Novel Scaffolds Benzimidazole: A Review

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Abstract: The point of this review is an endeavor to feature the advancement in biotechnology and science and to introduce a layout of different natural exercises of benzimidazole. The biological activity of benzimidazole like analgesic, antibacterial, anticonvulsant, anti-fungal, anti-histamine, anti-inflammatory, anti-tuberculosis, and anti-tumor were discussed. Numerous substituent particles are liable for a particular activity. Benzimidazole is a remarkably successful mixture and there are various audits accessible for biochemical and pharmacological investigations which affirmed that these particles are helpful against a wide assortment of microorganisms. Benzimidazole and its subordinates have been showing confident movement in the treatment of a few illnesses, thus, they accomplished a lot of consideration as significant pharmacophore in restorative science this review points are to gather writing work expressed by researchers on benzimidazole for their different remedial exercises and report the ebb and flow reports and advancements made on this ring.

Keywords: Benzimidazole, Analgesic activity, Antibacterial activity

1. INTRODUCTION:
Benzimidazoles are a class of heterocyclic, sweet-smelling escalating that share a primary basic characteristic of six-membered benzene merged to five-membered imidazole moiety. Benzimidazole assumes a significant part in the restorative science and medication disclosure with numerous pharmacological exercises which have made a fundamental anchor for the revelation of novel helpful specialists. Replacement of benzimidazole core is a significant manufactured methodology in the medication disclosure process. The fuse of benzimidazole core, an organically acknowledged pharmacophore in restorative mixtures, has made it a flexible heterocyclic moiety having a wide range of organic exercises. This bicyclic compound might be seen as combined rings of the fragrant mixture of benzene and imidazole. It is drab and strong. All things considered, the first benzimidazoles was ready in 1872 by Hoebrecker, who acquired 2,5 (or 2,6)-dimethyl benzimidazole by the decrease of 2-nitro-4-methylacetanilide [1].

Benzimidazole is shaped by the combination of benzene and imidazole moiety, and the numbering framework as indicated by the IUPAC is portrayed in Figure 1.

The natural use of benzimidazole core is found way back in 1944 when Woolley hypothesized that benzimidazoles look like purine-like construction and evoke some organic application. [2]. A preferred IUPAC name is 1H-1,3 Benzimidazole. The utilization of benzimidazole began numerous years back in 1990 ahead, and countless benzimidazole analogs amalgamation were accounted for, which brought about expanded strength, bioavailability, and huge natural action. The chemical formula of benzimidazole is C₇H₆N₂.

The molar mass is about 118-139 g/mol, the melting point varies from 170°C -172°C, and the pKₐ of benzimidazole is about 12.8 [3]. Benzimidazole is created by condensation of o-phenylenediamine with formic acid. The pharmacological utilization of benzimidazole analogs observed intense inhibitors of different catalysts included and helpful utilizations including analgesic, antidiabetic, anticancer, antimicrobial, analgesics, antiviral, allergy med, and neurological, endocrinological, and ophthalmological drugs. This review is an attempt that gives the biological activities of benzimidazole like analgesic, antibacterial, anti-convulsant, anti-fungal, anti-histamine, anti-inflammatory, and anti-tuberculosis.

2. ANALGESIC ACTIVITY
EP Jesudason et al [4] incorporated N-Mannich bases of benzimidazoles through the cow-like cornea and evaluated their pain-relieving movement. The compound with Piperidin and methyl group substituted with benzimidazole (fig. 2a) at 40 mg/kg was viewed as more strong than Diclofenac with 43.80% of security.

![Fig.2a](image)

A progression of 2-methylaminobenzimidazole subsidiaries was integrated by K Achar et al[5] and assessed for their pain-relieving movement. The compound like chloraniline attached to N-(5-bromo-1H-benzimidazol-2-yl) at a specific position (fig.2b) displayed intense pain relieving at 100 mg/kg b.w. with an 89% of assurance whereas the standard medication Nimesulide shows 100 percent assurance at 50 mg/kg.

![Fig.2b](image)

Gaba M et al[6] looked for GI cordial pain-relieving and mitigating utilizing a benzimidazole subordinate. The compound 3,4-Dimethyl-N-(1-phenylsulfonyl)-1H-benzo[d]imidazol-2-yl)methyl]benzenamine (fig.2c) showed an intense movement with 57.58% of security when contrasted with a standard medication Acetyl salicylic corrosive.

![Fig.2c](image)

Subbed benzimidazole subordinates were combined and assessed for their pain-relieving action by S Brishty et al [7]. The compound 1-(4-Methoxybenzyl)-2-(4-methoxyphenyl)-3-(4-methoxybenzyl)-1H-benzimidazole (fig.2d) is depicted as an intense compound with 88.24% of security at a portion of 50 mg/kg body weight in the examination of standard with diclofenac.

![Fig.2d](image)

S Srivastava et al [8] blended a progression of novel 2-phenylhydrazinomethyl and 2-(2-hydroxyphenyl)- benzimidazole subsidiaries subbed at the N1-position of benzimidazole core and evaluated for their pain-relieving activity. The compound 1H-benzimidazole attached by phenylhydrazin, methyl, and ethanamine in an appropriate position (fig.2e) showed a huge action with a 74.88% of pain-relieving action with a dose of 20 mg/kg when contrasted and the standard medication diclofenac sodium.
A progression of N-subbed benzimidazole subordinates was integrated by Asma eswayah et al [9] and evaluated for their pain-relieving action. The compound 1H-benzoimidazol attached by phenyl methylene-, phenyl diazenyl, phenyl and methenamine at a specific position (fig.2f) showed a strong movement diminished the number of works to 17% contrasting with control with a portion of 50 mg/kg as contrasted and standard medication ibuprofen.

3. ANTIBACTERIAL ACTIVITY
O Guven et al [10] combined a progression of novel phenyl-and benzimidazole-subbed benzyl ethers and assessed for their enemy of bacterial action. Compound with Dichlorobenzyloxy and phenyl ethyl molecules attached to a 1H-benzimidazole at an effective position (Fig.3a) displayed the most powerful antibacterial action with the least MIC upsides of 3.12 and 6.25 µg/mL against S. aureus and MRSA, individually.

Blend of a progression of novel and functionalized benzimidazole subsidiaries by Vinodkumar R et al [11] and evaluated for their enemy of bacterial action. The compound with Methyl, phenylethynyl, and phenyl groups attached to 1H-benzimidazole at an appropriate position (Fig.3b), and compound with Dimethylthiocroman, ethynyl, phenyl and trifluoromethane sulfonyl attached to 1H-benzimidazole in a specific position (Fig.3c) showed a huge enemy of bacterial movement showed total hindrance against S. Typhimurium.

Series of novel actinonin subordinates containing a benzimidazole heterocycle connected as amide isostere have been planned and blended by D Zang et al [12] and evaluated for their enemy of bacterial action. The compound with Butyl, hydroxyl, methyl and propylsuccinamide attached at a specific place in benzimidazole moiety (Fig.3d) and showed an intense movement against Staphylococcus aureus, Klebsiella pneumonia and Sarcina lutea with a MIC worth of 2, 0.5 and 4 µg/ml respectively.
N Al-Mohammed et al [13] novel benzimidazole subsidiaries and assessed for their enemy of bacterial action. The compound with Methylbenzenesulfonyl, methylbenzene sulfonyl, benzimidazole and methylthio attached to a benzimidazole moiety at a specific position (Fig.3e) showed a strong anti bacterial activity with MIC upsides of 0.05 mg/mL against *Bacillus subtilis*.

New benzimidazole subsidiaries were combined by Küçükbay H et al [14] and evaluated for their enemy of bacterial action. The compound with ethyl,phenylethyl and selenone attached to a benzimidazole at a specific position (Fig.3f) against *Candida albicans* and *Candida tropicalis* with a MIC upsides of 800,800,800 and 800µg/mL.

A progression of bis-benzimidazole diamidine compounds containing different focal linkers has been integrated and assessed by Hu L et al [15]. The compound with phenylene, sopropyl and carboximidamide attached to 1H-benzo[d]imidazole at a specific positions (Fig.3h) showed a powerful anti bacterial movement against *S. aureus* ATCC 29213 with a MIC of 0.25µg/mL.

F Naaz et al [16] incorporated a sulphonamide subsidiaries of benzimidazole and evaluated for their enemy of bacterial movement. The compound 1H-benzimidazole with chloro and tosyl at a prescribed (Fig.3i) and Chloro and chlorophenylsulfonyl attached to a 1H-benzimidazole moiety at a prescribed position (Fig.3j) showed great movement against *E. coli* with MIC of 3.1 µg/mL and 6.2 µg/mL, separately and *P. aeruginosa* with a MIC of 12.5 µg/mL and 6.2 µg/mL, separately.

### 4. ANTI CONVULSANT ACTIVITY

M Shaharyar et al [17] synthesized a novel benzimidazole subordinate and evaluated for their enemy of convulsant action by MES strategy. The compound with 4-fluorophenyl, methyldene, phenoxy methyl and acetohydrazide in 1H-benzimidazol moiety at a
definite position (Fig.4a) and 1H-benzimidazol with nitrophenyl, methylidene and phenoxy methyl and acetohydrazide at a definite position (Fig.4b) showed a powerful movement with a defensive file of 40.5% and 24.7% individually.

A progression of some novel benzimidazole acetohydrazide subsidiaries was integrated by G Dangi et al [18] and evaluated for their enemy of convulsant movement by MES technique. The compound with Benzyl and acetohydride attached to -1H-benzimidazole at a specific position (Fig.4c) with security of 31.52% and with an intensity of 53.70%.

Siddiqui N et al [19] synthesized an original series of benzimidazole and assessed for their and against convulsant movement. The compound with chlorobenzyl, methyl, methoxyphenyl, hydrazine carbothioamide attached with 1H-benzo[d]imidazole in a specific position (Fig.4d) was viewed as generally intense at the portion of 100 mg/kg (1/1 animal safeguarded) after 4.0 h and at the portion of 300 mg/kg (4/5 creatures secured) after 0.5 h organization.

5. ANTI FUNGAL ACTIVITY

Marcoss M et al [20] integrated a clever three series of benzimidazole framework bearing hydrazone and evaluated for their enemy of parasitic action. The compound with Chlorobenzylidene, nitrophenyl and carbohydrazide attached to 1H-benzimidazole at a specific position (Fig.5a) showed the most note worthy inhibitory action against lanosterol 14α-demethylase (CYP51) with IC_{50} esteem = 0.19 μg/mL.

A progression of novel benzimidazole subordinate integrated and assessed for their enemy of contagious action by N Chandrika et al [21]. The compound 6-(4-methylpiperezin-1-yl)- 2-· (4-((1E,3E)- penta-1,3-dien-1-yloxy)phenyl)- 1H,3H-2,5-bibenzod[d]imidazole showed phenomenal movement (Fig.5b) with MIC of 1.95 µg/mL against C. parapsilosis ATCC 22019 (strain J)
V Padalkar et al [22] blended a novel benzimidazole subordinate and evaluated for their enemy of contagious movement. The compound Benzothiazol with diethylamino and phenol at a definite position (Fig. 5c) shows incredible inhibitory development on account of *C. albicans* with a MIC worth of 250µg/mL.

A progression of mannich bases of benzimidazole subordinates were orchestrated by Aanandi M et al [23] and assessed for their enemy of parasitic action. The compound 1H-Benzimidazole with dimethylamino benzoal, methyl-amino and benzoic acid at assigned position (Fig. 5d) showed a strong movement with a zone of restraint of 11mm and 10mm against *Candida albicans* and *Aspergillus niger* separately.

6. ANTI HISTAMINE ACTIVITY
The benzimidazole center of the particular non-mind infiltrating H1-allergy medicine mizolastine was utilized to recognize a progression of cerebrum entering H1-allergy medicines for the possible treatment of sleep deprivation by Coon T et al [24]. The compound with flurobenzyl, methyl, Hpyrazol and piperidin attached to a 1H-benzo[d]imidazole at a definite position (Fig. 6a) displayed a powerful action with a hERG esteem IC<sub>50</sub> of 809 nM.

Lavrador-Erb K et al [25] recognized a progression of 2-(3-aminopiperidine)-benzimidazoles as specific H1-allergy meds and evaluated for their allergy med movement. The compound containing fluoro, methyl piperidin, methyl and phenol attached to a 1H-benzo[d]imidazole in a definite position (Fig. 6b) showed a huge action with a hERG IC<sub>50</sub>/H1 Ki = 800nM.
A progression of benzimidazole subsidiaries have been incorporated and assessed for H1 allergy med movement by X Wang et al [26]. The compound with chlorobenzyl, piperidin and methyl attached to a 1H-benzo[d]imidazole in a correct position (Fig.6c) showed incredible inhibitory impact on the quantities of degranulated pole cells (DMC) with a fixation subordinate way with IC$_{50}$ = 3.1 nmol/L.

S Ravula et al [27] concentrated on the primary action relationship of 2-(piperdin-3-yl)-1H-benzimidazoles, 2-morpholine and 2-thiomorpholin-2-yl-1H-benzimidazoles. The compound with methoxy benzyl and thiomorphine attached to 1H-benzo[d]imidazol-2yl) at a specific position (Fig.6d) showed a powerful movement with a hERGIC$_{50}$ of 1500Nm.

7. ANTI INFLAMMATORY ACTIVITY
Recently orchestrated benzimidazole subsidiaries bearing oxadiazole and morpholine rings were assessed for their calming movement by A Rathore et al [28]. The compound with Morpholino methyl, tolyl,oxadiazol and methyl substituted to a 1H-benimidazole moiety at a specific position (Fig.7a) and Methoxyphenyl,oxadiazol,methyl and morpholinomethyl attached to 1H-benimidazole at a specific position (Fig.7b) were likewise found to show great COX-2 hindrance with IC$_{50}$ upsides of 11.4 and 13.7 µM respectively.

M Maghraby et al [29] integrated another atomic crossovers of 2-methylthiobenzimidazole and evaluated for their mitigating movement. The compound with chlorophenyl, phenylthiazol, hydrazono propyl, methylthio,thiazol and amine groups are attached to a 1H-benzo[d]imidazole in a specific position (Fig.7c) was the most powerful double inhibitor COX-2 with IC$_{50}$ = 0.045 μM.

Novel coumarin-benzimidazole subordinates were planned and incorporated by R Arora et al [30] and inspected for their calming action. The compound substituted with bromo chromen to benzimidazole moiety (Fig.7d) and chloro chromen to benzimidazole moiety (Fig.7e) displayed great calming with 45.45%, and 46.75% inhibition, separately.
Another series of benzimidazole subsidiaries were read up and researched for their calming movement by S Bukari et al [31]. The compound with aminopyridine, phenyl and carboxamide groups are attached to a 1H-benzo[d]imidazole in a specific position (Fig.7f) showed a strong action by restraining a COX-1 and COX-2 with an IC\textsubscript{50} of 13.50 ± 3.21µM and 22.41 ± 3.16µM individually.

K Achar et al [32] blended a progression of 2-methylaminobenzimidazole subsidiaries and inspected for their mitigating action. The compound 1H-benzimidazol with methyl and chloroaniline at a specific position (Fig.7g) showed a strong mitigating with 100 percent hindrance at 100 mg/kg body weight.

A progression of coumarin-benzimidazole subordinates were combined by P Sethi et al [33] and assessed for their calming movement. The compound containing methyl coumarin in methyl substituted benzimidazole. (Fig.7h) and coumarin in methyl substituted benzimidazole (Fig.7i) showed a most extreme calming action with 45% of restraint.

8. ANTI TUBERCULOSIS ACTIVITY

Y Yoon et al [34] blended a novel benzimidazole subordinate and inspected for their enemy of tubercular action. The compound with ethyl, trifluoromethyl, phenyl, morpholinoethyl and carboxylate attached to a 1H-benzo[d]imidazole at a definite position (Fig.8a) was viewed as the most dynamic with IC\textsubscript{50} of 11.52 µM.

A progression of 1-[(2E)-3-phenylprop-2-enoyl]-1H-benzimidazole subsidiaries were orchestrated by V Kalalbandi et al [35] and assessed for their enemy of tuberculosis movement. The compound with phenyl, tolyl and propenone attached to 1H-benzo[d]imidazol at a specific position (Fig.8b) showed a strong movement with IC\textsubscript{50} > 10µg/mL.
M Sirim et al [36] blended a benzimidazole-acrylonitrile cross breed subsidiaries and assessed for their enemy of tubercular activity. The compound 1H-Benzo[d]imidazol attached with methylphenyl,piperazin,phenyl and acrylonitrile at a definite position (Fig.8c) was viewed as the most dynamic compound with MIC of 0.78 mg/mL.

A progression of N'-subbed 2-(5-nitrofuran or 5-nitrothiophen-2-yl)- 3H-benzo[d]imidazole-5-carboxyhydrazide subsidiaries were integrated by J Camacho et al [37] and inspected for their enemy of tubercular movement. The compound with Benzoyl,nitrofuran and carboxyhydrazide attached to a 3H-benzo[d]imidazole at an appropriate position (Fig.8d) showed a strong movement with IC$_{50}$ of 12.5 µg/mL.

Novel benzimidazole subordinates were blended by Y Yoon et al [38] and evaluated for their enemy of tuberculosis movement. The compound with ethyl,ethoxycarbonyl,aminophenyl,piperazine,ethyl, fluorophenyl,pyridine,phenyl and carboxylate groups attached to a 1Hbenzo[d]imidazole at a specific position (Fig.8e) showed a powerful movement with MIC of 0.112 µM.
ANTI TUMOR ACTIVITY

Novel tertiary sulfonamide subsidiaries containing benzimidazole moiety integrated by J Song et al [39]. The compound containing methyl and trimethoxy phenyl groups in dihydro-1H-benzo[d]imidazo- methyl moiety (Fig.9a) showed a steady movement with against MGC-803 cells (IC$_{50}$ =1.02 mM), HGC-27 cells(IC$_{50}$ =1.61 mM), SGC-7901 (IC$_{50}$ = 2.30 mM).

Y Yoon et al [40] combined an original 15 novel benzimidazole subordinates. The compound with ethyl,ethyl amino,ethylphenyl,hydroxyethyl and carboxylate attached to 1H-benzo[d]imidazole at a specific position (Fig.9b) showed the best inhibitory action for SIRT1 (IC$_{50}$ = 58.43 µM) as well with respect to SIRT2 (IC$_{50}$ = 45.12 µM).

Novel Benzimidazole-Chalcone Hybrids were combined and inspected for their enemy of growth movement by W zhou et al [41]. The compound with Bromophenyl,fluorobenzyl and propenone substituted to 1H-benzo [d] imidazole at a respective position (fig.9c) and molecules like Methylbenzyl,trimethoxyphenyl and propenone attached to a 1H-benzo[d]imidazol at a specific position (fig.9d) hindrance of A549 cells clonogenic with the IC$_{50}$ upsides of 0.54 µM and 0.47 µM individually.

Conclusion

From the writing survey, it is seen that practical gathering present on atom assumes significant part in physicochemical properties appearing by particle. To find better therapeutic specialist, analyst ought to get the overall commitments of each useful gathering. Benzimidazole particle assumed a significant part in restorative science as it is bioactive and basically straightforward hetetocyclic compound. It can turn into a piece of advancement and revelation of new medications with possible organic action. During last ten years endeavors has been taken to combine therapeutically significant benzimidazole subordinates and scientists found numerous benzimidazole subordinates showing promisingorganic movement. In a present audit, endeavors are taken to sum up the amalgamation of a different subsidiary of benzimidazole alongside their organic movement. It is trusted that this audit will benefit growing analysts in the field of benzimidazole-based drug planning.

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