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Some Approved Medicines containing Benzimidazole Moiety: A Mini Review

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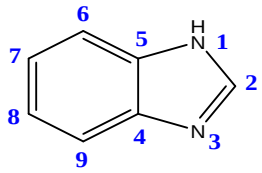
Abstract: Benzimidazole derivatives are of wide interest because of their presence in numerous categories of medicinal drugs; such as anticancer, anticoagulants, antihypertensives, anti-inflammatory, antimicrobials, antiparasites, antivirals, antioxidants, immunomodulators, proton pump inhibitors, hormone modulators, CNS stimulants as well as depressants, lipid level modulators, antidiabetics etc., makes it a moiety of great importance in medicinal chemistry. Because of this great importance, it attracts the researchers to synthesize more effective benzimidazole derivatives for several biological activity screening.
Keywords: Benzimidazole; moiety ; medicinal drugs; antiparasites ; biological activity;

I. INTRODUCTION

The benzo derivative of imidazole is referred to as benzimidazole.[1] Although benzimidazole is the commonest name of the parent compound of the series, other names such as benzimidazole and 1,3-benzodiazole are often used.



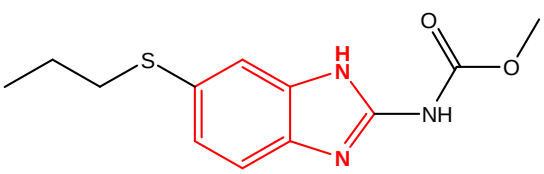
In 1872, Hoebrecker synthesized benzimidazole first time as 2, 5- or 2, 6-dimethylbenzimidazole (tautomers) through reduction of 2-nitro-4-methylacetanilide in presence of Sn/HCl reducing agent.[2] After Hoebrecker, in 1875 Ladenburg extensively explored the benzimidazole synthesis by condensation between O-amino aniline and carbonyl compounds (aldehyde and ketone) and others by using.[3]. Subsequently, Phillips explored Ladenburg synthesis to the condensation between O-amino aniline and carboxylic acids (acetic acid). Hence the synthesis reaction of benzimidazole from O-amino aniline is known as Ladenburg synthesis or Phillips synthesis or Ladenburg – Phillips synthesis. [4]

Active involvement of benzimidazole nucleus reported in various therapeutic agents like antiparasitics, anticonvulsants, analgesics (Etonitazene), antihistaminics (astemizole), antihelmintics (albendazole, mebendazole, thiabendazole), antiulcers, antihypertensives (candesarten cilexitil, telmisartan), antiviral (enviradine), anticancers, antifungals (Benomyl, Carbendazim), anti-inflammatory agents, proton pump inhibitors (omeprazole, lansoprazole, pantoprazole) and anticoagulants. [5] In this review letter, some approved medicines will be discussed.

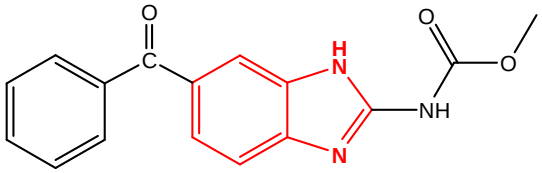
A. Some Benzimidazole Drugs

Albendazole (albendazolum) [CAS Number- 54965-21-8] is used for various parasitic worm infections. It is useful for giardiasis, trichuriasis, filariasis, neurocysticercosis, hydatid disease, pinworm disease, and ascariasis, among others. It is taken by mouth. [6]

Mebendazole (MBZ) (CAS Number- 31431-39-7) is a medication used to treat a number of parasitic worm infestations. This includes ascariasis, pinworm disease, hookworm infections, guinea worm infections, hydatid disease, and giardia, among others. It is taken by mouth. [7]



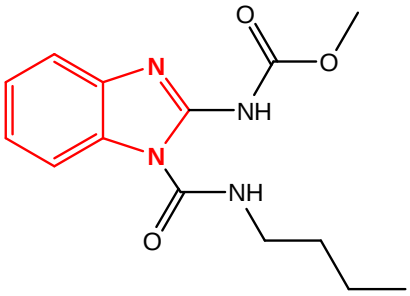
Albendazole



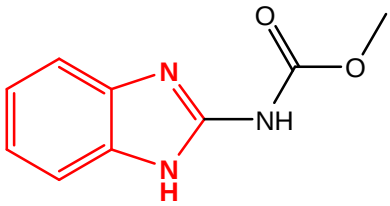
Mebendazole

Triclabendazole (brand name Egaten)(CAS Number- 68786-66-3) is a medication used to treat liver flukes, specifically fascioliasis and paragonimiasis. It is very effective for both conditions. Treatment in hospital may be required. It is taken by mouth with typically one or two doses being required.[8]

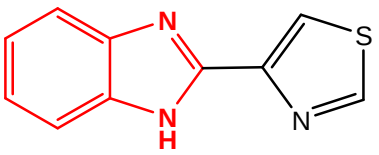
Benzimidazole fungicides are a class of fungicides including benomyl, carbendazim (MBC), thiophanatemethyl, thiabendazole and fuberidazole. They can control many ascomycetes and basidiomycetes, but not oomycetes. They are applied to cereals, fruits, vegetables and vines, and are also used in postharvest handling of crops.[9]



Benomyl

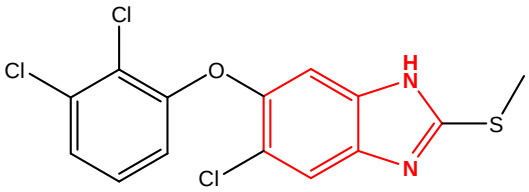


Carbendazim

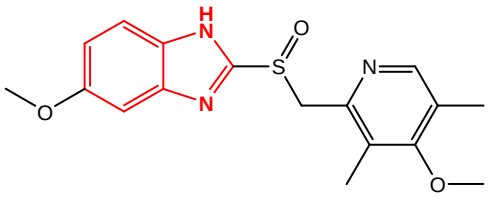


Thiabendazole

Proton-pump inhibitors (PPIs) are a group of medications whose main action is a pronounced and long-lasting reduction of stomach acid production. Within the class of medications, there is no clear evidence that one agent works better than another. PPIs are among the most widely sold medications in the world, and the first one, omeprazole, is on the World Health Organization's List of Essential Medicines, the safest and most effective medicines needed in a health system. [10]



Triclabendazole

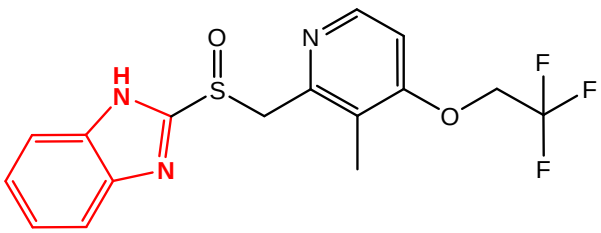


Omeprazole

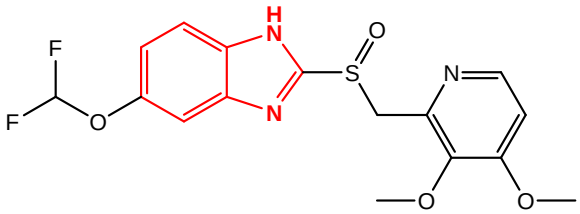
Omeprazole (brand names Prilosec and Losec) (CAS Number: 73590-58-6) is a medication used in the treatment of gastroesophageal reflux disease, peptic ulcer disease, and Zollinger–Ellison syndrome. It is also used to prevent upper gastrointestinal bleeding in people who are at high risk. Omeprazole is a proton-pump inhibitor (PPI) and its effectiveness is similar to other PPIs. It can be taken by mouth or by injection into a vein. [11,12,13]

Lansoprazole (brand name Prevacid) (CAS Number: 103577-45-3) is a medication which reduces stomach acid. It is used to treat peptic ulcer disease, gastroesophageal reflux disease, and Zollinger–Ellison syndrome. Effectiveness is similar to other proton pump inhibitors (PPIs). It is taken by mouth. Onset is over a few hours and effects last up to a couple of days. [14,15]

Pantoprazole (brand name Protonix) (CAS Number: 102625-70-7) is a medication used for the treatment of stomach ulcers, short-term treatment of erosive esophagitis due to gastroesophageal reflux disease (GERD), maintenance of healing of erosive esophagitis, and pathological hypersecretory conditions including Zollinger–Ellison syndrome. It may also be used along with other medications to eliminate *Helicobacter pylori*. Effectiveness is similar to other proton pump inhibitors (PPIs). It is available by mouth and by injection into a vein. [16,17]



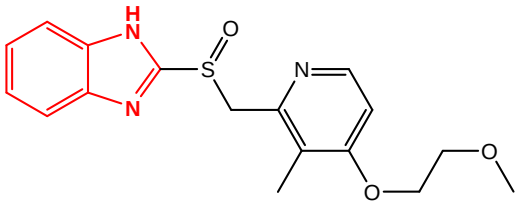
Lansoprazole



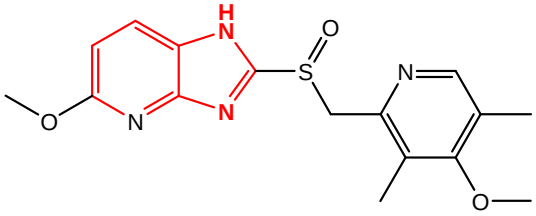
Pantoprazole

Rabeprazole (brand name Pariet) (CAS Number:117976-89-3) is a medication that decreases stomach acid. It is used to treat peptic ulcer disease, gastroesophageal reflux disease, and excess stomach acid production such as in Zollinger–Ellison syndrome. It may also be used in combination with other medications to treat *Helicobacter pylori*. Effectiveness is similar to other proton pump inhibitors (PPIs). It is taken by mouth.[18,19]

Tenatoprazole (113712-98-4) is a proton pump inhibitor drug candidate that was undergoing clinical testing as a potential treatment for reflux oesophagitis and peptic ulcer as far back as 2003. The compound was invented by Mitsubishi Tanabe Pharma and was licensed to Negma Laboratories (part of Wockhardt as of 2007).[20,21]



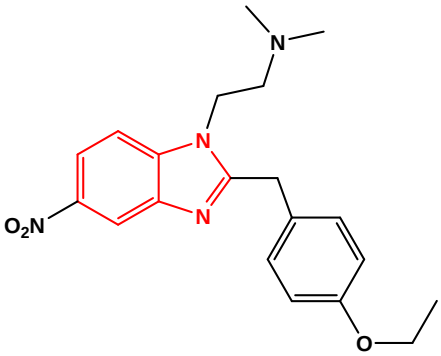
Rabeprazole



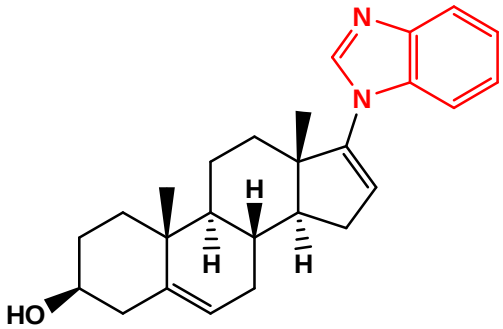
Tenatoprazole

Etonitazene (CAS Number: 911-65-9) is a potent analgesic drug first reported in 1957 which has been shown to have approximately 1000–1500 times the potency of morphine in animal models, but only 60 times in man. It is one of several benzimidazole opioids, and is structurally related to clonitazene (where the *p*-ethoxybenzyl group is replaced by a p-chlorobenzyl group; however, clonitazene itself has only 3 times the potency of morphine).[22]

Galeterone (developmental code names TOK-001, VN/124-1) (CAS Number: 851983-85-2) is a steroidal antiandrogen which was under development by Tokai Pharmaceuticals for the treatment of prostate cancer. It possesses a unique dual mechanism of action, acting as both an androgen receptor antagonist and a CYP17A1 inhibitor, the latter of which prevents the biosynthesis of androgens. As a CYP17A1 inhibitor, galeterone shows selectivity for 17,20-lyase over 17α-hydroxylase. [23,24,25]



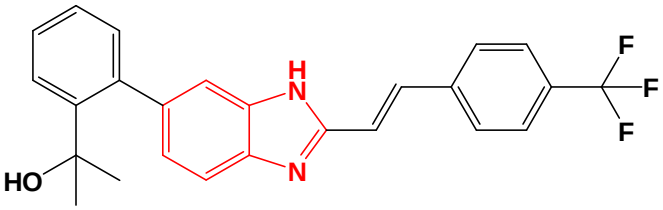
Etonitazene



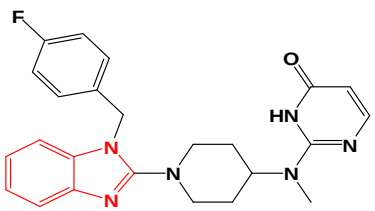
Galeterone

Mavatrep (JNJ-39439335) (CAS Number: 956275-94-5) is a TRPV1 receptor selective competitive antagonist. It is an investigational analgesic that may be a potential treatment for analgesia and/or inflammation. Phase I trials have been completed in healthy Japanese and Caucasian volunteers. Potential common adverse effects include thermohypoesthesia, chills, feeling cold, and feeling hot.[26]

Mizolastine (Mizollen) (CAS Number:108612-45-9) is a once-daily, non-sedating antihistamine. It blocks H_1 receptors and is commonly fast-acting. It does not prevent the actual release of histamine from mast cells, it just prevents it binding to receptors. Side effects can include dry mouth and throat.

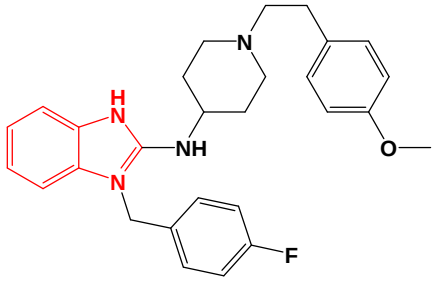


Mavatrep



Mizolastine

Astemizole (brand name Hismanal, developmental code R43512) (CAS Number: 68844-77-9) was a second-generation antihistamine drug that has a long duration of action. Astemizole was discovered by Janssen Pharmaceutica in 1977. It has been withdrawn from the market in most countries because of rare but potentially fatal side effects (QTc interval prolongation and related arrhythmias due to hERG channel blockade).[27]



II. CONCLUSION

These drugs reveal the importance of benzimidazole moiety, and motivates towards research for further design and development of new drugs containing benzimidazole unit. It's also a point of study & research development that which position on benzimidazole ring is important for substation with which particular substituent.

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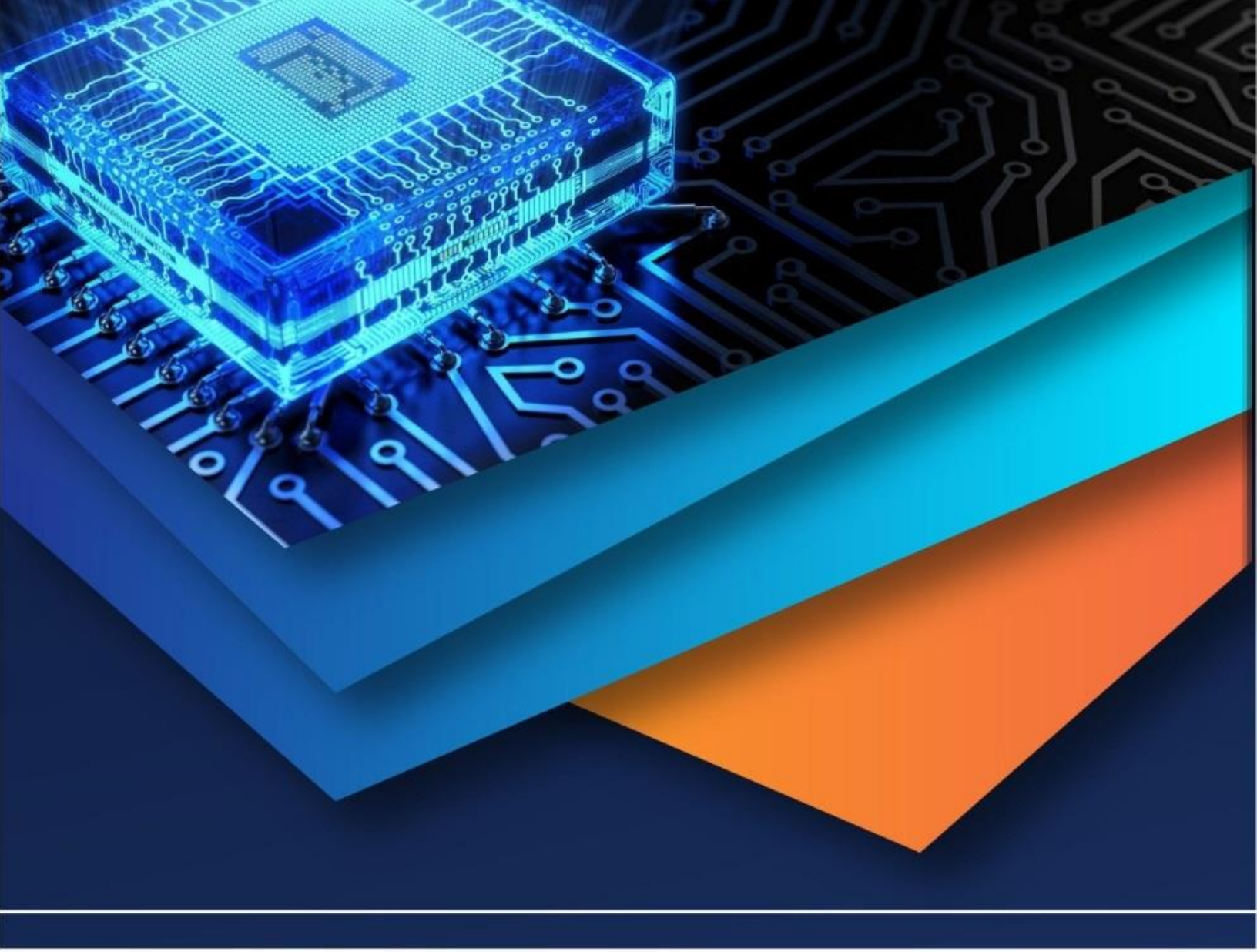

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