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Recent Advances and Potential Pharmacological Activities of Benzimidazole Derivatives

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ABSTRACT

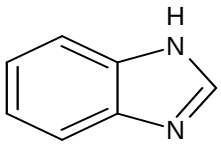
Benzimidazoles display a broad spectrum of potential pharmacological activities and are present in a number of pharmacologically active molecules such as Albendazole/ Mebendazole/ Thiabendazole (antihelmentic), Omeprazole (anti-ulcer). These compounds carrying different substituents in the benzimidazole structure are associated with a wide range of biological activities. Changes in their structure have offered a high degree of diversity that has proven useful for the development of new therapeutic agents having improved potency and lesser toxicity. In this context, the recently synthesized 2-Substituted benzimidazole derivatives possessing important pharmacological activities have been highlighted.

Keywords: Benzimidazole derivatives, Anti-hypertensive agent, Potential pharmacological activities.

INTRODUCTION

The benzimidazole heterocycle is represented in nature as an integral part of the structure of vitamin B12 and has been incorporated into pharmaceutical agents to form enzyme inhibitors, and DNA intercalators. Benzimidazoles are very useful intermediates/subunits for the development of molecules of pharmaceutical or biological interest. Substituted benzimidazole derivatives have found applications in diverse therapeutic areas including antiulcer, antihypertensives, antifungals, anticancers, and antihistaminics [1]. Some benzimidazole derivatives show diverse biological activities with significant clinical potential, including the

treatment of leukaemia and cancer. These compounds may also possess potent antiviral activity. It plays a crucial role in the development of theory in heterocyclic chemistry.



1*H*-benzimidazole

(fig.1)

Due to their wide range of pharmacological activity, industrial and synthetic applications, a number of methods have been reported for the synthesis of benzimidazoles, which include the coupling of phenylenediamines and carboxylic acids [2] or their derivatives (nitriles, imidates, or orthoesters) [3], the reaction between N-ethoxycarbonylthiomides with 1,2- diamines [4], and the reaction of aldehydes with 1,2-diamines followed by N-halosuccinimides (X = Cl, Br, I) [5]. Recently, azalactones [6], 2-aryl-1,1-dibromoethane [7], nitriles [8] and amino amides [9] have been used as starting materials for this synthesis of benzimidazoles. Benzimidazoles are remarkably effective compounds both with respect to their bacteria inhibitory activity and their favorable selectivity ratio. Extensive biochemical and pharmacological studies have confirmed that these molecules are effective against various strains of microorganisms. This review summarizes the chemistry of different derivatives of substituted benzimidazole along with their activity.

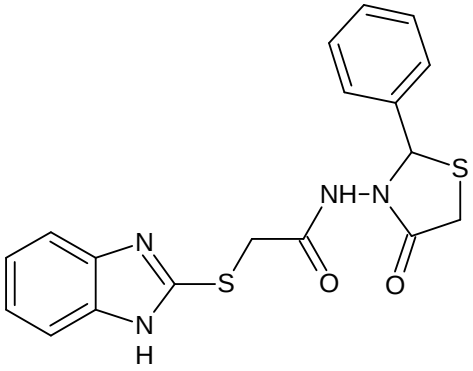
Pharmacological Activities

2-Benzimidazoles display a broad spectrum of potential pharmacological activities and are present in a number of pharmacologically active molecules such as albendazole/ mebendazole/ thiabendazole (antihelmentic), omeprazole (anti-ulcer), etc. Considerable interest has been focused on the benzimidazole structure. The discovery of this class of drugs provides an outstanding case history of modern drug development and also points out the unpredictability of pharmacological activity from structural modification of a prototype drug molecule. It is having a variety of medicinal applications. Benzimidazole derivatives carrying different substituents in the benzimidazole structure are associated with a wide range of biological activities including anticancer, antiviral, antibacterial, antifungal, antihelmintic, anti-inflammatory, antihistaminic, proton pump inhibitor, antioxidant, antihypertensive and anticoagulant activities. Their derivatives were also found to exhibit cytotoxic activity.

Antiepileptic activity

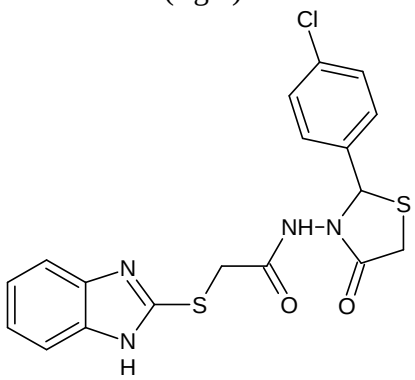
R.V.Shingalapur et al. synthesized (1H-benzimidazol-2-ylsulfanyl)-thiazolidin-4-one derivatives and studied their antiepileptic action by maximal electroshock seizure (MES). The existence of a hydrophobic unit in benzimidazole ring, an electron donor group and hydrogen bonding domain was essential for anticonvulsant activity as depicted by the models and also evidenced by active drug phenytoin and carbamazepine. A study of structure–activity relationship revealed that compounds include 2-(1*H*-benzimidazol-2-ylsulfanyl)-*N*-(4-oxo-2-phenyl-1,3-thia zolidin-3-yl) acetamide and its derivatives exhibited their ability to diminish tonic-extensor seizures. The presence of a hydroxyl –OH function at 2 and 4 position of the phenyl ring as seen with

compounds and was found to be the main structural requirement for maintaining anticonvulsant activity. The extensor phase time was remarkably reduced for these compounds. This requirement was further evidenced by compounds 3-(1H-Benzimidazol-2-ylsulfanylmethyl)-2-(4-chloro-phenyl)-thiazolidin-4-one and 3-(1H-Benzimidazol-2-ylsulfanyl methyl)-2-p-tolyl-thiazolidin-4-one where –OH function was replaced by a –Cl, –CH3 function, which resulted in complete loss of activity due to the disappearance of this function and can be explained in terms of interaction at the binding site by the pharmacophoric models. From the present study, four compounds have emerged as lead moieties. Further structural modifications might lead to the discovery of more potent anticonvulsant agents. [10]



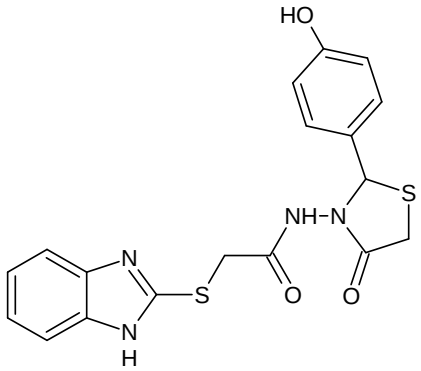
2-(1*H*-benzimidazol-2-ylsulfanyl)-*N*-(4-oxo-2-phenyl-1,3-thiazolidin-3-yl)acetamide

(fig.2)



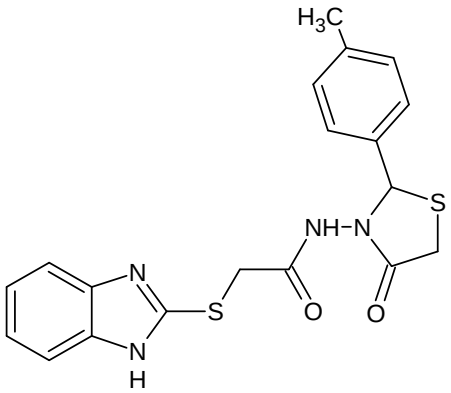
2-(1*H*-benzimidazol-2-ylsulfanyl)-*N*-[2-(4-chlorophenyl)-4-oxo-1,3-thiazolidin-3-yl]acetamide

(fig.3)



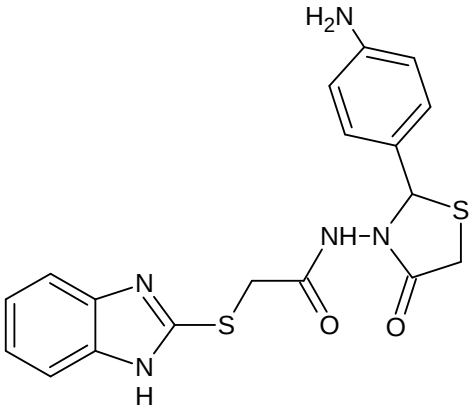
2-(1*H*-benzimidazol-2-ylsulfanyl)-*N*-[2-(4-hydroxyphenyl)-4-oxo-1,3-thiazolidin-3-yl]acetamide

(fig.4)



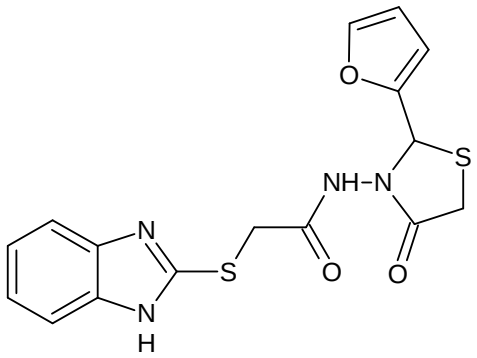
2-(1*H*-benzimidazol-2-ylsulfanyl)-*N*-[2-(4-methylphenyl)-4-oxo-1,3-thiazolidin-3-yl]acetamide

(fig.5)



N-[2-(4-aminophenyl)-4-oxo-1,3-thiazolidin-3-yl]-2-(1*H*-benzimidazol-2-ylsulfanyl)acetamide

(fig.6)

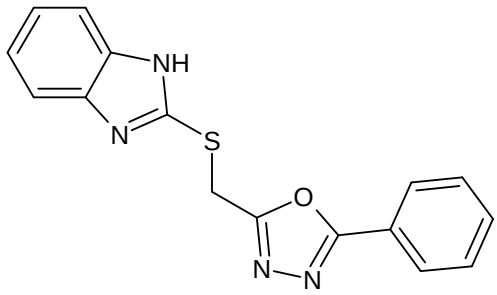


2-(1*H*-benzimidazol-2-ylsulfanyl)-*N*-[2-(furan-2-yl)-4-oxo-1,3-thiazolidin-3-yl]acetamide

(fig.7)

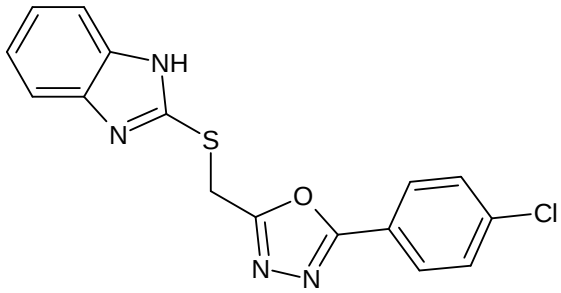
Antidiabetic activity

R.V.Shingalapur et al. synthesized four 2-(5-phenyl-[1, 3, 4]-oxadiazole-2-ylmethylsulfanyl)-1H-benzimidazole derivatives and was evaluated for their antidiabetic activity. Four compounds showed better reduction in blood–glucose levels on 9th day compared with glibenclamide. They were considered as significant compared to diabetic control group. Therefore, the best potent activity was found to be associated with 3-[5-(1H-Benzimidazol-2-ylsulfanylmethyl)-[1, 3, 4]-oxadiazole-2-yl]-naphthalene-2-ol. Several other compounds 2-(5-Phenyl-[1, 3, 4]-oxadiazole-2-ylmethylsulfanyl)-1H-benzimidazole,2-(5-Chloro-phenyl-[1,3,4]-oxadiazole-2-ylmethylsulfanyl) -1Hbenzimidazole and 3-[5-(1H-Benzimidazol-2-ylsulfanylmethyl)-[1, 3, 4]-oxadiazole-2-yl]-naphthalene-2-ol,5-[5-(1H-Benzimidazol-2ylsulfanylmethyl)-[1, 3, 4]-oxadiazole-2-yl]-benzene-1,2,3-triol and 2-[5-(4-Nitro-phenyl)-[1,3,4]-oxadiazole-2-ylmethylsulfanyl]-1H-benzimidazole were significant compared to normal control group during Oral Glucose Tolerance Test. [11]



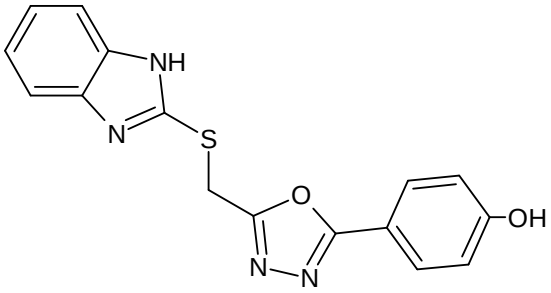
2-{[(5-phenyl-1,3,4-oxadiazol-2-yl)methyl]sulfanyl}-1*H*-benzimidazole

(fig.8)



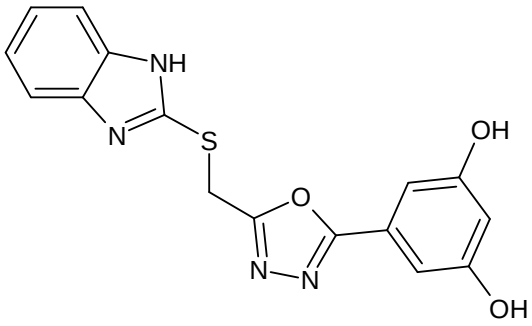
2-({[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]methyl}sulfanyl)-1*H*-benzimidazole

(fig.9)



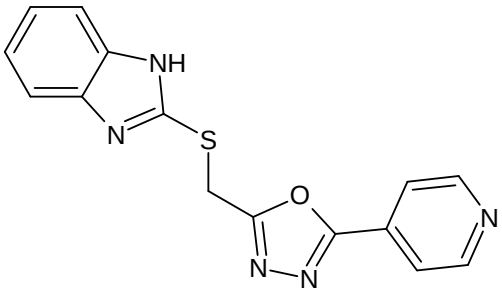
4-{5-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-1,3,4-oxadiazol-2-yl}phenol

(fig.10)



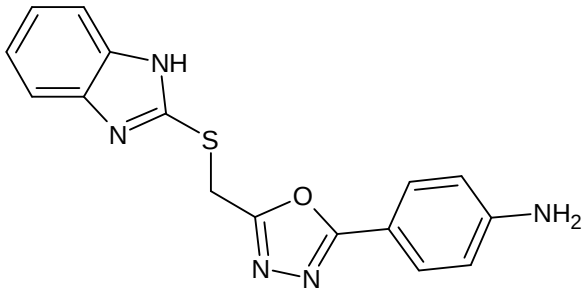
5-{5-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-1,3,4-oxadiazol-2-yl}benzene-1,3-diol

(fig.11)



2-({[5-(pyridin-4-yl)-1,3,4-oxadiazol-2-yl]methyl}sulfanyl)-1*H*-benzimidazole

(fig.12)



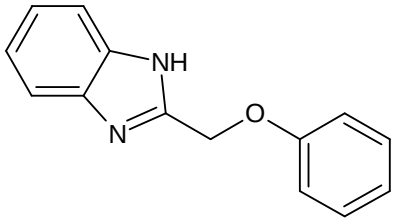
4-{5-[(1*H*-benzimidazol-2-ylsulfanyl)methyl]-1,3,4-oxadiazol-2-yl}aniline

(fig.13)

Antibacterial activity

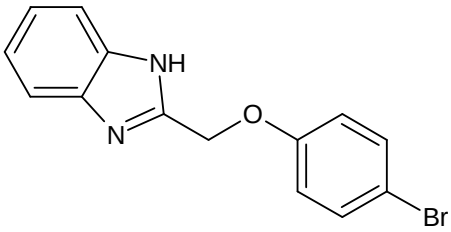
Varadaraj et al. synthesized a series of 2-substituted phenoxymethyl benzimidazoles and 1-alkyl-2-substituted phenoxymethyl benzimidazoles and evaluated for their antibacterial activity. The target molecules were tested for antibacterial activity against the variety of test organisms Escherichia coli, Pseudomonas aeruginosa (gram-negative bacteria) and Coagulase positive Staphylococcus aureus (COPS) (gram positive bacteria) by the punch well and Disc diffusion methods on the Muller Hinton agar medium using Gentamycin(100µg/ml) as the standard drug. The antibacterial screening was carried out with three different concentration of the synthesized novel molecules i.e. 1µg/ml, 10µg/ml, 100µg/ml using 50% Dimethylformamide as solvent. The screening results indicate that all compounds show promising activity against E. coli and P. aeruginosa and fewer compounds against COPS at all concentration levels. The compounds showed activity which is comparable with Gentamycin against E. coli in increasing order. All the compounds were far less active than the standard drug (gentamycin) taken. [12]

Afaf et al. synthesized and found antibacterial activities of 5-[2-(2-Methylbenzimidazol-1-yl) ethyl] [1,3,4]oxadiazole-2(3H)-thione containing arylidine hydrazones moiety in their structure. All the compounds were far less active than the standard drug (gentamycin) taken. [13]



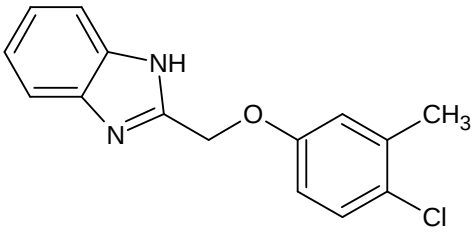
2-(phenoxymethyl)-1*H*-benzimidazole

(fig.14)



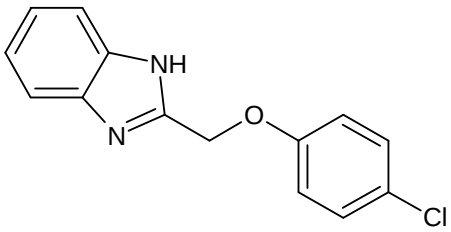
2-[(4-bromophenoxy)methyl]-1*H*-benzimidazole

(fig.15)



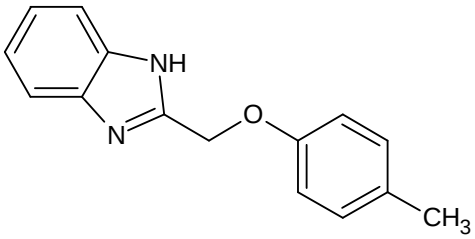
2-[(4-chloro-3-methylphenoxy)methyl]-1*H*-benzimidazole

(fig.16)



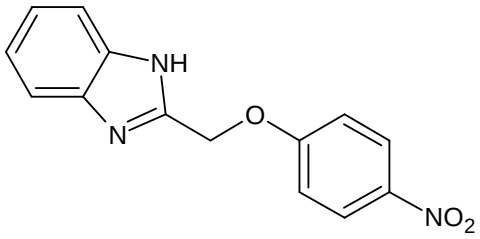
2-[(4-chlorophenoxy)methyl]-1*H*-benzimidazole

(fig.17)



2-[(4-methylphenoxy)methyl]-1*H*-benzimidazole

(fig.18)

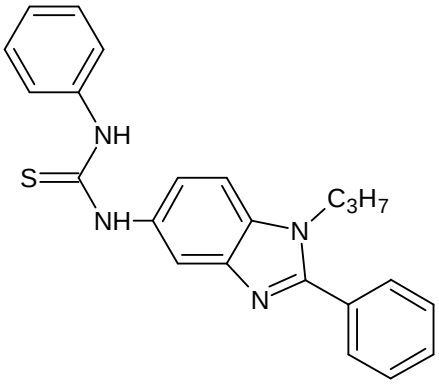


2-[(4-nitrophenoxy)methyl]-1*H*-benzimidazole

(fig.19)

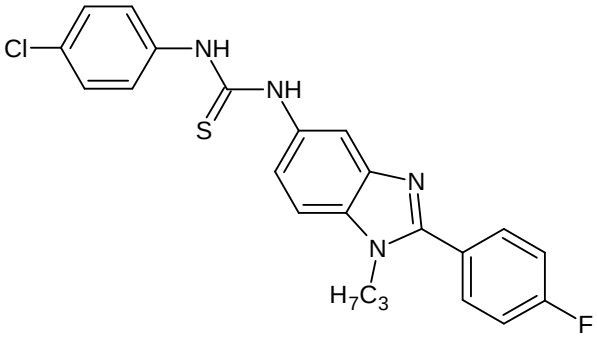
Antifungal studies:

Kilcigil et al. synthesized a series of benzimidazole derivatives were tested for antifungal activity against the variety of test organisms Candida albicans and Aspergillus niger by the punch well and Disc diffusion methods on the Sabourads Dextrose Agar Broth using Fluconazole(100 µg/ml) as the standard drug. The antifungal screening was carried out with three different concentration of the synthesized novel molecules i.e. 1µg/ml, 10µg/ml, 100µg/ml using 50% Dimethyl formamide as solvent. The screening results indicate that all compounds show promising activity against Candida albicans, of which only 1-alkyl-2-substituted phenoxymethyl benzimidazoles and its derivatives showed comparable activity with the standard Fluconazole. Fewer compounds exhibited activity against Aspergillus niger, substituted phenoxymethyl benzimidazoles showed higher activity than the standard Fluconazole. Some of the compounds exhibited a non-linearity between the concentration used and the zone of inhibition. [14]



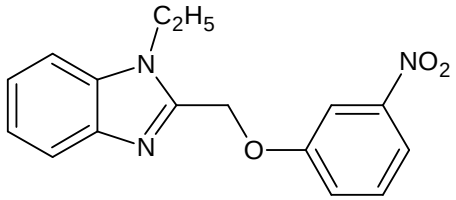
1-phenyl-3-(2-phenyl-1-propyl-1*H*-benzimidazol-5-yl)thiourea

(fig.20)



1-(4-chlorophenyl)-3-[2-(4-fluorophenyl)-1-propyl-1*H*-benzimidazol-5-yl]thiourea

(fig.21)

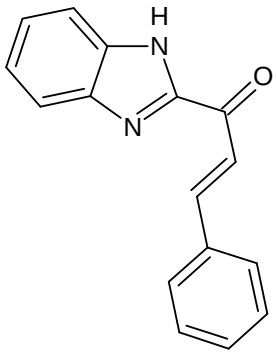


1-ethyl-2-[(3-nitrophenoxy)methyl]-1*H*-benzimidazole

(fig.22)

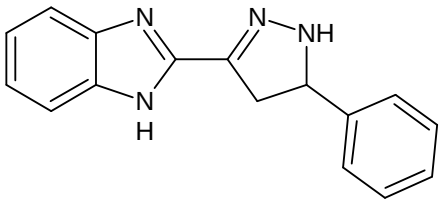
Antitubercular activity:

Jaseela et al. synthesized a series of 1-(1H-benzimidazol-2-yl)-3-(substituted phenyl)-2-propen-1-one were allowed to react with hydrazine hydrate and phenyl hydrazine in submitted reactions to get pyrazoline, phenyl pyrazoline and benzimidazole derivatives were tested for antifungal activity against the Mycobacterium tuberculosis H37RV strain using Lowenstein-Jensen Medium and Isoniazid and Rifampicin as standard drug. The media was prepared as per the procedure recommended by the international union against tuberculosis. All the compounds exhibited very good anti tubercular activity even at 1µg/ml against M. tuberculosis strain H37RV compared to the standards viz., Rifampicin and Isoniazid. [15]



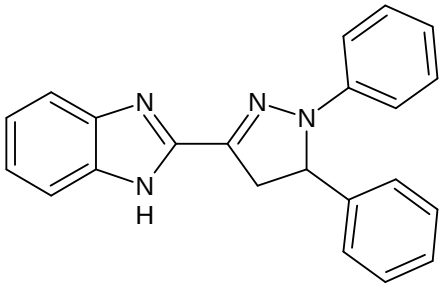
(2*E*)-1-(1*H*-benzimidazol-2-yl)-3-phenylprop-2-en-1-one

(fig.23)



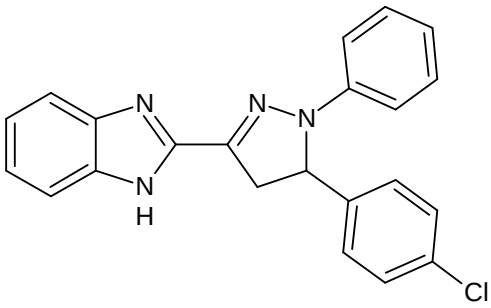
2-(5-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-1*H*-benzimidazole

(fig. 24)



2-(1,5-diphenyl-4,5-dihydro-1*H*-pyrazol-3-yl)-1*H*-benzimidazole

(fig.25)

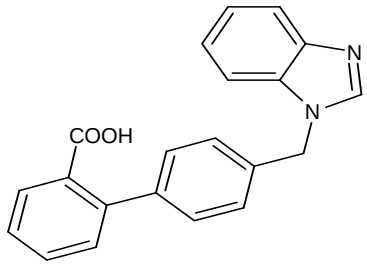


2-[5-(4-chlorophenyl)-1-phenyl-4,5-dihydro-1*H*-pyrazol-3-yl]-1*H*-benzimidazole

(fig.26)

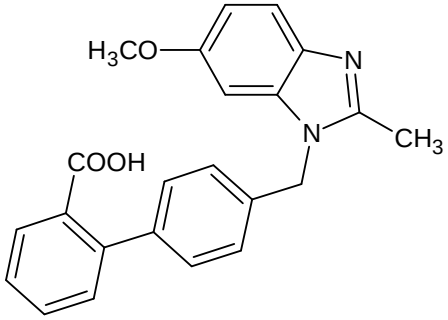
Antihypertensive Activity

Sharma *et al*. synthesized 6-Chloro-5-nitro-benzimidazole derivatives and evaluated their anti hypertensive activity. All the synthesized benzimidazole incorporated antihypertensive activity with standard drug compared all synthesized compounds. Almost all the newly synthesized substituted 6-Chloro-5-nitro-benzimidazole showed good antihypertensive activity with the goal of investigating the structure–activity relationships of benzimidazole, based molecules, fifteen analogs compounds were synthesized Synthesis has been carried out of selected benzimidazole derivatives having electron donor and acceptor substituents at 5-position nitro group and 2-postions different aryl groups. [16] [17]



4'-(1*H*-benzimidazol-1-ylmethyl)biphenyl-2-carboxylic acid

(fig.27)

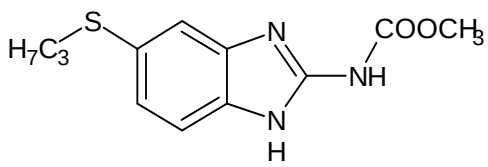


4'-[(6-methoxy-2-methyl-1*H*-benzimidazol-1-yl)methyl]biphenyl-2-carboxylic acid

(fig.28)

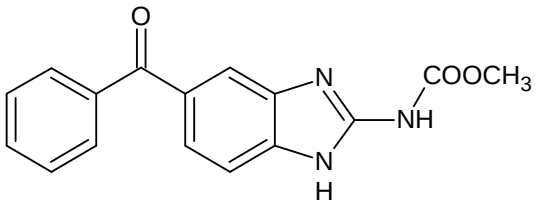
Antihelmintic Activity

The first of this class, thiabendazole, was discovered in 1961 and subsequently a number of further benzamidazoles were introduced as broad spectrum anthelmintics [18]. There is an extensive literature on these compounds reporting a number of different biochemical effects. Nonetheless, it is clear that their anthelmintic efficacy is due to their ability to compromise the cytoskeleton through a selective interaction with b-tubulin (Borgers and de Nollin, 1975; for review see Lacey, 1990). The effects of benzimidazoles on C. elegans, which include impaired locomotion, reproduction and a detrimental effect on oocytes, are consistent with disruption of processes requiring integral microtubules. The sensitivity of C. elegans to benzimidazoles is mediated by a single gene, ben-1, which encodes b-tubulin (Driscoll et al., 1989). This has provided a platform to investigate the molecular basis of benzimidazole resistance in parasitic nematodes. It has been noted that benzimidazole resistance in Haemonchus contortus seems to be associated with the presence of specific alleles for b-tubulin in the drug resistant isolates (Kwa et al., 1994).



methyl [5-(propylsulfanyl)-1*H*-benzimidazol-2-yl]carbamate

(fig.29)



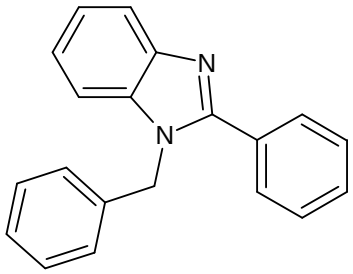
methyl (5-benzoyl-1*H*-benzimidazol-2-yl)carbamate

(fig.30)

Antioxidant activity

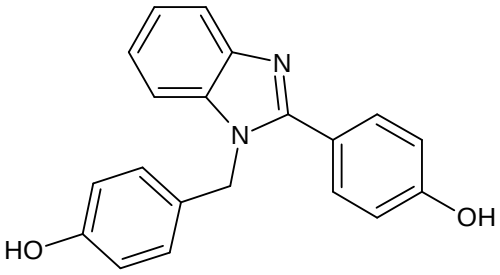
Sandhya Rani et al synthesized nine new [1-benzyl-2-phenyl-Substituted]-1H-5,6-substituted-benzoimidazoles were synthesized by reacting with substituted *o*-phenylenediamine with substituted benzaldehydes. All these compounds were characterized by means of their IR, 1H NMR and Mass Spectroscopic data. Antioxidant activity of these compounds was evaluated by ferrous induced lipid peroxidation in rat brain homogenate. It was found that the compounds possessing electron releasing groups such as dimethylamino, methoxy and hydroxyl substituent, at position 1 and 2 of benzimidazoles, considerably enhanced the activities when compared to the benzimidazoles having no substituents on the rings. [19]

Janssen et al. synthesized a large series of benzimidazole derivatives Compounds bearing benzimidazole moiety are reported to possess a number of interesting biological activities such as antitubercular, anticancer, antihelmintic, antiallergic, antimicrobial, antioxidant activities. [20] Guelguen et al. reported some new 1-[(thio carbamoyl hydrazine carbonyl) methyl]-2-phenyl-1Hbenzimidazole, N-[(2-phenylbenzimidazol-1-yl-methyl)-[1,3,4]-thiadiazole-2-yl arylamines & their in vitro effects on lipid peroxidation in the rat liver. [21]



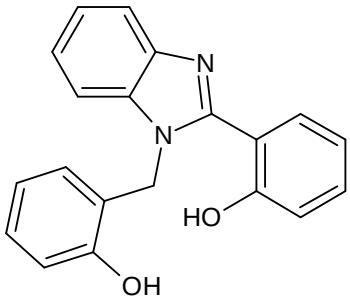
1-benzyl-2-phenyl-1*H*-benzimidazole

(fig.31)



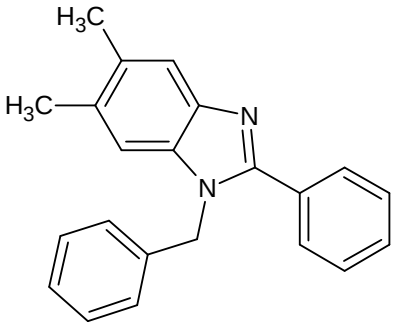
4-[1-(4-hydroxybenzyl)-1*H*-benzimidazol-2-yl]phenol

(fig.32)



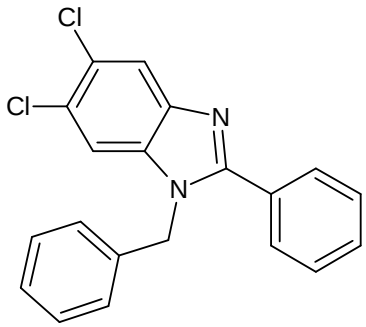
2-[1-(2-hydroxybenzyl)-1*H*-benzimidazol-2-yl]phenol

(fig.33)



1-benzyl-5,6-dimethyl-2-phenyl-1*H*-benzimidazole

(fig.34)

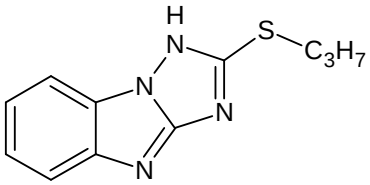


1-benzyl-5,6-dichloro-2-phenyl-1*H*-benzimidazole

(fig.35)

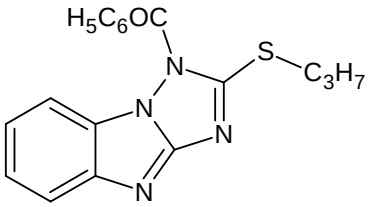
Analgesic and anti-inflammatory activity

B. G. Mohamed *et al*. synthesized and evaluated biological activity of 1-acyl-2-alkylthio-1, 2, 4-triazolobenzimidazoles. They were found to be analgesic and anti-inflammatory in nature. [22] Black et al. and Kalgutkar et al. reported the vital role of the p-chlorobenzoyl substituent for the activity of indomethacin and related compounds. The tested compounds could be considered as 3-aza-indolotriazole derivatives and they induce anti-inflammatory and analgesic effects. [23]



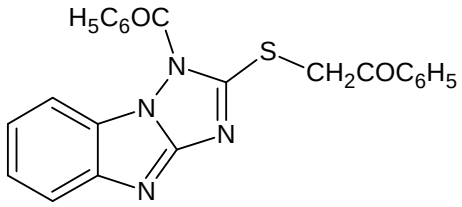
2-(propylsulfanyl)-1*H*-[1,2,4]triazolo[1,5-*a*]benzimidazole

(fig.36)



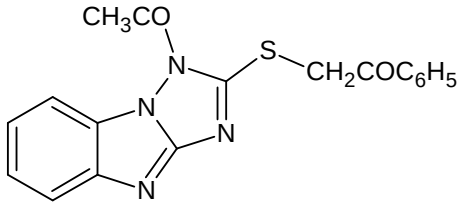
phenyl[2-(propylsulfanyl)-1*H*-[1,2,4]triazolo[1,5-*a*]benzimidazol-1-yl]methanone

(fig.37)



2-[(1-benzoyl-1*H*-[1,2,4]triazolo[1,5-*a*]benzimidazol-2-yl)sulfanyl]-1-phenylethanone

(fig.38)

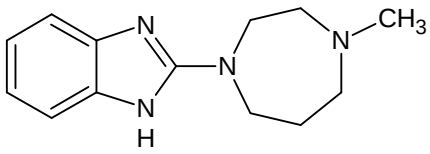


2-[(1-acetyl-1*H*-[1,2,4]triazolo[1,5-*a*]benzimidazol-2-yl)sulfanyl]-1-phenylethanone

(fig.39)

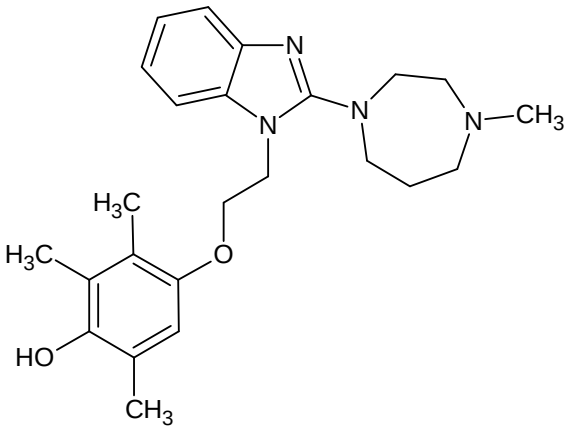
Anti Allergic activity

Toshio et al. synthesized, 1-[2-[2-(4-hydroxy-2,3,5-trimethylphenoxy)ethoxy]ethyl]-2-(4-methyl-1-homopiperazino)benzimidazole potently suppressed histamine release from rat peritoneal mast cells triggered by the antigen-antibody reaction, inhibited 5-lipoxygenase in rat basophilic leukemia-1 (RBL-1) cells, and prevented the NADPH-dependent lipid peroxidation induced by Fe31–ADP in rat liver microsomes, in addition to an antagonizing the contraction of guinea pig ileum caused by histamine. [24]



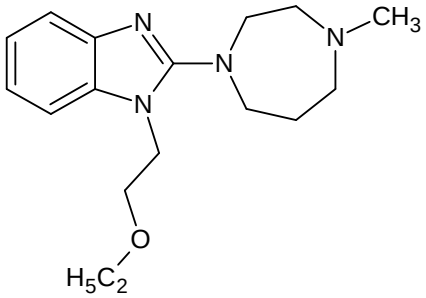
2-(4-methyl-1,4-diazepan-1-yl)-1*H*-benzimidazole

(fig.40)



1-[2-(4-Hydroxy-2,3,5-trimethylphenoxy)ethyl]-2-(4-methyl-1-homopiperazino)-1H-benzimidazole

(fig.41)



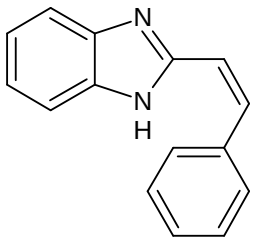
1-(2-ethoxyethyl)-2-(4-methyl-1,4-diazepan-1-yl)-1*H*-benzimidazole

(fig.42)

Anti viral and Anti cancer activity

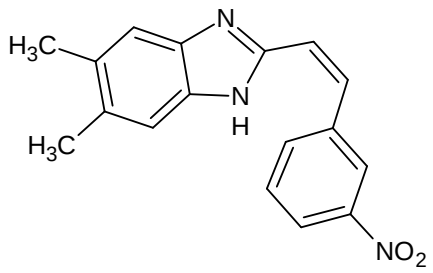
Gabriella et al. synthesized a class of benzimidazole 5-carboxamide derivatives and similar compounds as specific inhibitors of the NS5B polymerase of the hepatitis C virus (HCV) and some of benzimidazole derivatives show both antiviral and anticancer activity.

Göker et al., Valdez et al. and Aguirre *et al.*, synthesized 1*H*-Benzimidazole rings, which exhibit remarkable basic characteristics due to their nitrogen content, comprise the active substances of several drugs. A number of biological activities, such as anticancer, antibacterial, antifungal, antimicrobial, and antiprotozoal and antihelmintic activities have been attributed to these compounds. [25]



2-[(*Z*)-2-phenylethenyl]-1*H*-benzimidazole

(fig.43)



5,6-dimethyl-2-[(*Z*)-2-(3-nitrophenyl)ethenyl]-1*H*-benzimidazole

(fig.44)

Antiulcer activity

Katsura et al prepared compounds with substitution of dimethyl imidazopyridine at sixth position of benzimidazole showing strong antisecretory activity. Pantoprazole synthesis by Bernhard et al explained role of methoxy group of pyridine for maximum biological activity. Introduction of rigid ring with benzimidazole and their conversion to biological active sulfonamide in acidic media has been verified by Shin-ichi et al in 1994. Kohl et al substituted pyridine by triazole 3-yl 1-3 dithiane and reported promising results when biologically evaluated against H.Pylori. [26] Grast et al in 2003 substituted benzimidazole at first position by pyridyl sulfinyl and resulted in potentially active compounds. Recently substitution was carried out by n-propyl and N-(1 cyclohex-3-enylmethyl) piperidin-4-yl)-5-carboxamide and resulted in significant antiulcer activity, explained by shrinivasulu et al. [27]

Keiji Kubo et al [10] reported the synthesis of 2-[(3-methyl, 4- trifluro ethoxy)2- pyridyl) methyl , sulfinyl] benzimidazole which showed antisecretory, antiulcer, cytoprotective activity. After examining the pharmacological and toxicological properties Lansoprazole was selected as a promising antiulcer agent.

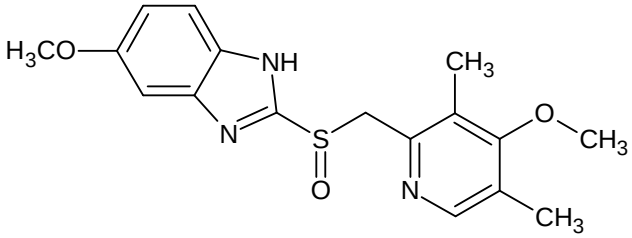
Brumagniez et al reported the synthesis of 2-(thiopropyne) - 5- (imidazole-1-yl.) benzimidazole, which exhibited moderate antiulcer activity against ulcer induced by anti inflammatory agents in rats orally.

Kovalev et al reported the synthesis of 9-(diethyl amino ethylene) 2 – phenyl imidazo [1, 2-a] benzimidazole, which was found to be more potent than omeprazole.

Braendstroem et al reported the synthesis of 2- [(3, 4 dimethoxy, 2 –pyridyl) methyl, sulfinyl] 5-acetyl, 6-methyl benzimidazole, which inhibited gastric acid secretion in dogs. [28]

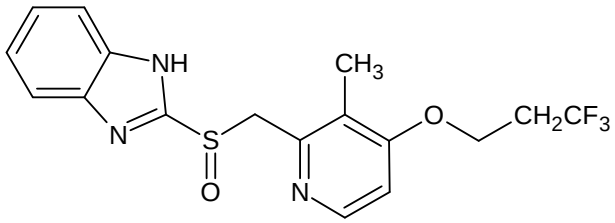
Shin-ichi et al reported the synthesis of 2- [(4- methoxy, 6,7,8,9- tetra hydro- 5H – cyclohepta (b)pyridine-9-yl)sulfinyl] 1-H benzimidazole sodium salt, which showed promising antiulcer activity and stability on isolated H^+/K^+-ATPase of rabbit gastric mucosa. [29]

Kamiyama et al reported the synthesis of 1- methyl acetate, 2- [(3-methyl, 4-trifluro ethoxy 2-pyridyl) methylsulfinyl] benzimidazole showed excellent antiulcer, gastric acid secretion inhibitory, mucosa protecting, anti H pylori effect in vivo. This compound also showed low toxicity, high stability to acid, higher absorption rate than enteric preparation and long lasting effect. Shrinivasulu et al reported the synthesis of 2- n propyl, 5 (N methyl 3, 4 cyclo hexane, 4 amino piperidine) keto, 6-ethoxy, benzimidazole, which exhibited good antiulcer activity. [30]



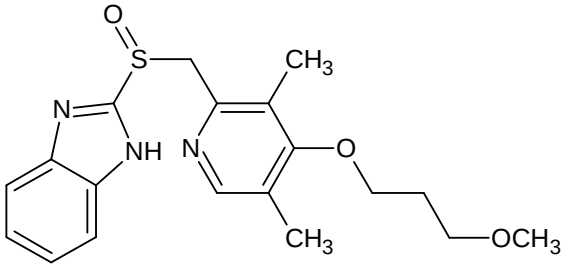
5-methoxy-2-{[(4-methoxy-3,5-dimethylpyridin-2-yl)methyl]sulfinyl}-1*H*-benzimidazole

(fig.45) (Omeprazole)



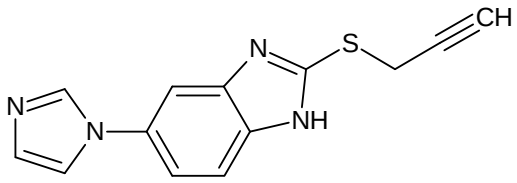
2-({[3-methyl-4-(3,3,3-trifluoropropoxy)pyridin-2-yl]methyl}sulfinyl)-1*H*-benzimidazole

(fig.46) (Lansoprazole)



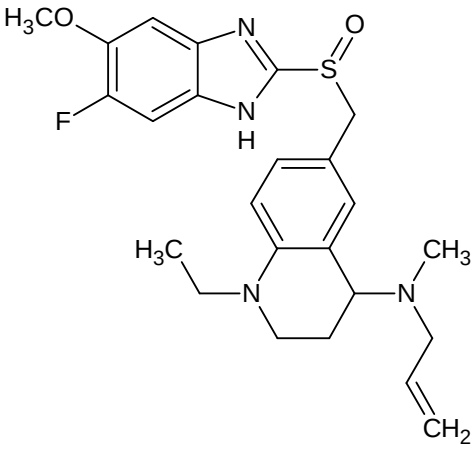
2-({[4-(3-methoxypropoxy)-3,5-dimethylpyridin-2-yl]methyl}sulfinyl)-1*H*-benzimidazole

(fig.47)(Rabeprazole)

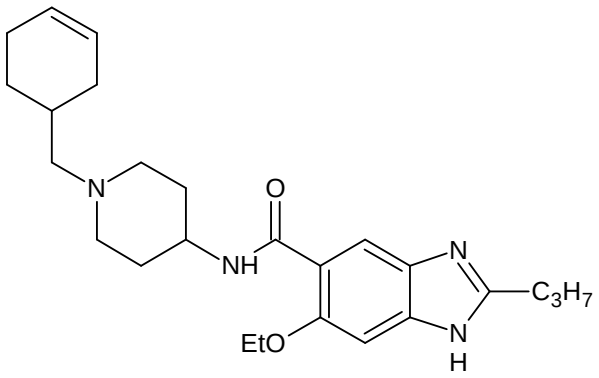


5-(1*H*-imidazol-1-yl)-2-(prop-2-yn-1-ylsulfanyl)-1*H*-benzimidazole

(fig.48)



2-[[(1- ethyl , 4- N-methyl – N – (1 propene) 1,2,3,4 tetrahydro quinoline-8 yl) methylsulfinyl] 5- fluro, 6- methoxy benzimidazole (fig.49)



2- n propyl, 5 (N methyl 3, 4 cyclo hexane, 4 amino piperidine) keto, 6 ethoxy, benzimidazole (fig.50)

Current aspect of benzimidazole derivatives

Most of the synthesized compounds exhibited good activity against the studied set of microorganisms. Since a fewer species have been used in this study, it is warranted to screen these compounds with varied species and resistant strains. All the compounds showed very good antituberculars activity even at less concentration. Hence, it is evident that the 2- Phenoxymethyl benzimidazoles are potent candidates for extensive Antitubercular studies. Researchers have been attracted toward designing of reversible, shorter, and rapid acting acid pump antagonist.

Thus, acid pump antagonists are the important future drugs for treatment of acid-peptic disorders.

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REFERENCES

[1] G.L. Gravatt, B.C. Baguley, W.R.Wilson, W.A. Denny, *J. Med. Chem.* **1994**, 37, 4338–4345.
[2] J.D. Geratz, F.M. Stevens, K.L. Polakoski, R.F. Parrish, *Arch. Biochem. Biophys*. **1979**, 197, 551–559.
[3] T.A. Fairley, R.R. Tidwell, I. Donkor, N.A. Naiman, K.A. Ohemeng, R.J. Lombardy, J.A. Bentley, M. Cory, *J. Med. Chem*. **1993**, 36 , 1746–1753.
[4] B. George, E.P. Papadopoulos, *J. Org. Chem*. **1977**, 42, 441–443.
[5] H. Fujioka, K. Murai,Y. Ohba, A. Hiramatsu,Y. Kita, *Tetrahedron Lett*. **2005**, 46, 2197-2199.
[6] S. Peddibhotla, J.J. Tepe, *Synthesis*, **2003**, 1433–1440.
[7] D.H. Huh, H. Ryu, Y.G. Kim, *Tetrahedron* , **2004**, 60, 9857–9862.
[8] J.M. Mitchell, N.S. Finney, *Tetrahedron Lett*. **2000**, 41, 8431–8434.
[9] S.L. You, J.W. Kelly, *Org. Lett*. **2004**, 6, 1681–1683.
[10] Ramya V. Shingalapur, Kallappa M. Hosamani, S. Keri, *European Journal of Medicinal Chemistry*, **2010**, 45, 1753–1759.
[11] S. Hemalatha, T. Ayyappan, S. Shanmugam, S. Nagavalli, T.S. Kurubha, *Indian Journal of Trade Knowledge*, **2006**, V, 468–470.
[12] Vijaya B Reddy, Rajeev K Singla Varadaraj Bhat G and Gautham G Shenoy, *Asian Journal of Research Chem*. **2009**, 2(2), 162-167.
[13] Kamdar, G. C.; Chavda, A. C.; Parikh, A. R. *J. Indian Chem. Soc*. **1987**, 64, 298.
[14] L.L. Kruse, D.L. Ladd, P.B. Harrsch, F.L. McCabe, S.M. Mong, L. Faucette and R. Johnson, *J. Med. Chem*. **1989**, 32, 409-417.
[15] V.L. Khairnar. S.R. Lockhande and B.G.Khadse, *Chemical Abstract*, **1981**, 95, 203.
[16] I. Wiedemann, H. Peli, H. Justus, S. Adamus, V. Brantl, H. Lohamann, Arzneim-. Forsch., *Drug Res*.**, 1985,** 35, 964-969.
[17] K. Kubo, Y. Kohara, E. Imamiya, Y. Sugiura, Y. Inada, Y. Furukawa, K.Nishikawa, T. Naka, *J. Med. Chem*. **1993**, 36, 2182-2195.
[18] V.J. Habernickel, *Drugs made in Germany*, **1992**, 35, 97.
[19] B. Can-Eke, M.O. Puskullu, E. Buyukbingol and M. Iscan, *Chemico-Biological Interactions*, **1998**, 113, 65-77.
[20] G. Ayhan-Kilcigil, C. Kus, T. Coban, B. Can-Eke and M. Iscan, *Journal of Enzyme Inhibition and Medicinal Chemistry*, **2004**, 19, 129-135.
[21] Guelguen, *Archive Pharmacol. Res*. **2004**, 27, 156-163.
[22] K. Ito, H. Kagaya, T. Fukuda, K. Yoshino and T. Nose, *Arzneim. Forsch*. **1982**, 32, 49–55.
[23] M. V. Kulkarni and V. D. Patil, *Arch. Pharm*. **1981**, 314, 440–447.
[24] Hiroyuki, Tsutomu, Nobuhide, *Chem. Pharm. Bull*. **1999**, 47(11), 1573—1578.

[25] Vitale G., Loriga M., Sanna G., Busonera B., La Colla P., Paglietti G. XVII Convegno Nazionale della Divisione di Chimica Farmaceutica della Società Chimica Italiana, Pisa, September **2004**, 6-10, P197.
[26] B.Kohl, E.Sturm, J.S.Blifinger,W.Alexander,S.V, *J. Med. Chem*., **1992**, 35, 1049-1057.
[27] S.Yamada,T.Goto , E.Shimanuki and S. Narita , *Chem. Pharm. Bull*., **1994**, 42 (3), 718—20.
[28] K.Bernhard, G.Gerhard, S.B.Joerg, O.Wolfgang, World Patent No.9501351, **(1995)**.
[29] G. Michael, S. George, S.J. Moo, US Patent No.6559167 , **(2003).**
[30] S.G. Reddy, P.P. Hegde, P.C.Ranjan, *Het. Comm*., **2005**, 11(1), 23-28.