MANTECH Publications

Journal of Pharmaceutical Chemistry and Drug formulation
Volume 3, Issue 1, January-April, 2021

A Review on Benzimidazole and its Biological Activities

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Abstract

Benzimidazole is a heterocyclic organic compound having an important pharmacophoric group that is used in the medicinal industry. The presence of a specific group was determined by FTIR spectroscopy. Benzimidazole derivatives play an important role in the medical field with so many Pharmacological activities such as antimicrobial, antiviral, antidiabetic, anthelmintic and anticancer activity. The potency of these clinically useful drugs in treating microbial infections and other activities encouraged the development of some more potent and significant compounds. Benzimidazoles are remarkably effective compounds. Extensive biochemical and pharmacological studies have confirmed that these molecules are effective against various strain sof microorganisms. This review is summarized to know about the chemistry of different derivatives of substituted benzimidazoles along with their pharmacological activities.

Keywords*: - Benzimidazole, Pharmacological Activity*

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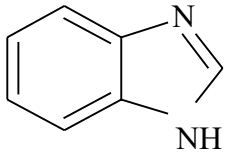
INTRODUCTION

Benzimidazole is an important heterocyclic aromatic organic compound having an important pharmacophore and a privileged structure in medicinal chemistry. It is Bicyclic in nature which Consists of an imidazolering containing 2 nitrogen atoms at an adjacent position fused to the benzene ring.

Nitrogen atom and the position of Narein 1st and 3rd position of the molecule. Various natural products, including purine,

histamine, histidine and nucleic acid, benzimidazole derivatives, being major constituents, have occupied a unique place in the field of medicinal chemistry. Thus, incorporating the benzimidazole nucleus to prepare or synthesize novel benzimidazole derivatives has always carried the attention of many medicinal chemists and proved to be a vital synthetic drug discovery strategy.



Structure of Benzimidazole ring

Benzimidazole derivatives is used in different ways such as analgesic, anti-inflammatory, antibacterial antimicrobial, antifungal, antiviral, anti-helminthic, anticonvulsant anticancer, antihyperten--sive, antiphrastic activity. Firstly benzimidazole was synthesized by Hoebrecker in 1872, who obtained 2, 5(or 2, 6)- dimethyl benzimidazole by the using of 2- nitro-4- methylacetanilide 2.

Now a day is a moiety of choice which possesses many pharmacological properties. The most prominent benzimidazole compound in nature is N-ribosyl-dimethyl benzimidazole, which serves as anaxial ligand for cobalt in vitamin B12. In 1990 various benzimidazole derivatives were synthesized with substitution of fluorine, propylene, tetrahydroquinoline and cyclised compound which resulted in compounds with increased stability, bioavailability and significant biological activity. In 1991 benzimidazole derivatives were synthesized by derivatization at N-H of benzimidazole by electron donating group and substitution with long chain of propyl, acetamido, thio, thiazole-amino, tetramethylpiperidine on pyridine resulting in good analgesic activity.

Nowadays Infectious microbial diseasesare causing problems world-wide, because of resistance to number of antimicrobial agents (β-lactam antibiotics, macrolides, quinolones, and vancomycin). A variety of clinically significant species of microorganisms has become an important health problem globally. One way to fight with this challenge is the appropriate usage of the available marketed antibiotics the other is the development of novel anti-microbial agents. Hence, there will always be a vital need to discover new benzimidazole derivatives as a chemo--therapeutic agent

PHYSICALPROPERTIES

Amphotericity:

Benzimidazole is amphotricin nature i.e. acts as acid and as a base.

Molecular formula: $C_7H_6N_2$

Molecular weight: 118.14g/mol

Meltingpoint : 170^0C-172^0C

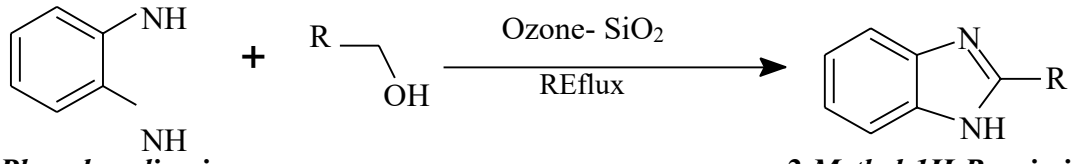
Activity (PKa) : 12.8(for benzimidazole) & 5.6 (for the conjugate acid)

CHEMICAL PROPERTIES:

Benzimidaole undergoes following types of organic reactions:

1. AdditionReaction: -

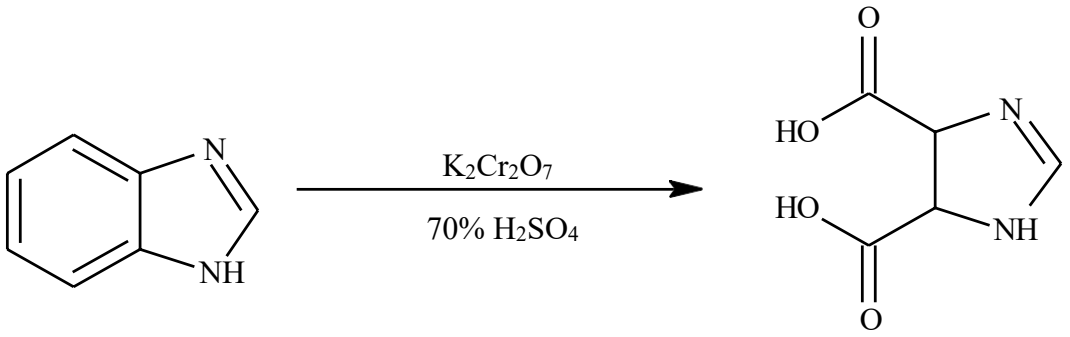
O-Phenylenediamine addition in the presence of ethanol and silicon oxidation to form a 2-methyl-1H-benzimidazole.



O-Phenylenediamine ***2-Methyl-1H-Benzimidazole***

2. OxidationReaction:

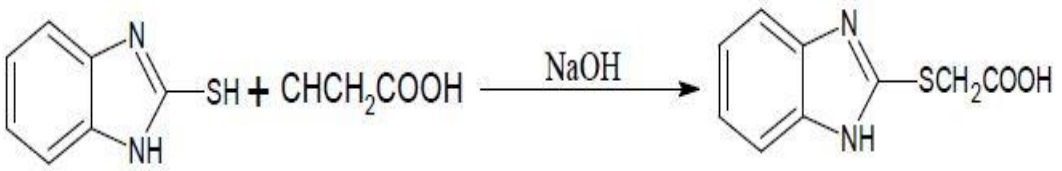
Benzimidazole oxidation in the presence of Potassium dichromate and 70% $H_2SO_4$to form a 4, 5-dihydro-1H-imidazole -4, 5-dicarboxylic acid.



Benzimidazole ***4,5-Dihydro-1H-Imidazole-4,5-DicarboxylicAcid***

3. Substitution Reaction:

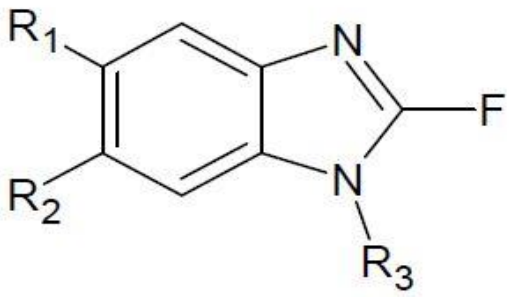
1H-benzimidazole-2-thiol substitution in the presence of carboxylic acid and NaOH to forma [(1H-benzimidazole-2-yl) sulfanyl] acetic acid.



1H-Benzimidazole-2-Thiol *[(1H-Benzimidazole-2-Yl) Sulfanyl] Acetic Acid*

SYNTHESIS AND BIOLOGICAL ACTIVITY OF BENZIMIDAZOLE

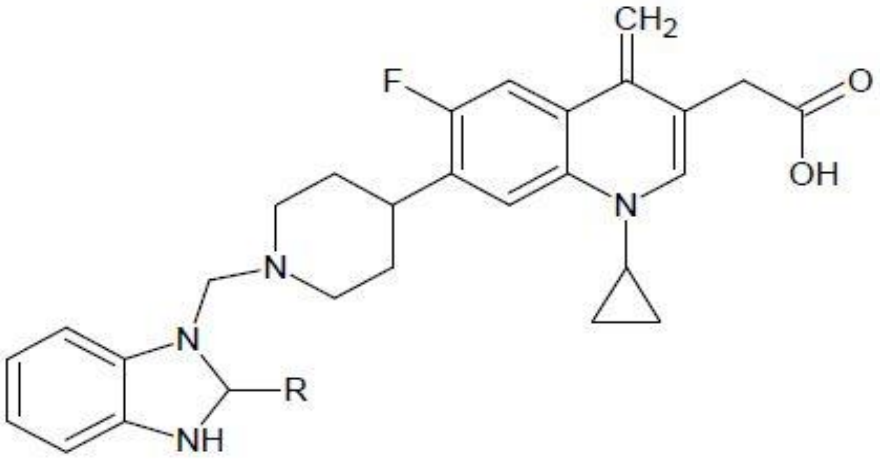
1. WaliaR *et.al* has reported the syntheses of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for antimicrobial activity. Against staphylococcus saureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (GramNegative) and candida Albicans and Aspergillus Nigerbytwod illusion method. The compound 2-(Trifluoromethyl)-1H benzimidazole derivatives was found to be more active antibacterial compound than other compound.



2. HS. Lamba *etal* have reported the synthesis of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for Antimicrobial and anti fungal activity Isoxazolyl substituted compounds were screened for activity against Gram Negative species like E.coli and Proteus vulgaris, Gram positive like Bacillus mycoides and staphylococcus au.

Some Benzimidazole compounds possessing hydrazone moiety were studied in order to investigate their possible antibacterial and antifungal activity. Most of the test compounds found to be significantly effective against Proteus vulgaris, Staphylococcus typhimurium, Klebsiella pneumoniae and Pseudomonas aeruginosa gram-negative bacterial strains some fluroquinolones substituted Benzimidazole derivatives have been reported by microwave assisted method.

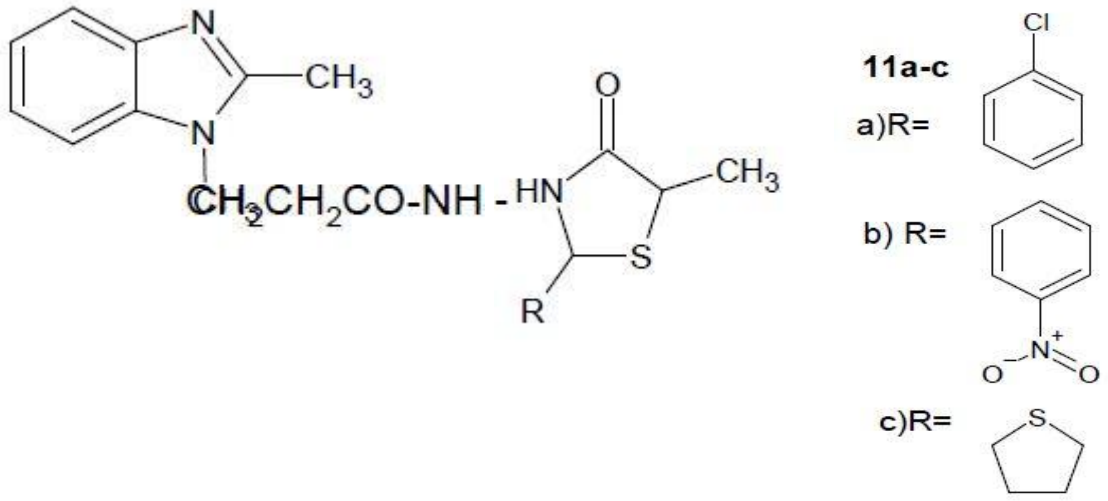
The synthesized compounds are reported to be the derivatives of Ciprofloxacin.



3. AfafH *et al*

Have reported the synthesis of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for antimicrobial activity.

Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method. The compound 3-(2-methylbenzimidazol-1-yl)propanoic acid hydrazide was found to be more active antimicrobial compound than other compound. CS2/KOH gave oxadiazole which underwentMannich reactiontogive. Compound2was treated withhydrazinehydrate togive was treated with both aldehydes and acetic anhydride. to give. acids gave 10 and **(11a-c)** respectively.



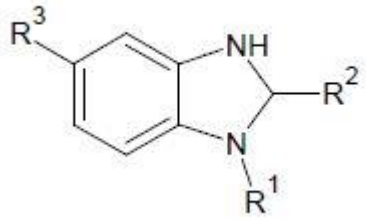
4. Khalid Iqbal *et al* have reported the syntheses of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for anticonvulsant activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus niger by two dilusionmethod.Thecompoundof1,2,5- tri-substituted benzimidazoles derivatives was found to be more active anticonvulsant compound than other compound.

Benzimidazole derivative some potential anticonvulsant compounds have been synthesized, a series of 1, 2, 5-trisubstituted benzimidazoles derivatives has been reported.

5. Juan Valdez *et al* have reported the syntheses of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for antiparasitic activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicansand Aspergillus Niger by two dilusion method.

The compound 2- methoxycarbonylamino derivatives benzimidazoles derivative was found to be more active antiparasitic active Compound than other compound.

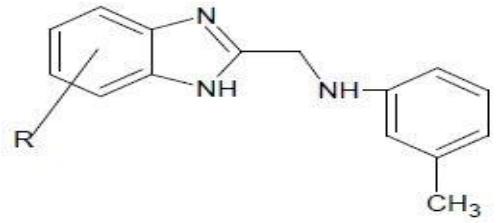
Synthesis and Antiparasitic Activity of 1H- Benzimidazole Derivatives. These are Compounds **1–14** have been synthesized and tested in vitro against the protozoa Giardia lamblia, Entamoeba histolyticaand the helminth Trichinella spiralis.



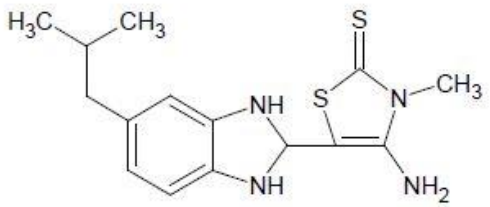
Where R1=Picoline,
R2=varying alkyl chain
R3=NO2

6. Achar KC *et al* have reported the syntheses of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for analgesic & anti-inflammatory activity. Against staphylococcus aureus, Bacillus subtilis,E-coil, pseudonomousasa enginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method.

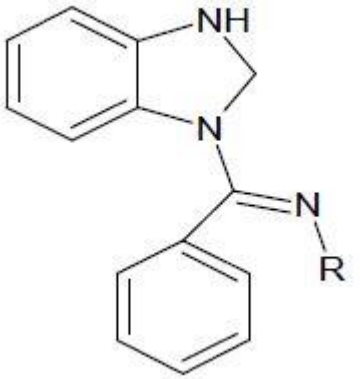
The compound 2-methylamino benzimida--zole derivative was found to be more active analgesic & anti- inflammatory compound than other compound. In- vivo analgesic and anti-Inflammatory activities of newly synthesized benzimidazole derivatives.



7. Hanan M. Refaat et al have reported the syntheses of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for anti cancer activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method. The compound 2-[(4-oxothiazolidin-2-ylidene) methyl and (4-amino2-thioxothiazol-5-yl) benzimidazoles derivatives was found to be more active anticancer active compound than other compound. The synthesized products were subjected to in vitro anticancer screening that revealed that all the tested compounds exhibited antitumor activity .

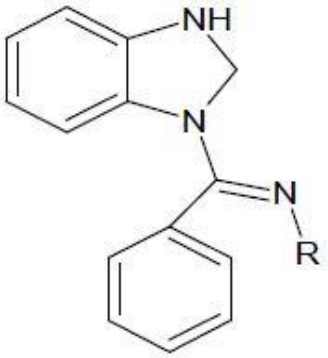


8. O¨ zden O¨ zel Gu¨ven,a,et al have reported the syntheses of N-substituted Benzimidazole derivatives.Newly synthesized compound were evaluated for anticancer activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method. The compound 3-(2-phenylpropyl)-1Hindole benzimidazoles derivatives was found to be more active anticancer active compound than other compound.



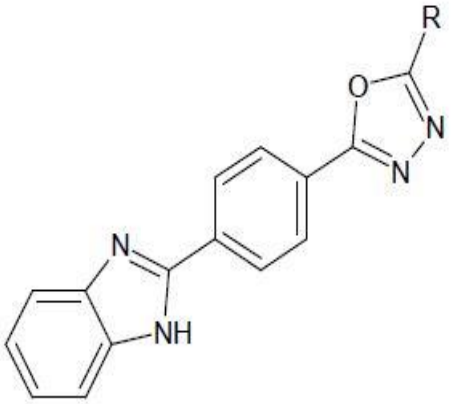
9. Asma Eswayah et al have reported the synthesis of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for analgesic activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method. The compound Nacylated benzimidazole derivative was found to be more active anticancer active compound

than other compound. Synthesis and Analgesic Activity Evaluation of Some New Benzimidazole Derivatives.



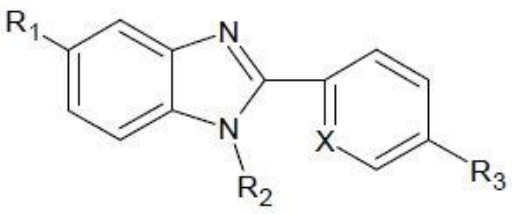
10. Muhammad Tahaa et al have reported the syntheses of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for alpha glycosidase inhibitory activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method.

The compound 3-methyl oxadiazole benzimidazoles derivative was found to be more active alpha glycosidase inhibitory active compound than other compound. Synthesis, α-glycosidase inhibitory potential and molecular docking study of benzimidazole.



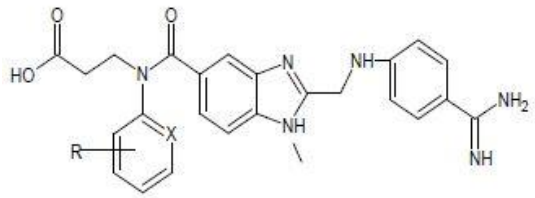
11. Azize Gizem et al have reported the syntheses of N-substituted Benzimidazole derivatives.Newly synthesized compound were evaluated for inhibitory activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method.

The compound 2-arylbenzimidazole derivative was found to be more active inhibitory active compound than other compound.

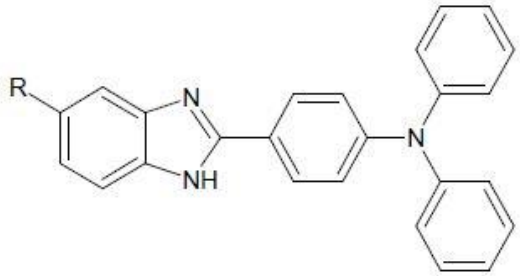


12. Jiaxu Fu et al have reported the synthesis of N-substituted Benzimidazole

derivatives. Newly synthesized compound were evaluated for biological activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method. The compound N, N-dimethylformamide benzimidazoles derivatives was found to be more active biological active compound than other compound. Microwave- assisted synthesis and biological activity in the luminescent properties of diphenylamine substituted mono and di- branched benzimidazole derivatives.



13. **Tianrong Zhang** et al have reported the synthesis of N-substituted Benzimidazole derivatives. Newly synthesized compound were evaluated for biological activity. Against staphylococcus aureus, Bacillus subtilis, E-coil, pseudonomous as aenginosa (Gram Negative) and candida Albicans and Aspergillus Niger by two dilusion method. The compound 3-methyl oxadiazole benzimidazoles derivative was found to be more active biological in vitro active compound than other compound.



CONCLUSION

Benzimidazole is a versatile Heterocyclic molecule with numerous pharmacological activities. Hence there is need to research on synthesis of numerous derivatives of benzimidazole and evaluation of their biological activities.

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