. The benefits of this treatment occur without the need for applications of ointments or other topical applications.
8. The imidazole nucleus is an important synthetic strategy in drug discovery. Many imidazoles have been prepared as pharmacological agents Azomycine, Clotrimazole, Miconazole, Ergothionine, Clonidine and Moxonidine. One of the most important applications of imidazole derivatives is their used as material for treatment of denture stomatities.
9. Imidazole has become an important part of many pharmaceuticals. Synthetic Imidazoles are present in many fungicides and antifungal, anti protozoal, and antihypertensive medications.
10. Imidazole is part of the theophylline molecule, found in tea leaves and coffee beans, which will stimulates the central nervous system. It is present in the anticancer medication mercaptopurine, which used in leukemia by interfering with DNA activities.
11. Imidazole also used in industry as a corrosion inhibitor on certain transition metals, such as copper. Conductivity of the copper decreases due to corrosion.

12. Many compounds of industrial and technological importance contain imidazole derivatives. The thermo stable polybenzimidazole imidazole fused to a benzene ring and acts as a fire retardant.
13. Imidazole can also be found in various compounds which are used for photography and electronics.

CONCLUSION

Imidazole moiety have been most frequently studied, many of its analoges are active against various pathological conditions, which are discussed in brief in this article. Imidazole is an entity which has interesting physical and chemical properties, in the present article focus lies on analysis of these properties which in turn may be exploited for different pharmacological activities and effective substitutions are also made in the entity which resembles structures of various natural compounds. On the basis of various survey, Imidazole and their derivatives are important scaffolds used in the treatment of many diseases like HIV-AIDS, cancer, tuberculosis, fungal infections, depression disorders and etc.

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