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Significance of Benzimidazole analogues for the creation of novel molecules in drug discovery

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A B S T R A C T

Fused heterocyclic derivatives have become an important scaffold nowadays, which could be used as a template in drug development and medicinal chemistry. Benzimidazole moiety is an imperious aromatic heterocycle which is frequently present in naturally occurring products such as purines, vitamin B 12 and histidine as well as synthesized bioactive compounds, indomethacin and albendazole, for example. This study comprises widespread and comprehensive literature analysis on chemical reactivity and biological properties associated with Benzimidazole containing molecules. Benzimidazole ring structure possesses an extensive variety of pharmacological activities in several medications of therapeutic interest against a variety of diseases such as hypertension, malaria, cancer, microbial diseases, inflammatory disorders, etc. Furthermore, this fused heterocycle benzimidazole core might interact with various anions and cations in addition to biomolecules over different reactions in the human body, therefore exhibiting wide-ranging biological activities such as antineoplastic, antibacterial and antifungal, anti-inflammatory and analgesic, antihypertensive, antiviral and antidepressant. In this review, we are focusing on the chemistry and recent biological activities, designing approaches, and SAR (structure-activity relationship) data of different benzimidazole-based analogues during the past years.

1. Introduction

Fused heterocyclic derivatives have become an important scaffold nowadays, which could be used as a template in drug development and medicinal chemistry. Benzimidazole may be considered as a common pharmacophore found in numerous natural compounds such as purines, vitamin B 12, and histidine.[1]This fused hetero-aromatic ring structures possesses an extensive variety of pharmacological activities[2-5]in several medications of therapeutic interest against a variety of diseases such as hypertension, malaria, cancer, microbial diseases, inflammatory disorders, etc. Moreover, amongst the fused benzimidazole analogs, pyrimido[1,2-a]benzimidazole was discovered as effective corticotropin releasing factor-1 (CRF-1) receptor antagonist towards the treatment of mental disorders.[6]Another derivative named as pyrrolo[1,2-a] benzimidazole was observed as the most effective CDK4/6(cyclin-dependent kinase 4/6) inhibitor in a chain of alicyclic ring-fused benzimidazole analogs.[7] Therefore, many efforts have been made by the research community to explore the therapeutic potential of benzimidazole analogs. Under these conditions, benzimidazole-based fused derivatives have been reported for the treatment of multifactorial diseases and create it a scaffold of therapeutic interest for multinational pharmaceutical companies and research groups. In this review, we are focusing on the chemistry and recent biological activities, designing approaches, and SAR (structure-activity relationship) data of different benzimidazole-based analogs during the past years.

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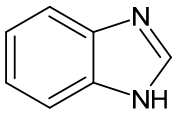
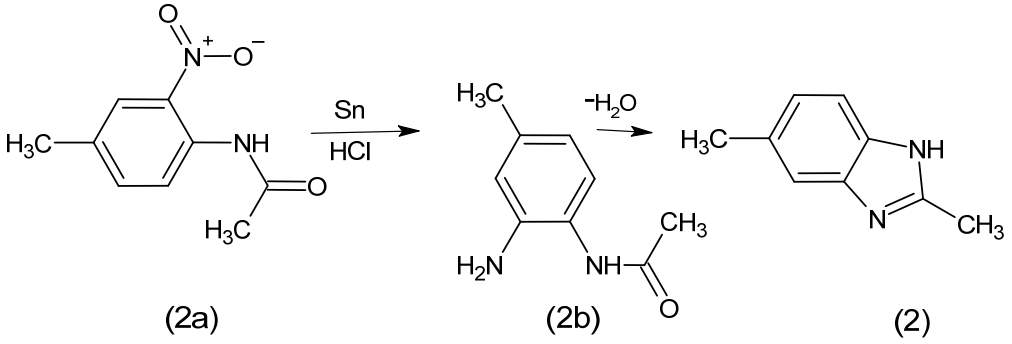
2. Chemistry of Benzimiadazole

As shown in the structure of benzimidazole (1), the benzimidazoles have a phenyl ring which is fused to an imidazole ring.[8]



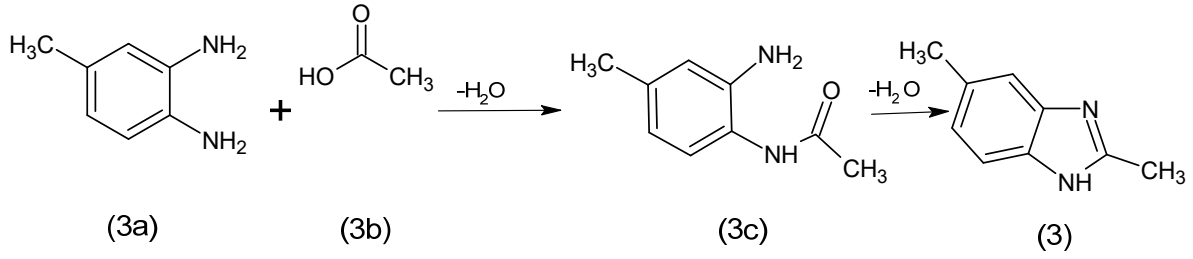
(1)

Hoebrecker [9-11] made the first benzimidazole compound (2) in the year 1872 by reducing 2-nitro-4-methylacetanilide to yield 2,5 / 2,6 dimethyl benzimidazole (Scheme No. 1).



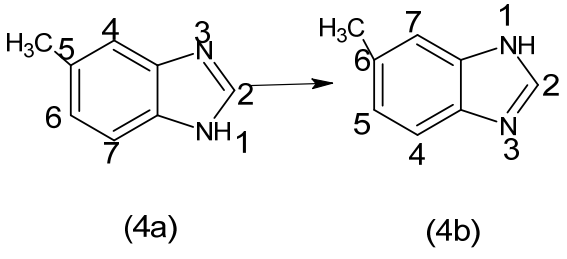
Scheme 1.

Ladenburg[12] obtained the same benzimidazole compound (3) several years later by using 3,4-diaminotoluene and acetic acid under reflux (Scheme No. 2).



Scheme 2.

Tautomerization is easy for benzimidazoles (4a and 4b) with a hydrogen atom linked to nitrogen in the 1-position[13]This can be shown as follows (Scheme No 3).



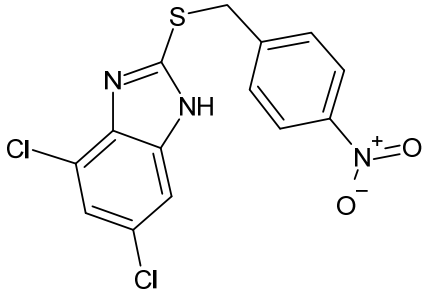
Scheme 3.

This is similar to the tautomerism found in amidines and imidazoles. In fact, benzimidazoles can be thought of as cyclic analogues of amidines. Due to the presence of tautomerism in benzimidazoles, several derivatives that appear to be isomers are actually tautomers; despite the fact that two nonequivalent structures might be written, only one compound is recognized.

3. Biological Activities of Benzimiadazole

3.1 Antiprotozoal activity

Kazimierczuk in 2002 prepared[14] some benzimidazole derivatives of thio-alkylated and thioarylated substituted and screened against the pathogen *Stenotrophonas malthophilia* nosocomial strain. Compound 4,6-dichloro-2-(4-nitrobenzylthio)-benzimidazole (5) was the most active compound and metronidazole (6) was used as reference drug.



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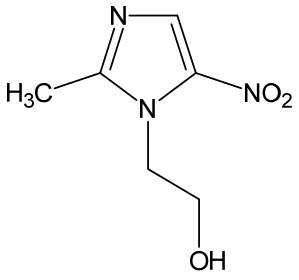
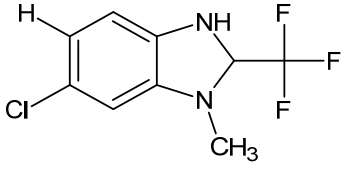


(6)

Vazquez in the year 2006 [15] have studied on analogues with 5- and 6-postion substituents (Cl,CF_3,CN) which were screened for their antiprotozoal activity against *Giardia intestinalis* and *Trichomonas vaginalis in vitro.* The compound [2,5 (6)-bis(trifluoromethyl)-1H-benzimidazole] (7) has shown potent antiprotozoal activity when albendazole (8) and metronidazole (6) were used as reference drugs.



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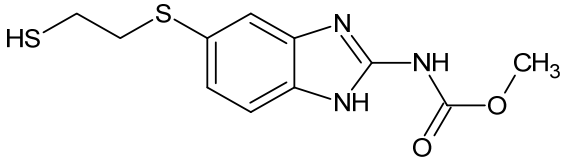
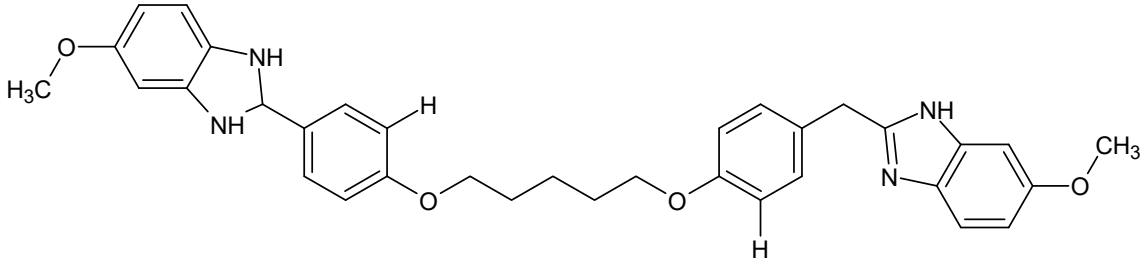


(8)

Gomez [16]in 2008 has been developed a new series of benzimidazole pentamidine hybrids and screened them against protozoa *in vitro*. The study showed that 1,5- bis [4--(5-methoxy-1H-benzimidazole-2-yl)phenoxy]pentane (9) was potent towards *G. Lamblia* when compared with pentamidine (10) and metronidazole (6).



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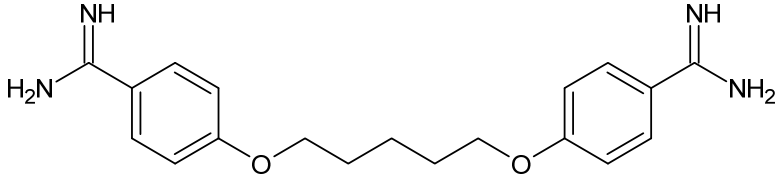
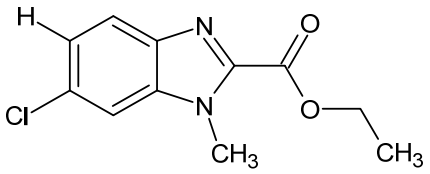


(10)

In 2009, Padilla[17] has synthesized and tested *in vitro* the antiprotozoal activity of 1- methyl benzimidazole derivatives. SAR studies have shown that substituting chlorine atoms enhances the activity and ethoxy carbonyl, Ethyl 1-methyl-1H- benzimidazole-2-carboxylated compounds (11), (12), (13) and (14) in this series are more potent when compared with metronidazole (6).



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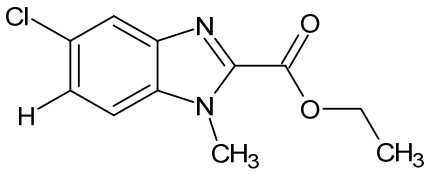

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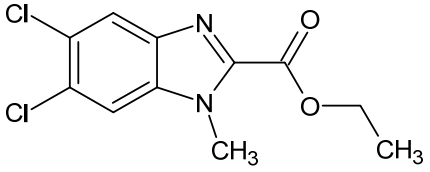

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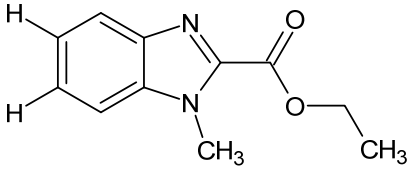
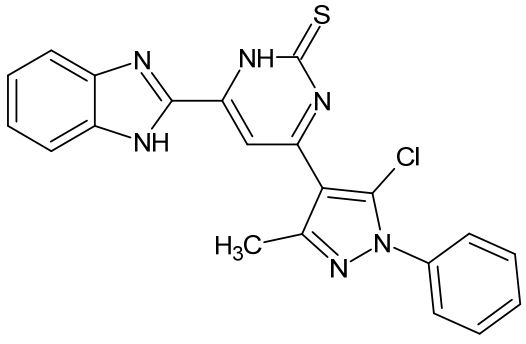


(14)

3.2 Antioxidant activity

Abd[18] in 2015, prepared some benzimidazole derivatives by incorporating chalcones, pyrazolines, oxazolines, pyrimidines,and oxiranes. They were tested for antioxidant activity by DPPH method. They discovered that 4-(1H-benzo[d]imidazol-2-yl)-6-(5-chloro-3-methyl-1-phenyl-1H-pyrazol-4-yl)- 5,6-dihydropyrimidin-2(1H)-one (15) and 2-(3-(5-chloro-3-methyl-1-phenyl-1Hpyrazol-4-yl) oxiran-2-yl)- 1H-benzo[d]imidazole (16) exhibited strong antioxidant activity when Ascorbic acid (17) was used as reference drug. Structure activity relationship has shown that epoxide ring and the pyrimidine thione were essential for their activity.



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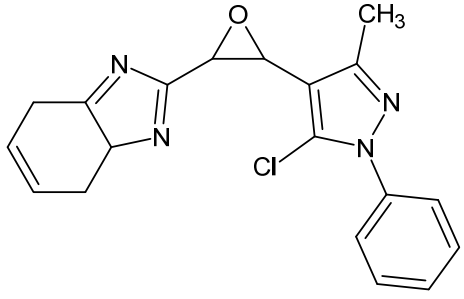

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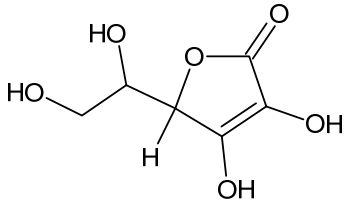

(17)

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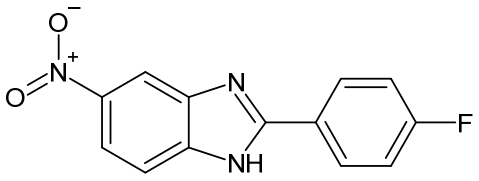
In the year 2017, Sabrina Rahman Archie [19]prepared benzimidazole derivative and screened for their antioxidant activity. All of the screened compounds have shown high antioxidant activity and compound 2(-4-fluoro-phenyl)-5-nitro-1H-benzimidazole (18) has shown promising antioxidant activity while butylated hydroxytoluene (BHT) (19) was used as reference.



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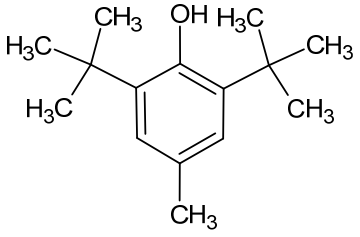
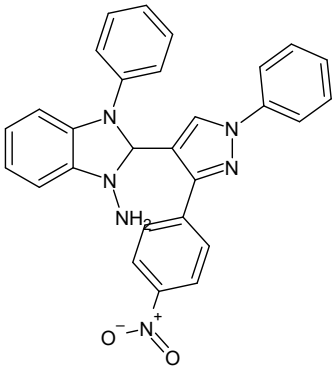


(19)

Mahesh Bellam[20] in 2017 prepared and investigated N-substituted pyrazole-containing benzimidazoles for screening antioxidant properties by assessing their radical scavenging ability against DPPH and H_2O_2. Results revealed that compounds (20) and (21) which were having inclusion of benzyl group on the nitrogen of imidazole showed good antioxidant activity.



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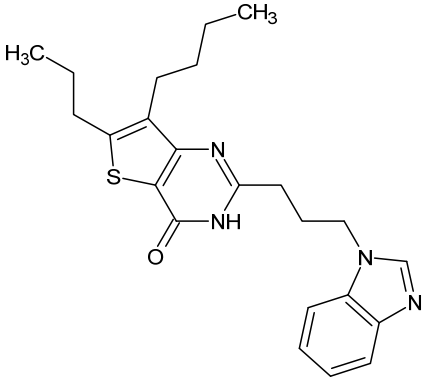
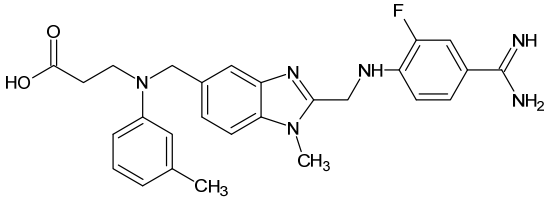


(21)

3.3 Anticoagulant activity

Yang Haoran[21] in 2016, prepared fluorinated benzimidazole analogues and evaluated for their anticoagulant activity. It was found that compounds (22),(23), and (24) displayed superior anticoagulant action than argatroban (25) in thrombin assay. When studied the SAR of these compounds, it shows that the presence of methyl groups at the ortho position in the benzene ring is favorable for anticoagulant medication.



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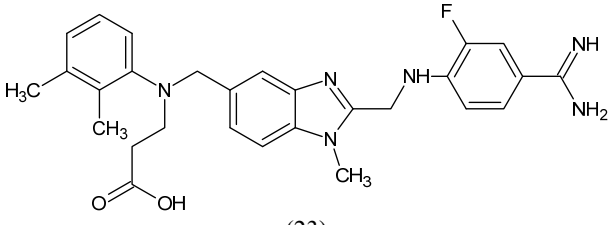

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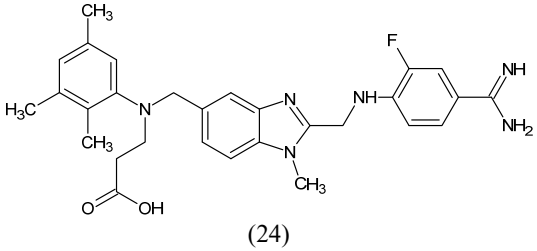

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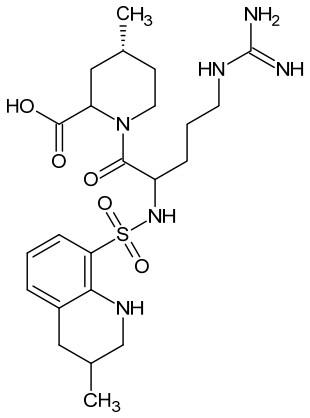

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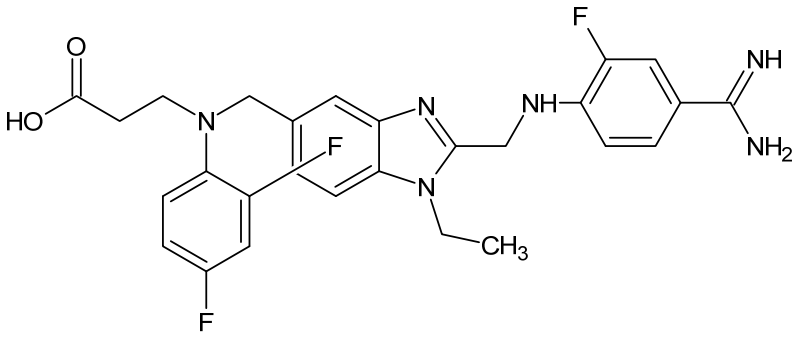
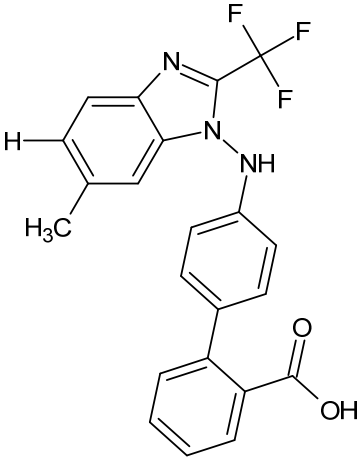


(26)

In the year 2016, Fei Wang et al.[22] prepared and evaluated 1-ethyl-1H-benzimidazole fluorinated derivatives for anti-thrombin activity. All substances tested surpassed the standard of drug argatroban (25) and compound (26) was identified as the most powerful derivative.

3.4 Antihypertensive Activity

Kankate in 2016 [23] synthesized a series of benzimidazole analogues and screened as Angiotensin-II blockers for antihypertensive activity. They reported that all compounds had potent antihypertensive activity in which the compound 4′ -((6- methyl-2-(trifluoromethyl)-1H-benzo[d]imidazol-1-yl)methyl)-[1,1′ - biphenyl]-2-carboxylic acid (27) was most effective antihypertensive agent when Losartatan (28) used as standard.



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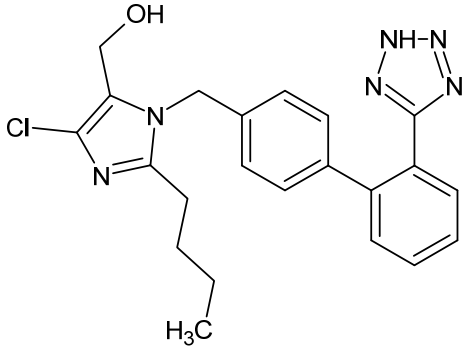

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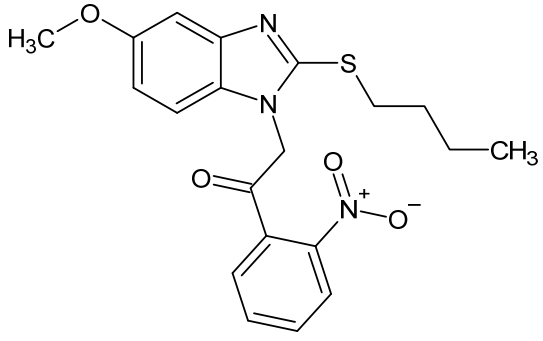

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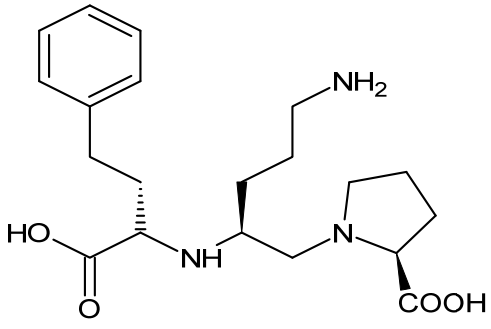
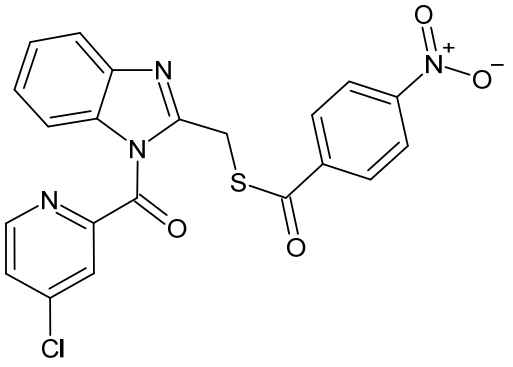


(30)

Abdulaziz Hammad in 2017 [24] developed a range of benzimidazole compounds and tested these as ACE inhibitors using molecular docking. They discovered compound 2-(2-(butylthio)-5-methoxy 1H indol-1-yl)-1-(2-nitrophenyl) ethan-1-one (29) as an equally active as ACE inhibitor in comparison to Lisinopril (30) as a reference medication using molecular docking and in silico toxicity studies.

3.5 Anti Helminthic Activity

Lingala Srikanth in year 2011 [25] prepared 4-chloropyridine-2-carbonyl and N-methyl picolinamide moieties from benzimidazole analogues and evaluation of their anthelmintic efficacy was conducted against indian adult earthworms (pheretima posthuma). In this study, six earthworms were divided in to four groups and samples were taken in 0.2% and 0.5% w/v with complete paralysis and death time recording. Compounds (31) and (32) showed higher efficacy when compared with albendazole (33) as a reference drug.



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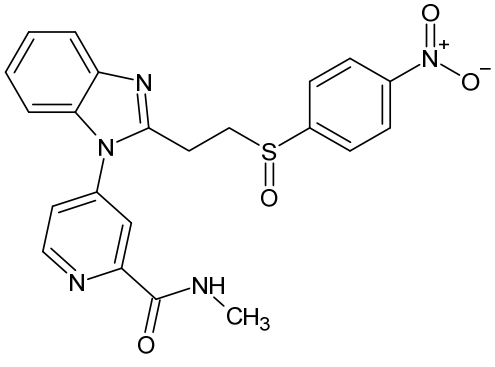

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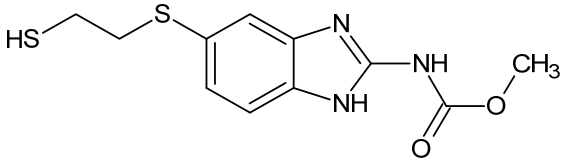
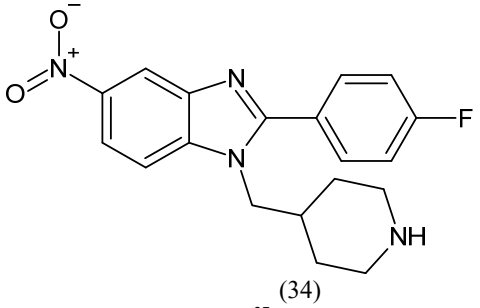


(33)

Faruk Alam in 2014 [26] synthesized 1 and 2-substituted-5-nitrobenzimidazole derivatives and tested their anthelmintic action on the adult Indian earth worm Pheretima posthuma. All prepared compounds demonstrated considerable anthelmintic action. When compared with the conventional piperazine citrate (34), compound 2-(4-flurorophenyl)-5-nitro-1-(piperidin1-ylmethyl)-1H-benzimidazole (35) demonstrated potential anthelmintic activity.



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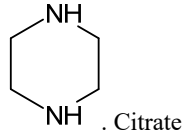
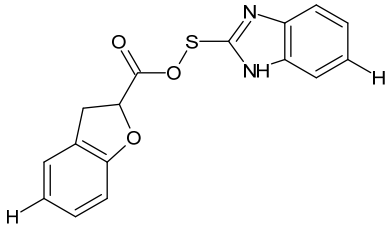


. Citrate

(35)

Kenchappa in 2016 [27] developed and tested a range of thiazolo[3,2-a] benzimidazole derivatives containing the benzofuran nucleus on the earthworm Pheretima posthuma. Results revealed that the compound 2-(1H-Benzimidazol-2-ylsulfanyl)-1-(1-benzofuran-2-yl)ethanone (36) and 1-(1-Benzofuran-2-yl)-2-[(6-bromo-1H-benzimidazol-2-yl)sulfanyl] (37) was highly active against earthworms, while (1-Benzofuran-2-yl)-2-(morpholin-4-ylmethyl)[1,3]thiazolo[3,2-a]benzimidazole (38) demonstrated good activity.



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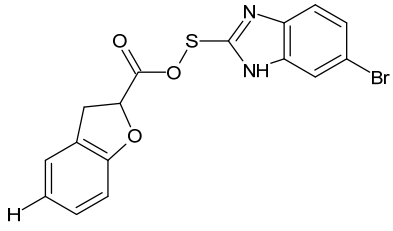

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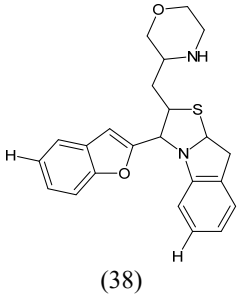
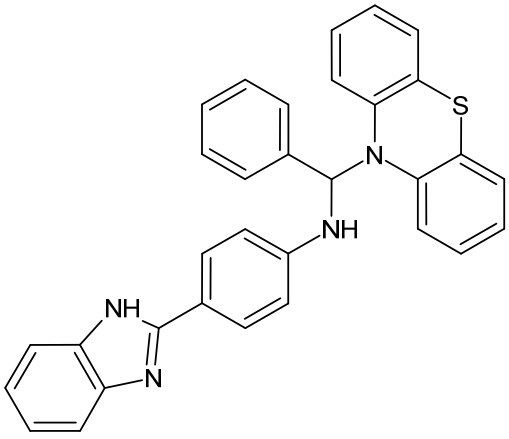


(38)

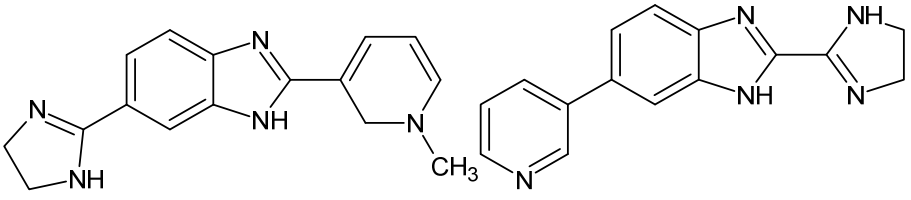
3.6 Antiviral Activity

Bishnoi in 1978, [28] synthesized 10-(a-p-benzimidazolyl-1-aminobenzyl) phenothiazine derivatives and evaluated against Japanese encephalitis virus and Herpes simplex virus *in vitro.* Antiviral assays of the compounds were performed in Swiss albino mice. The virus was maintained in mice by intracerebral passage and paralytic symptoms were observed in infected brain mice. Compounds (39) possesses highly potent antiviral activity.

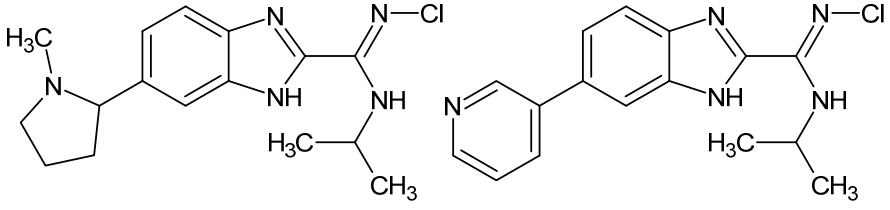


(39)

In the year 1999, Pandey and Shukla [29] prepared 7-(arylamidoalkyl)-3,4-diphenyl-isoquinolinyl-[1,5-c]- benzimidazoles derivatives which were screened against influenza virus *in vitro* and the virus was inoculated in hen's egg at allantoic cavity. The results revealed that the nicotinamido group is essential for isoquinonyl benzimidazole derivatives. Compounds (40),(41),(42), and (43) have shown higher activity.

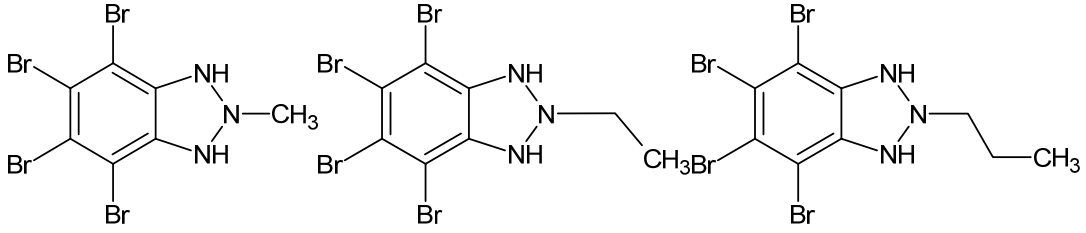


(40) (41)



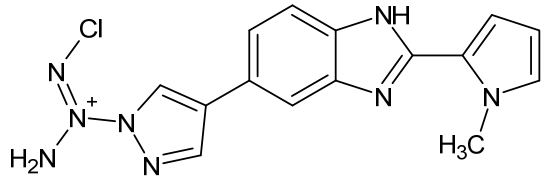
(42) (43)

Maria in 2005, [30]synthesized N-alkyl derivatives to improve antihelical activity and screened them against flaviviridae, hepatitis C virus (HCV), West Nile virus (WNV), Dengue virus (DENV) and Japanese encephalitis virus (JEV). The compounds (44), (45), and (46) which contain 4,5,6,7-tetrabromo-1H-benzotriazole have shown potent activity.

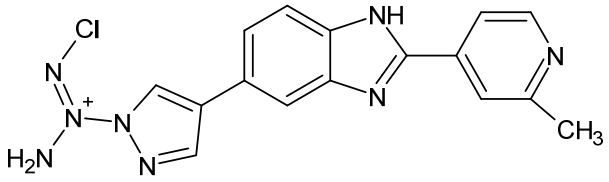


(44) (45) (46)

In the year 2007, Kristina [31] prepared 2-substituted-5-amidino-benzimidazole derivatives bearing amidino substituent at C-5 of the benzimidazole ring. All synthesised compounds were characterized by IR and ^{1}H NMR spectral data and evaluated against coxsackie virus and echo virus. Study revealed that compounds 2-(Methyl-H-pyrrol-2-yl)-H-benzimidazole-5-carboxamidine hydrochloride (47) and N-Isopropyl-2-pyridin-2-yl-H-benzimidazole-5-carboxamidine hydrochloride (48) are highly potent as antiviral. It also proves that the compound having pyridine ring at C-2 position has high inhibiting RNA replication potency in enterovirus.

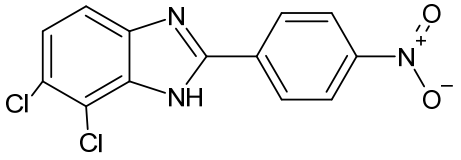


(47)



(48)

Michele et al.in 2010, [32] prepared 2-phenylbenzimidazole analogues and evaluated their antiviral activity for finding new antiviral agents against poxviruses, pestiviruses and even HCV, which are toxic for human society. Compounds (49), (50), (51), and (52) have shown good antiviral activity.



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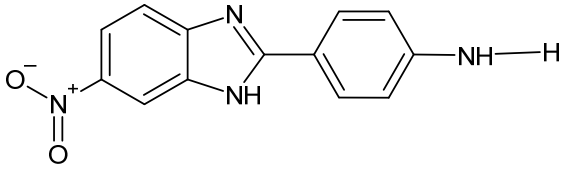

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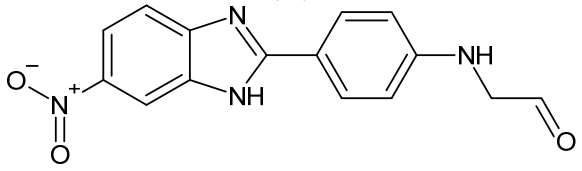

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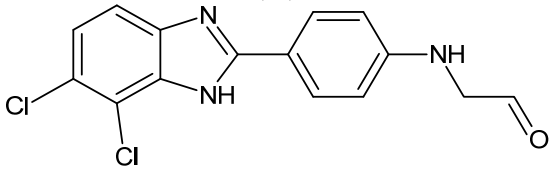
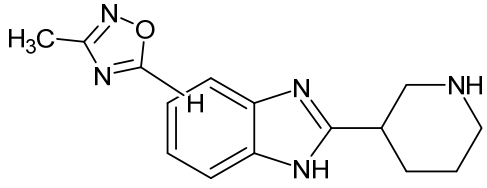


(52)

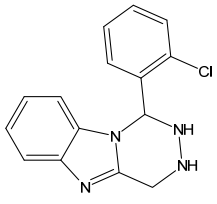
In the year 2013, Reyila et al [33] prepared incorporated oxadiazoles, thiadiazole and triazole substituent derivative of benzimidazole and evaluated against coxsackie virus B3 and B6.Among them, compound 5-(3-Methyl-1,2,4-oxadiazol-5-yl)-2-(pyridin-3-yl)-1H-benzimidazole (53) has shown highest activity.



(53)

3.7 Anticancer Activity

Hala Bakr El-Nassan in 2012[34] synthesized some 1,2,3,4-tetrahydro[1,2,4]triazino[4,5-a]benzimidazoles. All prepared compounds were screened *in vitro* against a human breast adenocarcinoma cell line using a 96-multiwell plate. Compound 1-(2-Chlorophenyl)-1,2,3,4-tetrahydro[1,2,4] triazino[4,5-a] benzimidazole (54) is much more potent against carcinoma cells. SAR study revealed that it might be due to the presence of aryl and heteroaryl groups at the first position, which enhances activity.



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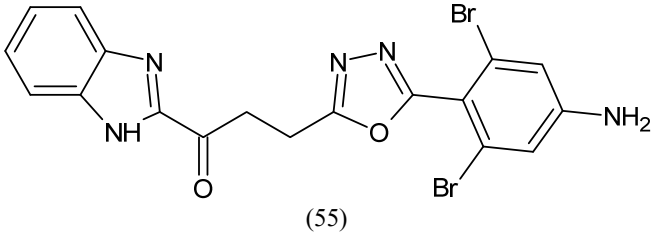
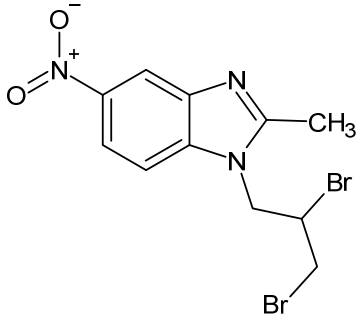


(55)

Asif [35]in 2012, synthesized some compounds bearing oxadiazole and triazolo-thiadiazole nuclei. All synthesised compounds were screened against human cell lines of which compound 3-(5-(4-amino-2,6-dibromophenyl)-1,3,4-oxadiazol-2-yl)-1-(1H-benzo[d] imidazol-2- yl) propan-1-one (55) was highly potent. This study also confirmed that compounds containing an oxadiazole ring had better anticancer activity than triazolo-thiadiazole nucleus containing compounds. In 2015, Yasser M. Shaker [36] prepared 1-substituted benzimidazole analogues and screened them against A549, HCT-116, and MCF-7cell lines. The results show that compound (56) is more effective against cell lines than doxorubicin (57).



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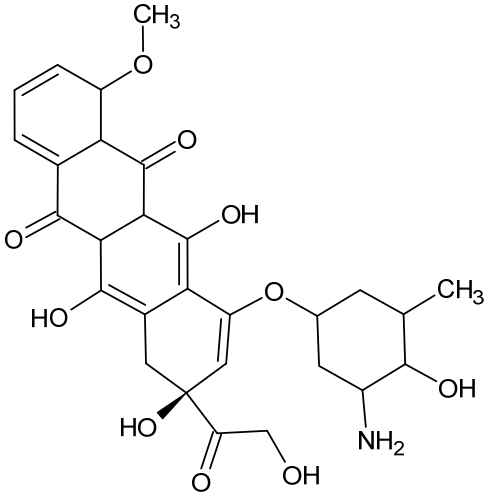
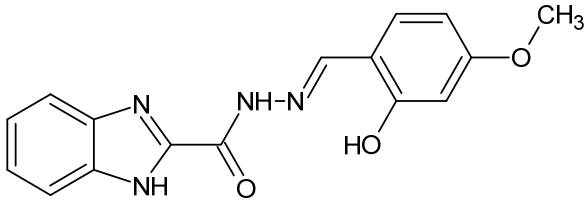
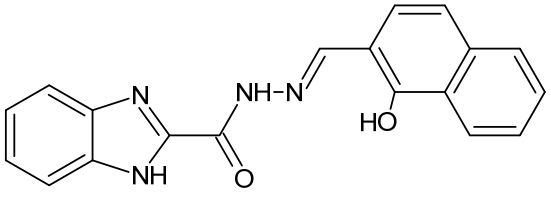


(57)

Valentina Onnis [37] in 2016, prepared a novel series of benzimidazole analogues and screened them for antiproliferative activity. SAR study revealed that hydrazones are essential for ant cancerous activity. Compounds (58) and (59) have shown promising activity against murine leukemia, human T-cell leukemia, human cervix carcinoma, and human pancreati carcinoma cells.

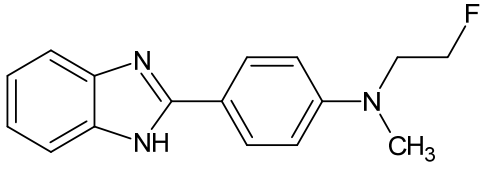


(58)



(59)

Goreti Ribeiro Morais in 2017, [38] synthesized a series of novel benzimidazole analogues having fluorinated or hydroxylated alkyl substituents with the purpose of screening the anticancer activity. The results revealed that compound 2-[N-methyl-N-(2′-fluoroethyl)-4′-aminophenyl]-1H-benzo [d]imidazole (60) displayed the most promising anticancer activity.



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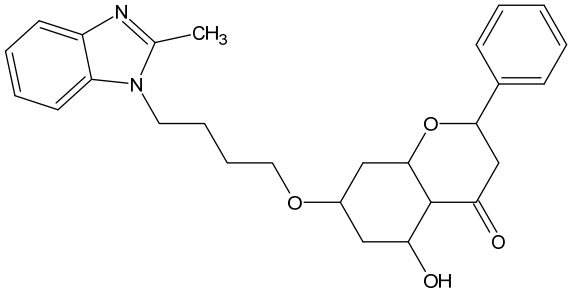
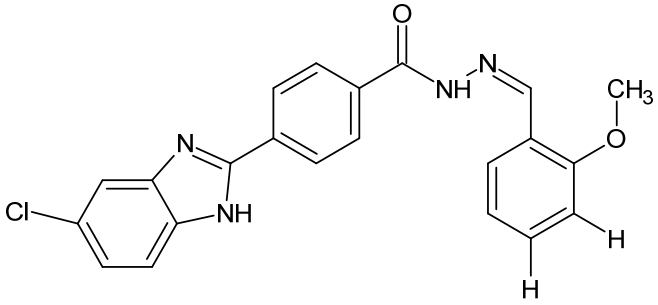


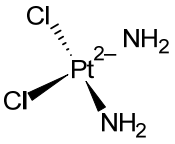
(61)

ZheWanga et al. in 2018, [39] reported chrysin benzimidazole compounds that have been found very potent against cell lines. Compound (61) had the most effective antiproliferative activity against MFC cells, and flow cytometry results revealed that the drug enhances MFC cell apoptosis in a dose-dependent manner. The anticancer efficacy of the compound

was further investigated in tumor-bearing animals, and it was discovered that it inhibited tumour growth. UlviyeAcarCevik in 2018, [40] produced 4-(5-chloro-1H-benzimidazol-2-yl)-benzoic acid benzylidene hydrazide derivatives. All synthesized compounds were characterized by 1H-NMR, 13C-NMR, and mass spectroscopy. A number of prepared compounds were subjected to anti-cancerous screening, which was showed that some compounds displayed activity against A549 and MCF-7 cancer cells. Compound 4-(5-Chloro-1H-benzimidazol-2-yl)benzoic acid 2-methoxylbenzylidene hydrazide (62) demonstrated a significant cytotoxic effect when cisplatin (63) was used as reference drug.



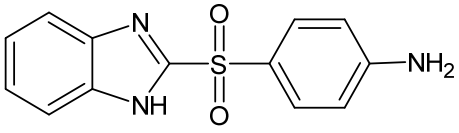
(62)



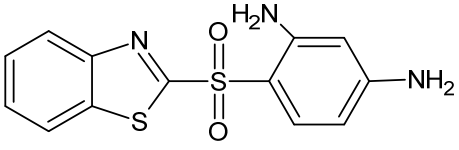
(63)

3.8 Antimicrobial Activity

Ghoneim et al in 1998, [41] prepared a series of 2-[(4-aminophenyl)sulphonyl] analogues and screened for the antimicrobial activity by using the agar diffusion method. It was found that all prepared compounds have significant antimicrobial activity, of which the compounds (64) and (65) were found to be the most active among all.

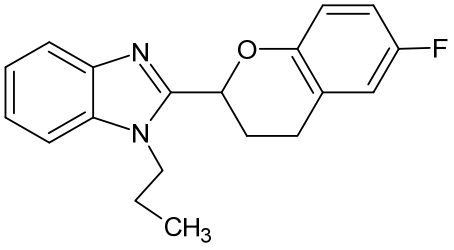


(64)



(65)

Kumar et al. in 2006, [42] used several electrophiles to make novel 2-(6-flurochroman-2-yl)-1-alkyl/acy/aroyl-1H-benzimidazoles. All compounds were characterized by ^{1}HNMR and IR spectroscopy. Antibacterial activity were screened against *Salmonella typhimurium* and *Staphylococcus aureus*. The compounds (66) and (67) have shown good activity against *Salmonella typhimurium*.



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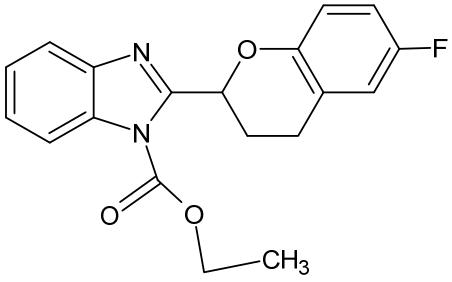
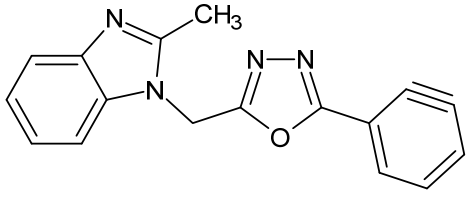


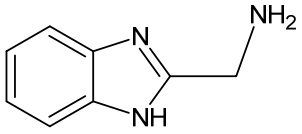
(67)

Ansari and Lal in 2009, [43] synthesized novel azetidine-2-one derivatives and screened against *Bacillus subtilis, Escherichia coli*, *Candida albicans*, *Aspergillus niger*, and *Aspergillus flavus*. The compounds that have been studied are more efficient against Gram-positive bacteria and 1-{[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]methyl}-2-methyl-1H-benzimidazol (68) was the most promising compound.



(68)

Ajani in 2016, [44] prepared a series of 2-substituted benzimidazole derivatives and screened them for their antimicrobial activity against Gram positive bacteria, and, Gram negative bacteria. Results revealed that the compound 1H-benzo[d]imidazol-2-yl)methanamine (69), demonstrated bigger zones of inhibition against these microorganisms when compared with gentamicin (70) as a standard drug.



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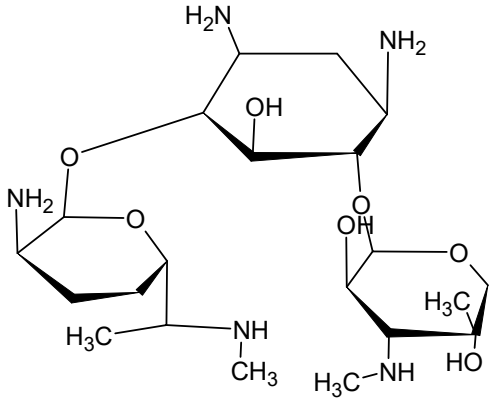
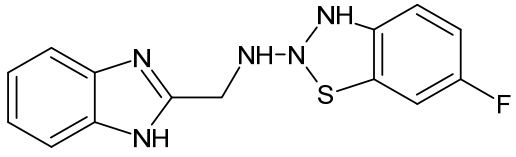


(70)

El-Gohary in 2017, [45] identified a series of benzimidazole derivatives which were evaluated for their antimicrobial activity. In this way, compound 2-[((6-Fluoro benzo- thiazol-2-yl)amino)methyl]-1H-benzimidazole (71) and1-((1H-Benzimidazol-2-yl)methyl)-3-methyl-1H-pyrazol-5(4H) (72) had promising activities towards *S. aureus* who inhibits cell wall biosynthesis. 5-Amino-N-((5-nitro-1H-benzimidazol-2-yl)methyl)-6-nitroquinoline (73) exhibited remarkable activity towards *B. cereus*. Ampicillin (74) and Fluconazole (75) were used as reference drugs.



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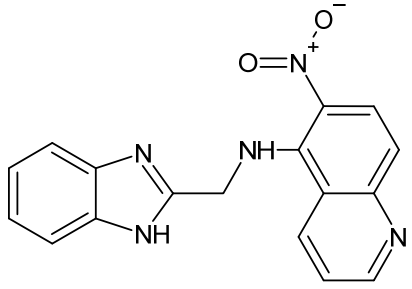

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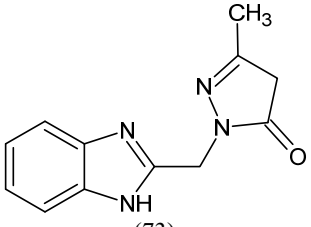

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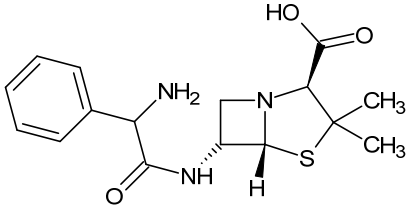

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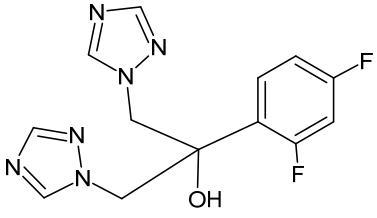
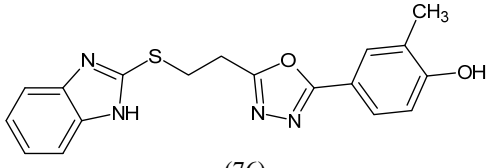


(75)

3.9 Antidiabetic Activity

Shingalapur in 2010, [46] screened 2-mercapto benzimidazole derivative for antidiabetic activity. Compounds (76 to 79) when compared with glibenclamide (80) demonstrated a better reduction in blood glucose levels.



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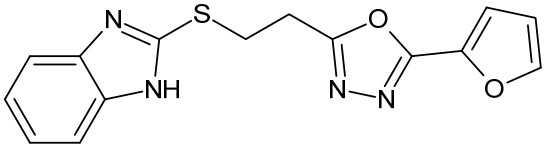

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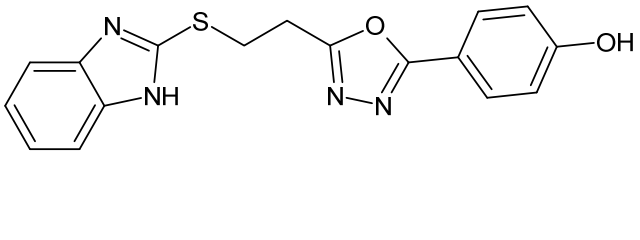

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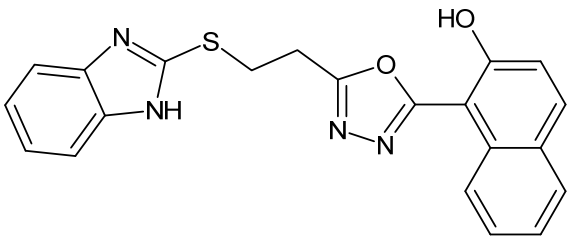

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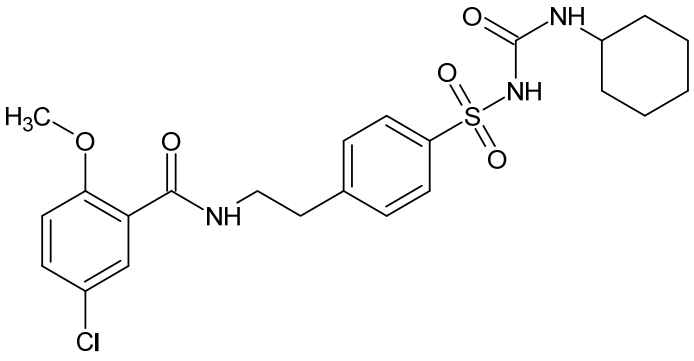
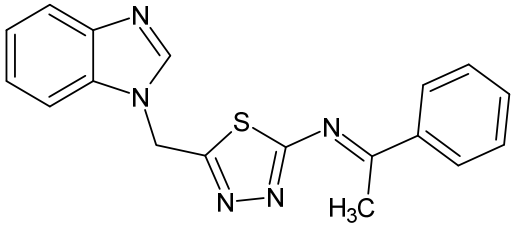


(80)

Nair in 2016, [47] prepared novel N-[(2-amino-5-methylene)-1,3,4-thiadiazole]-2-methyl benzimidazole analogues. All synthesized compounds were characterized by IR, 1 H-NMR, and mass spectral data and elemental analysis. Based on the Libdock score, compound (81) was selected as a potent *in vitro* antidiabetic and was found to have 49.25% inhibition at 100 µg conc. Acarbose (82) was used as the standard compound.



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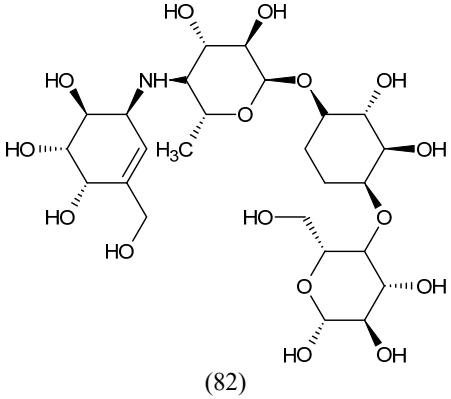
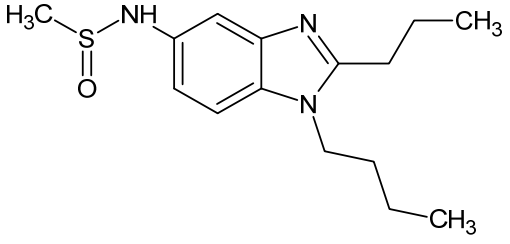


(82)

3.10 Anti-inflammatory Activity

Sharma in 2010, [48] prepared novel N-(1-alkyl-2-*n*-propyl-1*H*-benzo[*d*]imidazol-5-yl) methanesulfonamide benzimidazole analogues.The structure-activity relationship study indicated that the prepared compounds with variable number of alkyl groups and methanesulfonamides usually promoted inhibition of edema in rats induced by carrageenan. Compounds (83),(84), and (85) were found to have more more potent anti-inflammatory properties when compared to Rofecoxib (86) and Indomethacin (87) as standard drugs.



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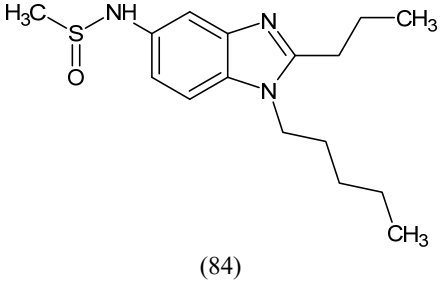
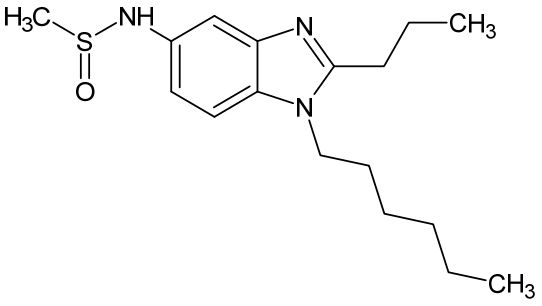


(84)



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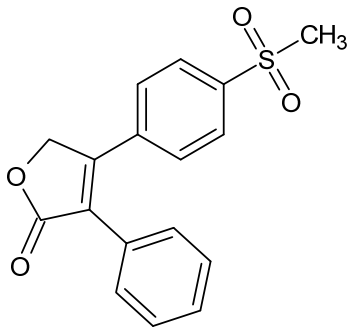

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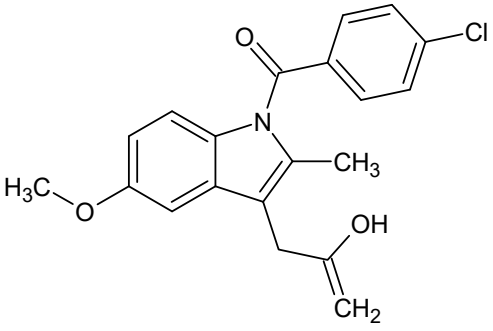
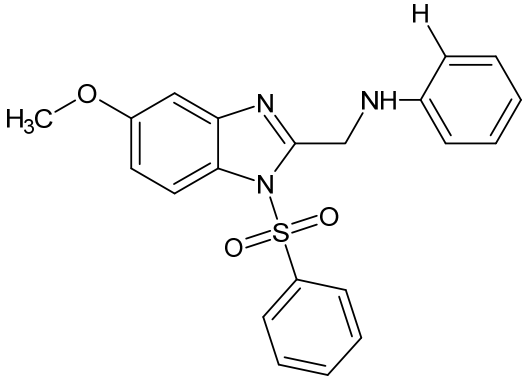


(87)

Gaba *et al*. in 2015, 49 prepared a series of 1, 2, and 5-substituted benzimidazole analogues and screened for in vivo anti-inflammatory studies using carrageenan-induced rat paw edema model. AnaloguesN-((5-Methoxy-1-(phenylsulfonyl)-1H benzo[d] imidazol-2-yl)methyl)benzenamine (88), N-((5-Methoxy-1-(phenylsulfonyl)-1H-benzo[d]imidazol-2-yl)methyl)-2-methylbenzenamin(89),N-((5-Methoxy-1- (phenylsulfonyl)-1H-benzo [d] imidazol-2-yl)methyl)-2-nitrobenzenaminee (90) were shown to have high antiinflammatory activity with depletion in edema. Indomethacin (87) was used as a reference drug.



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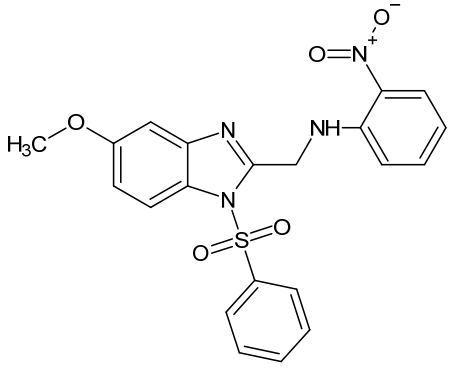

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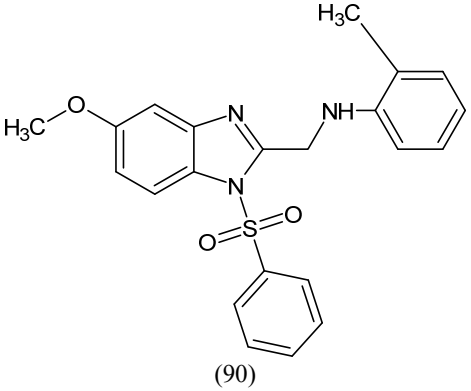
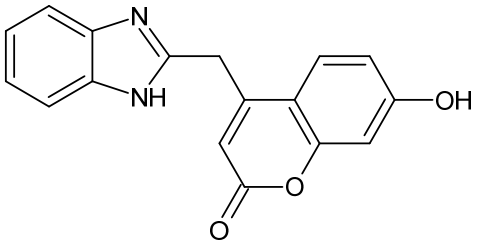


(90)

Purva Sethi et al. in 2017, [50] prepared new benzimidazole analogues from coumarin and Benzimidazole nuclei. All prepared compounds showed significant activity of which compounds (91 and 92) exhibited the highest anti-inflammatory activity, which is similar to the activity of indomethacin (87).



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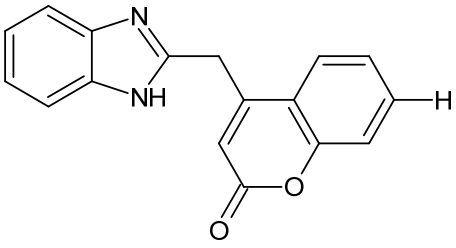
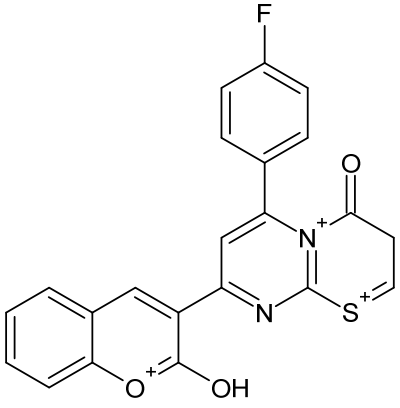


(92)

3.11 Antidepressant Activity

Abdel-Latif in 2005, [51] synthesized coumarin-based benzimidazole analogues and screened them for their antidepressant activity in rats. In all analogues,compounds (93) and (94) demonstrated higher activity than Tranylcypromine (95), as well as appreciable therapeutic windows and good safety margins.



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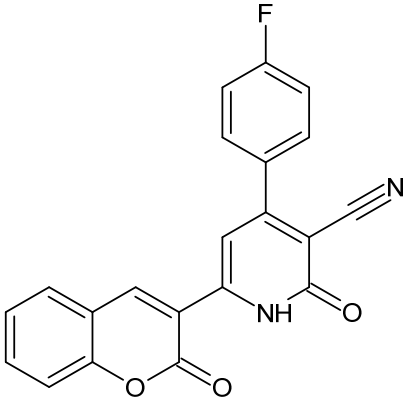

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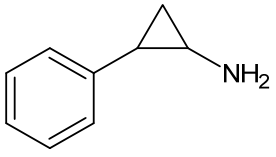
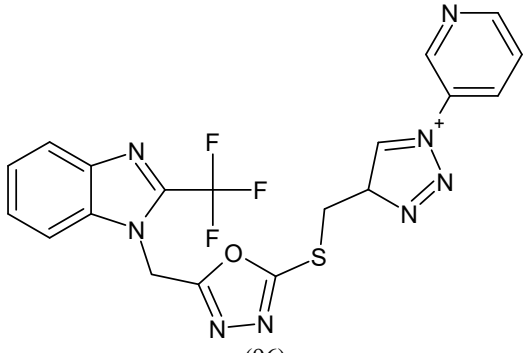
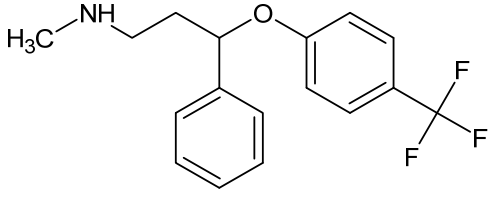


(95)

In the year 2016, Tantray *et al.* [52] were studied1,2,3-triazole and 1,3,4-oxadiazole fused benzimidazole derivatives and evaluated for their antidepressant activity in vitro and further screened in wistar rats by using fluxontine (97) as standard compound. The compound 1-((5-((1-(pyridin-3-yl)-1H-1,2,3-triazol-4-yl)methylthio)-1,3,4-oxadiazol-2-yl) methyl)-2-(trifluoromethyl)-1H-benzo[d] imidazole (96) exhibited significant GSK-3β inhibition with IC50 values.



(96)



(97)

4. Conclusion

Based on the assessment of the literature, it has been discovered that the functional group on a compound plays a prime role in the physicochemical properties displayed by the molecule. To develop a more effective medicinal agent, researchers must first understand the relative benefaction of each functional group. Numerous compounds derived from the benzimidazole nucleus are used in the treatment of a variety of diseases like anticancer, anti-inflomatory, antioxidant, antiviral etc. Benzimidazole is a bioactive and structurally simple heterocyclic compound, the molecule has played a key role in pharmaceutical chemistry in the development and discovery of new drugs with prospective biological activity. The

current review attempts to summarise the synthesis of various benzimidazole derivatives as well as their biological activity. It is hoped that this review will be useful to aspiring researchers working in the field of benzimidazole-based drug design.

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