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Research Article

Biological Activities of Substituted Benzimidazole Derivatives

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Abstract

Benzimidazole could be a heterocyclic aromatic chemical compound. It's one of the impotant pharmacophore having privileged structure in therapeutic and medicinal chemistry. It plays the most vital role with lots of helpful therapeutic activities such as: antiulcers, antihypertensives, analgesic, medication, anti-virals, antifungals, anticancers, and antihistaminics. The review of the literature shows that the benzimidazole derivatives square measure effective compound and range of reviews on the market for organic chemistry and medical specialty studies conformed that their molecules square measure helpful against a good style of micro-organisms. Due to their importance, the strategies for its synthesis became attention of artificial Organic Chemists. Thus within the gift review we have a tendency to tried to compile the chemistry numerous by product of substituted benzimidazole further as various medical specialty activities.

Keywords: Benzimidazole, Pharmacophore, Anti-viral, Anti-bacterial

Introduction

Imidazole was earlier known as glyoxalin because it firstly prepared by glyoxal and ammonia. Imidazole is known to be as azapyrrole in which nitrogen atom is separated by one carbon atom. Benzimidazole derivatives are of wide interest because of their diverse biological activity and clinical applications, they are remarkably effective compounds both with respect to their inhibitory activity and their favorable selectivity ratio (Ansari et al., 2009, Kazimierczuk et al., 2002, Grocer et al., 2002). Looking at the importance of benzimidazole and oxadiazole nucleus, it was thought that it would be worthwhile to design and synthesize some new benzimidazole derivatives bearing oxadiazole moiety and screen them for potential biological activities. We have previously reported the synthe-sis of some new biologically active benzimidazoles. Resistance to number of anti-microbial agents (β-lactam antibiotics, macrolides, quinolones, and vancomycin) among a variety of clinically signifi-cant species of bacteria is becoming increasingly important global problem. In particular, increasing drug resistance among Gram-positive a bacterium such as staphylococci, enterococci, and streptococci is a significant health matter. Benzimidazole ring displays an important heterocyclic pharmacophor in drug discovery. These compounds carrying differ-ent substituent's in the benzimidazole structure are associated with a wide range of biological activities including anti-cancer, anti-viral, anti-bacterial, anti-fungal, anti-helmintic, anti-inflammatory, anti-histaminic, proton pump inhibitor, anti-oxidant, Anti-hypertensive and anti-coagulant properties (Tuncbilek et al., 2009). In 1960, Fort et al. reported the discovery of benzimidazole derivatives as proton pump inhibitors. Further, synthesis and evaluation of different substituted benzimidazole derivatives resulted in the discovery of omeprazole, lansoprazole, rabeprazole, and pantoprazole (Patil et al., 2008).

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Chemistry of Benzimidazole

Benzimidazole is a heterocyclic aromatic organic compound. This bicyclic compound consists of the fusion of benzene and imidazole (Fig.1). The most prominent benzimidazole compound in nature is N-ribosyl-dimethylbenzimidazole, which serves as an axial ligand for cobalt in vitamin B12 (Barker et al., 1960).

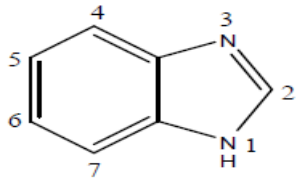


Figure 1.Structure of Benzimidazole is a heterocyclic aromatic organic

Benzimidazole, contains imidazole ring system, has been used as carbon skeletons for N-heterocyclic carbenes and its derivatives. These are often prepared by deprotonating an N, N'-disubstituted benzimidazolium salt at the 2-position in the presence of base (Jackstell et al., 2002; Huynh et al., 2005).

Benzimidazole is a white to slightly beige solid; having melts at 172 °C, boils at 360 °C. Solubility profile of benzimmidazole is slightly soluble in water, soluble in ethanol. Benzimidazole is a dicyclic compound contains imidazole ring (which containing two nitrogen atoms at nonadjacent positions) fused to benzene (Fig.2). Various derivatives of benzimidazole class are fungicides include benomyl, carbendazim, chlorfenazole, cypendazole, debacarb, fuberidazole, furophanate, mecarbinzid, rabenzazole, thiabendazole, thiophanate. Benzimidazole nucleus in some drugs acts as proton pump inhibitors and anthelmintic agents. Benzimidazole, is less basic than imidazole. Benzimidazoles display annular tautomerism in solution.

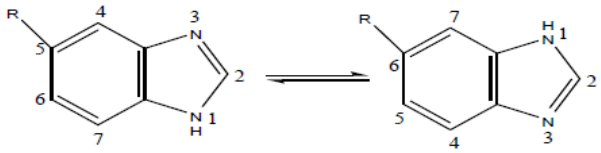


Figure 2. Structure of Benzimidazole bicyclic compound having imidazole ring

Nucleophile attacks on benzimidazoles at the 2-position. When on treatment with sodium amide in xylene, 1-alkylbenzimidazoles give the corresponding 2-amino compounds.

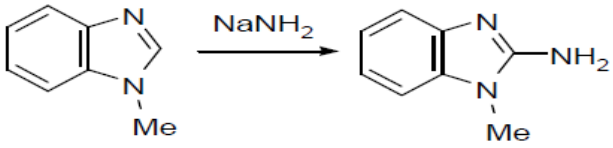


Figure 3.Structure of 1-alkylbenzimidazoles

The most convenient method for benzimidazoles is the cyclocondensation of o-phenylenediamine or substituted o-phenylenediamines with carboxylic acids or their derivatives (Fig. 4).

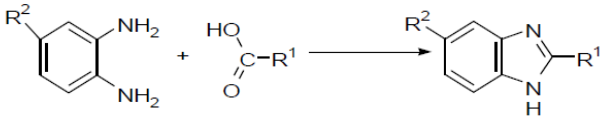


Figure 4.Structure of 2-halobenzimidazoles

Biological Profile of Benzimidazole

Anti-inflammatory

Synthesis and anti-inflammatory activity of phenyl benzimidazole (Fig.5) was reported by Leonardo et al. (Leonard et al., 2006). Compounds were screened for anti-inflammatory activity and they showed percent inhibition (22.1%, 52.2%, 54.6% and 49.6%) at 50 mg/kg each doses. By these values the compound showed maximum (54.6%) inhibition of edema at doses of 50 mg/kg.

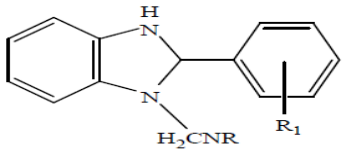
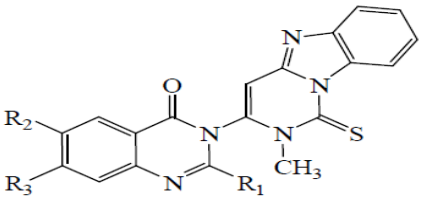


Figure 5.Structure of Phenyl benzimidazole

Diuretic

Synthesis of 3-(2-methyl-1,2-dihydropyrimido (1,2-c) benzimidazole-1-thionyl)-6,8- dibromo-2-substituted-3H-quinazolin-4-one (Fig.6) was reported by Srinivasan et al. (Srinivasan et al., 2008). Compound 2a and 2b showed moderate diuretic activity.



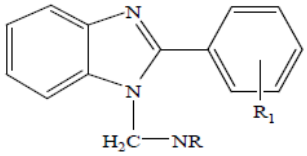
$R_1 = CH_3$, Br, $R_2 = C_6H_5$, H, R_3 = H, Br

Figure 6. Structure of 3-(2-methyl-1,2-dihydropyrimido (1,2-c)benzimidazole-1-thionyl)-6,8- dibromo-2-substituted-3H-quinazolin-4-one

Antimicrobial

Synthesis of benzimidazole as 1-(substituted-methyl)-2-(substituted-phenyl) benzimidazole (Fig.7) was reported by Leonardo et al (Leonard et al., 2006). Compounds 3a, 3b and 3c were screened for their antibacterial activity against S. aureus, B. pumillus and P. Aeurugenosa. Compound 3a showed MIC (6.25) at 100 µM/mL and exhibited good antibacterial activity. Synthesis of 2,3,4,-trisubstituted-1,2-

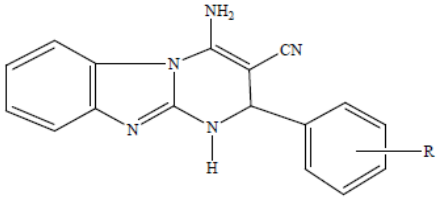
dihydropyrimido [1,2-a] benzimidazole derivatives (Fig.8) were reported by Deshmukh et al (Deshmukh et al.,2009). The compounds were tested for their fungicidal activities against Aspergillus niger MTCC-2255 and Penicillium chrysogenum-NCIM-723 using Greiseofulvin as control.



R= piperazine, dimethylamine, diethylamine

R_1= Cl

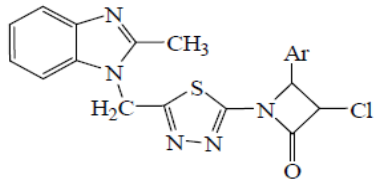
Figure 7. Structure of 1-(substituted-methyl)-2-(substituted-phenyl) benzimidazole



R = -OCH_3, -OH

Figure 8. Structure of 2,3,4,-trisubstituted-1,2-dihydropyrimido [1,2-a] benzimidazole

The efficient synthesis of novel 3-chloro-1-5-(2-methyl-1H-bezimidazol-2-yl)-4- (substituted) phenylazetidin-2-one (Fig.9) was reported by Ansari et al (Ansari and Lal, 2009). Compounds were screened for antimicrobial activity against B. substilis and E. coli and compound 5a, 5b and 5c shown MIC at 100 µg/mL, 100 µg/mL and 200 µg/mL doses.

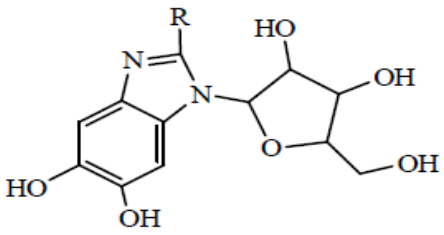


Ar = 2-C_6H_5Cl, 2-C_6H_5OH

Figure 9. Structure of 3-chloro-1-5-(2-methyl-1H-bezimidazol-2-yl)-4-phenylazetidin-2-one

Antiviral

Synthesis of 2-(benzylthio)-5, 6-dichloro-1-(β-D-ribofuranosyl)benzimidazoles (Fig.10) was reported by Devivar et al (Devivar and kawashima, 1994). Compounds 6a, 6b and 6c performed antiviral activity against HSV-1 and HCMV and compound 6c shown maximum activity at 90% inhibitory concentration (µM).

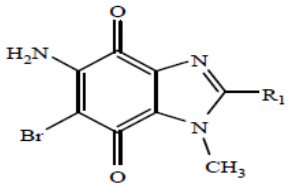


R = SCH_3, SO_2CH_3, $SO_2C_6H_5$

Figure 10.Structure of 2-(benzylthio)-5, 6-dichloro-1-(β-D-ribofuranosyl) benzimidazoles

Antitumor

Some new benzimidazole-4,7-diones substituted at 2-position (Fig.11) were synthesized and reported by Gellis et al (Gellis et al., 2008). Among compounds 7a, 7b and 7c (10µM, 8µM and 3µM), 7c performed excellent cytotoxic activity against colon (HT29), breast (T47D) and lung (A549) cancer cell lines and shown lowest IC_{50} values in µM i.e., (3µM).



R_1 = -$CH=CH_2(CH_3)_2$, -CH_2-$CH(CH_3)_2NO_2$

Figure 11. Structure of benzimidazole-4,7-diones substituted

Antiprotozoal

Synthesis and anti-protozoal activity of 2-(trifluoromethyl)-1H-benzimidazole (Fig.12) were reported by Vazquez et al (Vezquez et al., 2006). A series of 2-(triflouromethyl)-1H-benzimidazole derivatives with 5 and 6 position bio isosteric substituent (-Cl, -F, -CF3, -CN) were prepared by using short synthetic route. Analogues were tested in vitro against the protozoa Giardia intestinals and Trichomonas vaginalis compared with Albendazole and Metronidazole, have IC50 < 1 µM and compound (Fig.12), was more active than Albendazole against T. vulgaris and also showed moderate antimalarial activity against W2 and D6 strains of Plasmodium falciparum.

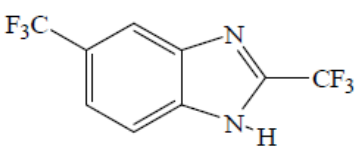


Figure 12.Structure of -(trifluoromethyl)-1H-benzimidazole

Antiulcer

Series of novel pyrimidyl-thio-methyl- benzimidazole (Fig.13) pyrimidyl-sulfinyl-methylbenzimidazole (Fig.14) were synthesized and reported by Bariwal et al (Bariwa et al., 2008). Compounds evaluated for the antiulcer activity. Compound 9 and 10 at 10 and 30 mg/kg doses reduced the ulcer formation significantly comparable to standard (Omeprazole) and 10 (sulfinyl derivative) compound was more effective than 9 (thio derivative).

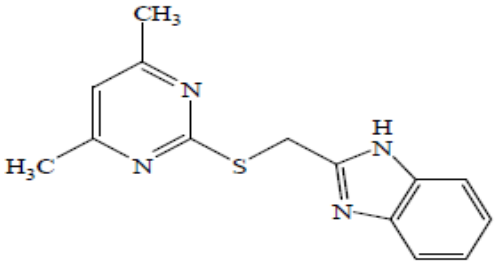


Figure 13.Structure of pyrimidyl-thio-methyl-benzimidazole

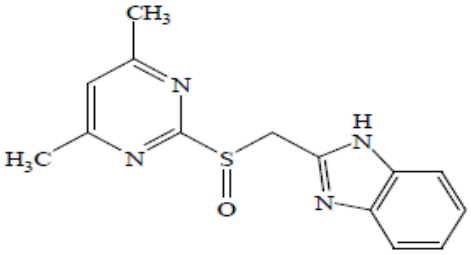
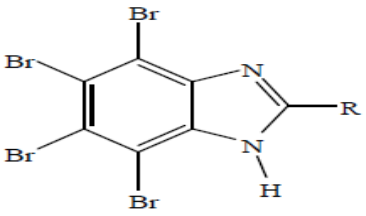


Figure 14. Structure of pyrimidyl-sulfinyl-methylbenzimidazole

Protein Kinase Ck2 Inhibitors

QSAR studies were carried out on 4,5,6,7 tetra-bromo benzimidazole (Fig.15) derivatives by Tripathi et al. (Tripathi and Mishra, 2008) and having the inhibitory activity data (IC_{50}) and the values converted in to –log IC_{50} (µM), compound 11a (0.797), 11b (0.177), 11c (0.607), by these values compound 11b shown effective inhibitory concentration.

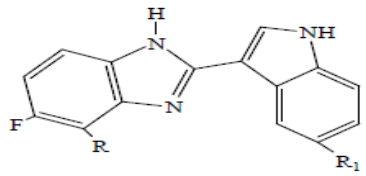


R = NH_2, Br, $NHCH_3$

Figure 15.Structure of 4,5,6,7 tetra-bromo benzimidazole

Antioxidant

Synthesis of some 6-flouro-5-substituted benzimidazole (Fig.16) were reported by Alagoz et al. (Alagoz and Coban, 2004) in which indole and 1,4,4,4-tetramethyl-1,2,3,4-tetrahydro naphthalene groups were attached to the 2-position ring and tested for antioxidant activity. Compound 12e showed strong super scavenging effect on superoxide anion at 10-3 M concentration.

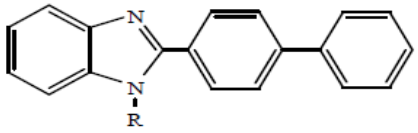


R = 4-$CH_3C_5H_{10}N$, 4-$CH_3C_5H_{10}N$, 4-$C_6H_5C_4H_9N_2$, 4-$C_6H_5C_4H_9N_2$, 4-$C_6H_5C_4H_9N_2$; R_1 = H, Br, OCH_3

Figure 16.Structure of 6-flouro-5-substituted benzimidazole

Anti-Asthmatic

Syntheses of novel and functionalized benzimidazole derivatives (Fig.17) were reported by Kumar et al (Kumar and Rao, 2006). Compounds were tested against PDE-1V for potential anti-asthmatic effect, compound 13a, 13b and 13c shown inhibitory activity (3.40%, 13.52% and 8.91%) at 1µm dose. The 13b compound showed potential anti-asthmatic activity.

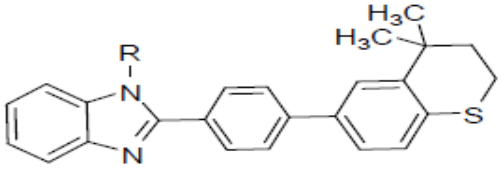


R= H, C_2H_5, $CH_2CH_2CH_3$

Figure 17.Structure of benzimidazole derivatives

Anti-Diabetic

A synthesis of a series of novel and functionalized benzimidazole derivatives (Fig.18) was reported by Kumar et al (Kumar and Rao, 2006). Compounds shown anti-diabetic activity against DPP-IV and PTP-IB. compound 14a and 14b shown inhibitory activity against PTP-IB (1.64 %, 2.42 %) at 30µM doses and 14c shown inhibitory activity against DPP-IV (3%) at 0.3 µM doses.

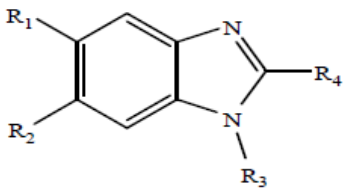


R= H, $CH_2CH_2CH_2CH_3$

Figure 18.Structure of benzimidazole derivatives

Cysticidal Activity

Synthesis of novel benzimidazole derivatives (Fig.19) were reported by Alonso et al (Alonso and Cook, 2009). Compounds 15a, 15b and 15c had shown their in vitro activity against Taenia crassiceps of WFU strain (22.6%, 9.3% and 5.0%) cysts's mortality percentage. Among three of them compound, 15c having good mortality rate.

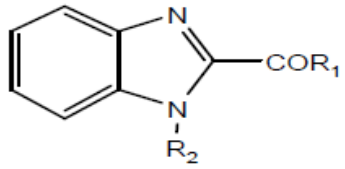


R_1 = 4-nitrobenzyl formate, 4-piperidine-carbaldehyde, -Cl
$R_2 = R_3 =$ H, $R_4 =$ $NHCOOCH_3$

Figure 19.Structure of benzimidazole derivatives having Cysticidal Activity

5-HT3 Receptor Antagonist

Synthesis of novel benzimidazole-2-carboxylic acid amides and esters (Fig.20) were reported by Orjales et al. (Orjales et al., 1999) with a quinolidine or a tropane moiety. It was evaluated for *in vitro* affinity for the 5-HT3 receptor. Synthesized compounds 16a, 16b, 16c having 5-HT3 receptor antagonist activity (12.7, 18.4, 24.4) with ED50 values of (10.6- 19.1) mg/kg i.v. among these compound 16a having higher affinity for 5-HT3 receptor.

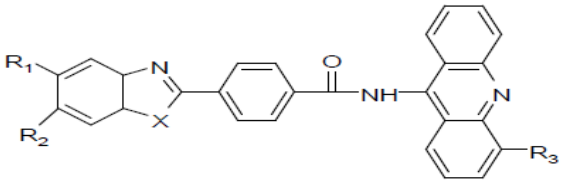


R_1= 7-methyl-7aza-bicyclo heptan-2-amine
R_2=isopropyl, benzyl

Figure 20.Structure of benzimidazole-2-carboxylic acid amides and esters

Analgesic

Syntheses of a series of N-(acridin-9-yl)-4-(benzo[d] imidazol/oxazol-2-yl) benzamides (Fig.21) have been reported by Sondhi et al (Sondhi et al., 2002). Compound containing R1 = NO2, R2 = H, R3 = H, X = NH showed significant in vitro activity against CDK-5 (IC50 = 4.6 lM) and CDK-1 (IC_{50} = 7.4 lM) and compound having R1 = Cl, R2 = H, R3 = H, X = NH showed moderate CDK-5 inhibitory activity (IC_{50} = 7.5 lM). The other compounds showed moderate anti-inflammatory and analgesic activities.

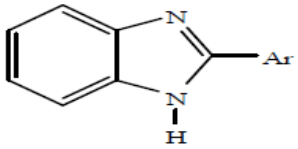


R1= Cl,NO_2,CH_3,H; R_2 = H,CH_3; R_3 = H,OCH_3;
X= NH,O

Figure 21. Structure of N-(acridin-9-yl)-4-(benzo[d] imidazol/oxazol-2-yl) benzamides

Spasmolytic

Syntheses of 2-(aryloxyaryl)-1H-benzimidazole derivatives (Fig.22) were reported by Vazquez et al (Vezquez et al., 2006). Compounds 18a, 18b and 18c showed significant antispasmodic effect in a concentration dependent manner, IC_{50} 1.94 µM, 1.19 µM and 1.8 µM, compound 18c shown potent relaxant smooth muscle activity.

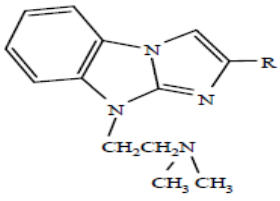


Ar = $C_6H_5COC_2H_5$, 4-OH-3-$OCH_3C_6H_5$,
2,3,4 -trimethoxybenzene

Figure 22.Structure of 2-(aryloxyaryl)-1H-benzimidazole derivatives

Hypotensive

Synthesis of 9-dialkylaminomethyl-2-oxy(dioxy) phenylimidazo[1,2-a] benzimidazole (Fig.23) was reported by Anisimova et al (Anisimova et al., 2006). Compounds 19a, 19b and 19c possessed hypotensive activity (ED_{50}: 2.8 mg/kg, 0.8 mg/kg, 0.13 mg/kg) ,(LD_{50}: 121.0 mg/kg, 182 mg/kg, 143 mg/kg) and (LD_{50}/ED_{50}: 43.2, 227.5, 1100), the most active compound out of these was 19c exceeded the reference drugs (Dibazole and Apressin) (ED_{50}: 22.1, 4.0) with respect to both the degree of the hypotensive action (ED_{50}) and the conditional therapeutic index (LD_{50}/ED_{50}).



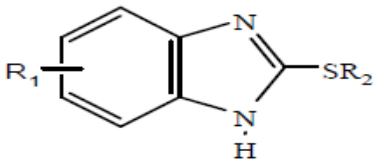
R= 1-4 dihydroxymethylbenzene,
1-3 dihydroxymethylbenzene,

Figure 23.Structure of 9-dialkylaminomethyl-2-oxy(dioxy)phenylimidazo[1,2-a] benzimidazole

Antimycobacterial

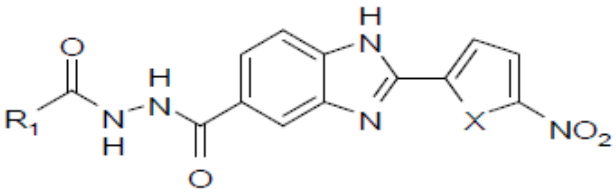
Synthesis of substituted 2-polyfluroalkyl and 2-nitrobenzyl sufanyl benzimiazole (Fig.24) were reported by Kazimierczuk et al (Kazimierczuk et al., 2005). Compounds were evaluated for their activity against mycobacterium strains and compounds which showed appreciable antimycobacterial activity compound 20a, 20b and 20c shown their MIC values 2 µmol L-1, 2 µmol L-1 and 4 µmol L-1.

Camacho et al. (Camacho et al., 2011) synthesised a series of N'-substituted-2-(5-nitrofuran or 5- nitrothiophe-2-yl)-3H-benzo[d]-imidazole-5-carbohydrazide derivatives (Fig.25) and investigated for their abilities to inhibit β-hematin formation, hemoglobin hydrolysis and in vivo for their antimalarial efficacy in rodent Plasmodium berghei. Selected analogues were screened for their antitubercular activity against sensitive MTB H37Rv and multidrug-resistant MDR-MTB strains, and cytotoxic activity against a panel of human tumor cell lines and two nontumorogenic cell lines.



R_1= Cl, Br
R_2= methylnitrobenzene, C_4F_9

Figure 24.Structure of 2-polyfluroalkyl and 2-nitrobenzyl sufanyl benzimiazole

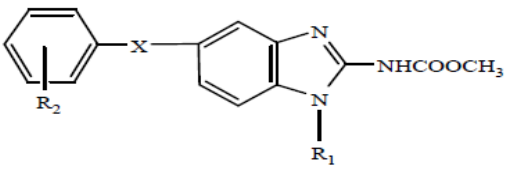


R_1 = H, Ar; X = O,S

Figure 25.Structure of 5- nitrothiophe-2-yl)-3H-benzo[d]-imidazole-5-carbohydrazide derivatives

Anthelmintic

Synthesis of 2-benzimidazole carbamic acid methyl ester derivatives (Fig.26) were reported by Solominova et al (Solominova et al., 2004). Compounds 22a and 22b shown anthelmintic activity against Nippostrongilus, Ankilostoma and Haemonhus larvae that exceeded 65% upon per oral administration in animals (rats, sheep, dogs) at a dose of 2.5-50 mg/kg. In another group of animal inhibition action is below 40% upon per oral administration in a dose of 50-100 mg/kg.

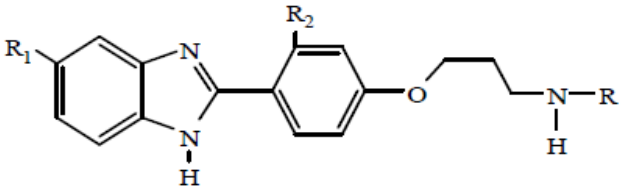


R_1= C O O CH_2CH_2 OCH_3, C O NH CH_2CH_2C O O C H_3
R_2= H, X= S

Figure 26.Structure of 2-benzimidazole carbamic acid methyl ester derivatives

Histamine H4-Receptor Antagonist

Synthesis of 2-arylbenzimidazole derivatives (Fig.27) were reported by Dutra et al. (Dutra et al., 2006) and found to bind with high affinity to the human histamine H4 receptor. Compounds 23a, 23b and 23c shown their antihistaminic activity, among three of them 23a showed moderate affinity for H4 receptor (Ki = 124 nM) and others (Ki = 65, 95)

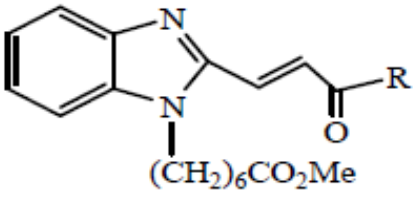


R = methylpiperazine, dimethylpyrrolidin-3-amine, 1-5diazocanemethylamine; R_1= Cl

Figure 27.Structure of 2-arylbenzimidazole derivatives

Prostaglandin Analogs

Syntheses of 2-(1-2-methylene-3-methylene-3-hydroxyoctyl)-N-(6-methoxy carbonylhexyl) benzimidazole (Fig.28) derivatives were reported by Bespalov et al (Bespolov et al., 1998). Synthesized compounds 24a and 24b shown comparable results with F2α prostaglandin preparation Enzaprost and spasmogenic action of these compounds significantly lower (4-6 times) than Enzaprost.

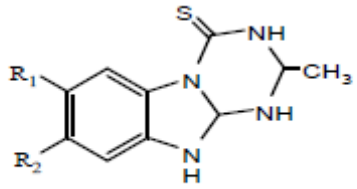


R= cyclopropylheptan-1-ol, cyclopropylheptan-1-one

Figure 28.Structure of 2-(1-2-methylene-3-methylene-3-hydroxyoctyl)-N-(6-methoxy carbonylhexyl) benzimidazole

Anti-Amoebic

Synthesis of pyrimido [1,6-a]benzimidazole derivatives (Fig.29) were reported by Sondhi et al (Sondhi et al., 2006). Compounds 25a and 25b were carried out in-vitro against E. histolytica and IC50 values obtained (1.82 µM, 2.62 µM) compared with the reference drug Metronidazole had 50% inhibitory concentration (IC_{50}) of 1.22 µM and the best IC_{50} value shown by 25a compound.

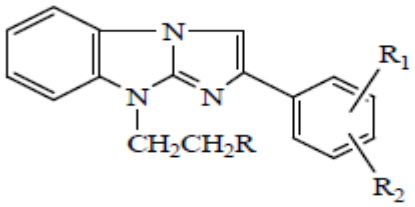


R_1= CH_3,COOH, R_2= CH_3, H

Figure 29.Structure of pyrimido [1,6-a]benzimidazole derivatives

Antiarrhythmic

Syntheses of 9-dialkylaminoethyl-2-oxy (dioxy) phenylimidazo [1,2-a] benzimidazole derivatives (Fig.30) were reported by Anisimova et al (Anisimova et al., 2006). Compounds exhibited the antiarrhythmic activity. Compound 26a, 26b and 26c were evaluated the activity in minimum effective concentration (MIC mole/L) 2.9×10-4m/L, 2.3×10-4 m/L, 2.1×10-4 m/L with reference to Quinidine (3.1×10-4 m/L). Hence the 26a MIC value was close to the reference drug. Concentrations but the values showed no significant result.

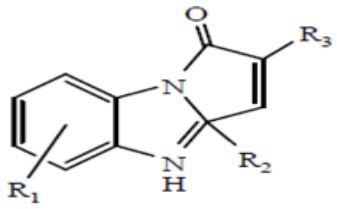


R= diethylamine, ethoxyethylethanamine
R_1= OH, R_2= H

Figure 30.Structure of 9-dialkylaminoethyl-2-oxy (dioxy) phenylimidazo [1,2-a] benzimidazole

Anticonvulsant

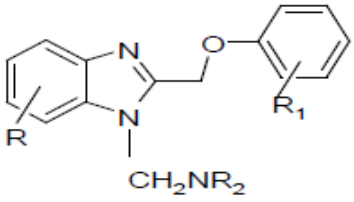
In this synthesis of novel 1H-pyrrolo (1,2-a)benzimidazole-1-one derivative (Fig.31) were reported by Chimrri et al (Chimrri et al., 2010). Compounds 27a, 27b and 27c showed (84 %, 67% and 69 %) by maximal electroshock method, at dose level 25 mg/kg orally. The compound 27a showed maximum anticonvulsant activity.



R_1= Cl, F, H, R_2= C_6H_5,CH_3, R_3= H

Figure 31.Structure of 1H-pyrrolo (1,2-a)benzimidazole-1-one derivative

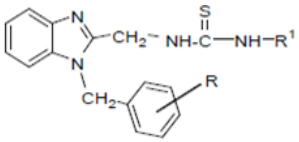
Shukla et al. (Shukla et al., 1982) synthesized a series of 1-heterocyclic amino/iminomethyl-2- substituted benzimidazoles (Fig.32) and were screened for their neuropharmacological and monoamine-oxidase inhibitory properties. A number of such compounds showed CNS stimulant, anticonvulsant and mono amine oxidase inhibitory activities.



R = H,Cl,F; R_1= H,CH_3,C_2H_5;
R_2 = H, C_6H_5

Figure 32.Structure of 1-heterocyclic amino/ iminomethyl-2- substituted benzimidazoles

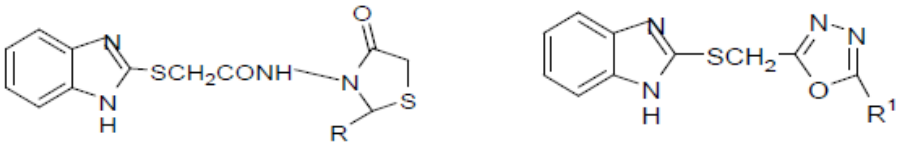
Siddiqui et al. (Siddiqui and Alam, 2010) synthesized a number of new 1-[(1-(2-substituted benzyl)-1H-benzo[d] imidazol-2-yl) methyl]-3-arylthioureas compounds (Fig.33). All the newly synthesized compounds were screened for their anticonvulsant activity in ip MES and sc PTZ model and were compared with the standard drug phenytoin. Majority of the compounds exhibited significant activity against both the animal models however compounds 29g, 29l and 29o displayed promising activity.



R = H, Cl ; R^1 = C_6H_5, 2-CH_3.C_6H_5, 3-CH_3.C_6H_5, 4-CH_3.C_6H_5, 2-OCH_3.C_6H_5, 3-OCH_3.C_6H_5, 4-OCH_3.C_6H_5,

Figure 33.Structure of 1-[(1-(2-substituted benzyl)-1H-benzo[d]imidazol-2-yl) methyl]-3-arylthioureas compounds

In seeking broad spectrum pharmacological activities of benzimidazole derivatives, a group of 4-thiazolidinones (**Fig.34**) and 1,3,4-oxadiazoles (Fig.34) containing 2-mercapto benzimidazole moiety were synthesized by Shingalapur et al. (Shingalapur et al., 2010) and screened for *in vivo* anticonvulsant activity by Maximal Electroshock (MES) model and antidiabetic activity using Oral Glucose Tolerance Test (OGTT). Compounds 30c, 30d, 30g and 30i exhibited potent anticonvulsant results and 31c, 31d, 31h and 31i showed excellent antidiabetic activities and also pharmacophore derived from active molecules suggested that presence of –OH group was a common feature in all active compounds. In DNA cleavage studies, compound 31d cleaved DNA completely as no trace of DNA was found. On the other hand, a sharp streak was found for compounds 30c, 31a and 31d.



$R = C_6H_5$, 4-C_6H_5Cl, 2-C_6H_5OH, 4-C_6H_5OH, 4-$C_6H_5CH_3$, 4-$C_6H_5OCH_3$;
$R^1 = C_6H_5$, 4-C_6H_6Cl, 2-C_6H_5OH, 4-C_6H_5OH, 3-C_6H_5OH, 4-$C_6H_5CH_3$, 4-$C_6H_5OCH_3$

Figure 34.Structure of benzimidazole derivatives, a group of 4-thiazolidinones and 1,3,4-oxadiazoles

Conclusion

The new classes of reviewed substituted benzimidazole have a wide variety of biological activities. The 1-(substituted-methyl)-2-(substituted-phenyl) benzimidazole has good antibacterial and antifungal activities respectively. The significant anticancer activities are shown by 7 benzimidazole-4,7-diones substituted at 2-position. The antiprotozoal activities shown by 2-(trifluoromethyl)-1H-benzimidazole derivatives, the antiulcer property shown by pyrimidyl-thio-methyl- benzimidazole . However the antioxidant effect shown by 6-flouro-5-substituted benzimidazole and the N-(acridin-9-yl)-4-(benzo[d]imidazol/oxazol-2-yl) benzamides derivatives shows analgesic effect. The anti-Amoebic effect shown by pyrimido [1,6-a]benzimidazole derivatives, but they are associated with some drawbacks like side effect, toxicity. So for minimizing these drawbacks there are need to synthesize some new chemical compounds with better results.

Conflict of Interest: None

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