A Brief Review of The Biological Activities of Benzimidazole Derivatives

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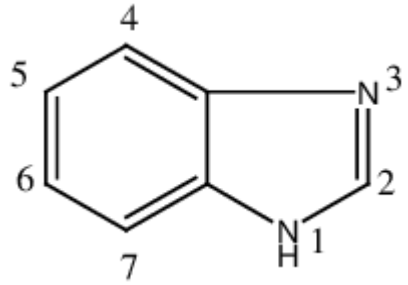
Abstract- *Benzimidazole derivatives are important in the medical profession. Because of their numerous pharmacological properties, including their antibacterial, anthelmintic, antiviral, antidiabetic and anticancer properties. In the world of modern medicinal chemistry, benzimidazole a fused hetero cycle containing both benzene and imidazole has drawn a lot of intrest. Benzimidazole is a valuable tool in the medicinal chemistry and drug development because of its numerous pharmacological properties. It is an essential component in the search for new therapeutic medicines. The purpose of this paper is to present the work that has been done on the chemistry and pharmacological activity of benzimidazole derivative in previous years.*

Keywords- Benzimidazole, antibacterial, antifungal, anthelmintic activity.

I. INTRODUCTION

Benzimidazole is a specific kind of heterocyclic aromatic coumpound.In medicinal chemistry, it is a privileged structure and a significant pharmacophore. The coumpound is bicyclic in nature arising from the combination of imidazole and benzene. There is a popular variety these days that has numuerous pharmacological qualities. Hobecker created the first benzimidazole derivative in 1872. The 1943 study by Goodman and Nancy Hart on the pharmacological characteristics of benzimidazole. Then, in 1944, Woolley reported on the antibacterial properties of certain benzimidazole derivatives. Following the hydrolysis of vitamin B-12 by acid. In 1949, 5, 6 -dimethyl benzimidazole was reported as degradation product by Norman GB and Karl Folker. After extensive investigation, it was determined that the biological activity of benzimidazole against the variety of pathogens and physical disorders made it an important heterocyclic system. Therapeutic agents such as antiviral, anticancer, anthelmintics, antiinflammatory, analgesic, antihistaminic, antiparasitic, anticonvulsant, antiulcer, antihypertensive, antifungal, proton pump inhibitors and anticonvulsants, among others, actively involve benzimidazole derivatives. Since they have a wide range of biological activities and clinical applications, benzimidazole derivatives are highly effective compounds in terms of both their inhibitory activity and overall potency.

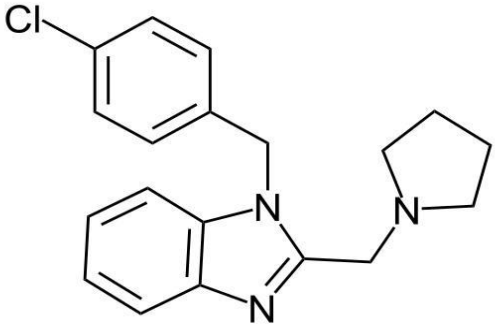


Benzimidazole

BIOLOGICAL ACTIVITY OF BENZIMIDAZOLE:

ANTIBACTERIAL ACTIVITY:

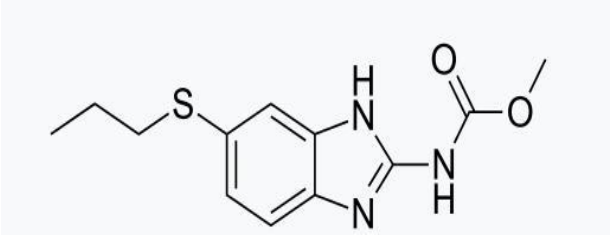
[(1)]The development of novel classes of antibacterial agents attracted a lot of interest due to the rise in bacterial resistance. A survey of literature reveals that 2-substituted benzimidazole derivatives are pharmacologically more strong , thus a promising field of study would be the creation and synthesis of 2-substituted benzimidazoles. This class of drugs known to be present in some used antibacterial medications, including furacillin, furazolidine and ftivazide. Hydrazone have drawn in lot of interest and been the subject of numerous studies in the past few years because of their potential as chemotherapeutics in the creation of new antimicrobial agents. Methicillin-resistant S. aureus and S. aureus with 1,2-disubstituted 1H-benzimidazole-N alkylated-5-carboxamidine derivatives are among the highly effective antibacterial compound.



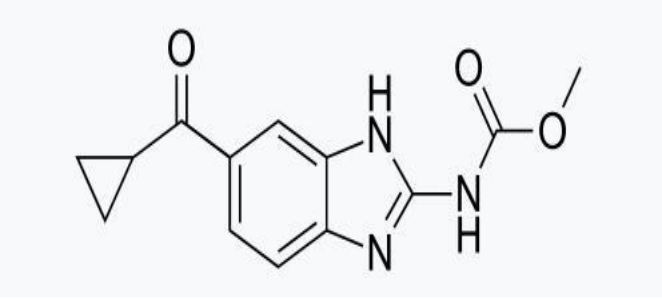
Clemizole peniciline

ANTHELMINTIC ACTIVITY:

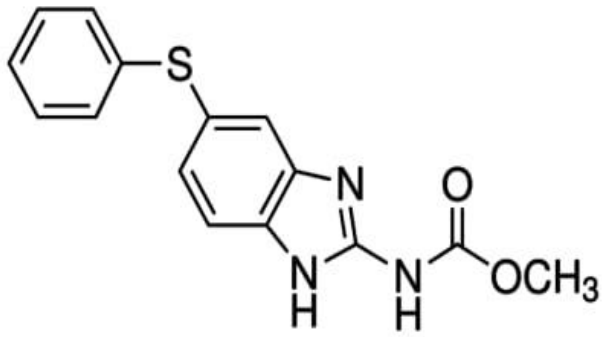
[20]Numerous benzimidazole including, albendazole, cyclobendazole, fenbendazole, flubendazole, mebendazole, oxibendazole, oxfendazole, thiabendazole, have been developed and are available as anthelmintic agents. A series of 5-nitro benzimidazole derivatives were synthesized by Faruk et al, and the anthelmintic activity against the adult Indian earth warm P.posthuma, Faruk et al, prepared the compounds. Preliminary biological experiments revealed that every chemical had a notable anthelmintic effect. The synthesis of a llibrary of 2-substituted benzimidazoles and an assessment of the anthelmintic efficacy against the adult earthworm E. fetida were reported by Vilasrao et al. Out of them, compounds demonstrated outstanding anthelmintic properties that are on par with those of regular albendazole. Created benzimidazole derivatives through the condensation of and O-phenylenediamine, then examined to determine the anthelmintic properties. The anthelmintic activity of all the compounds was significantly higher than t hat of piperazine citrate standard.



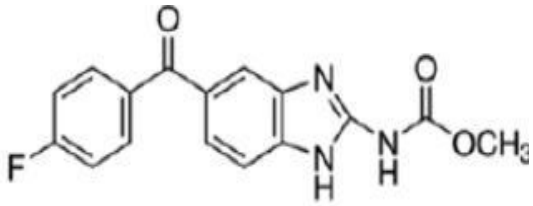
Albendazole



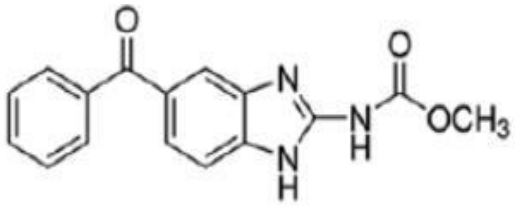
Cyclobandazole



Fenbendazole



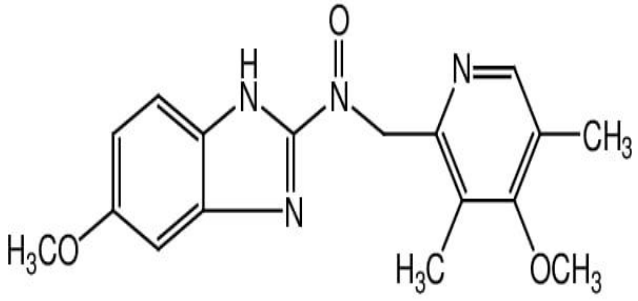
Flubendazole



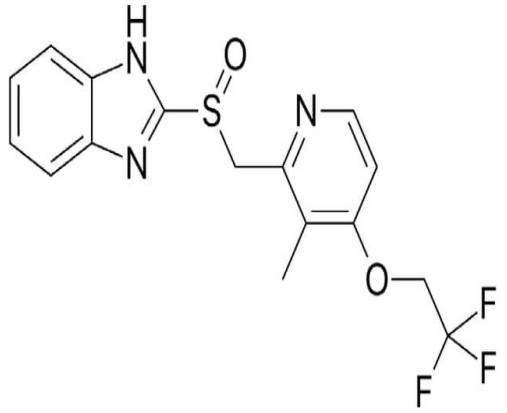
Mebendazole

ANTIULCER ACTIVITY:

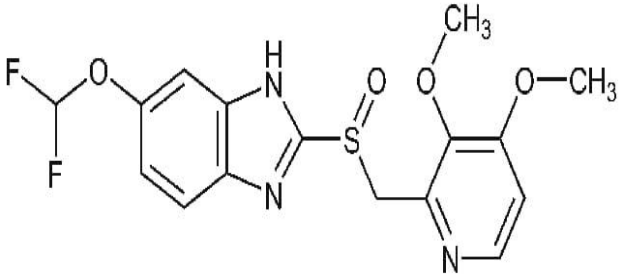
[3]Numerous derivatives of benzimidazoles have demonstrated antiulcer activity and have the potential to inhibit $H^{+/}$ K^{+} ATPase.[4] Because of the clinical importance of these medications in the treatment of peptic ulcers and other gastrointestinal disorders, new, significant and potent compounds have been developed, making benzimidazole more selective for proton pump inhibitors. [5]Good antiulcer activity was produced in 1991 by synthesizing benzimidazole derivatives by derivatizing benzimidazole at its N-H by an electron-donating group and substituting it with a long chain of propyl acetamido-thio, thiazole-amino and tetramethyl piperidine on pyridine. [6]The well-known antiulcer drugs with benzimidazole nucleus include omeprazole (racemic mixture), lansoprazole, rabeprazole, pantoprazole, and esomeprazole (absolute (S) configuration). Omeprazole works best when taken in enteric-coated capsules; otherwise, the medication will be broken down in the stomach's acidic area. Omeprazole's biological activity and chemical stability seem to be related to the way the benzimidazole ring's N-H substituent behaves and changes into sulfonamide.



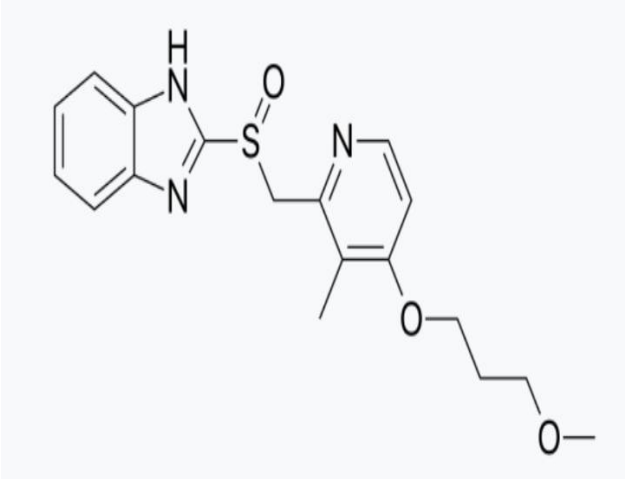
Omeprazole



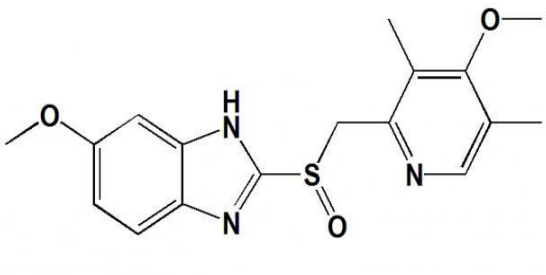
Lansoprazole



Pantoprazole



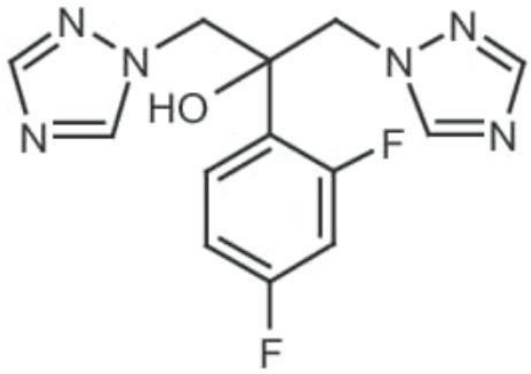
Rabeprazole



Esomeprazole

ANTIFUNGAL ACTIVITY:

[7] Over the past few decades, infectious diseases have posted a serious and growing threat to human health. A wide range of pathogens are becoming susceptible to anti-microbial agents currently in use, and resistance to multiple drugs is becoming more common in several microorganisms, particularly in gram positive bacteria and certain untreatable fungi. Their inhibitory qualities with relation to model fungi have been widely used. In particular, it is important to highlight that fluconazole, the first-line triazole antifungal medication recommend by world health organization (WHO), has a remarkable therapeutic record for treating Candida infection and as emerged as the treatment of choice for infections caused by Cryptococcus neoformas and Candida albicans because of its strong activity, good safety record, have advantageous pharmacokinetic properties. Fluconazole is not fungicidal, however, and it is inactive against invasive aspergillosis. Furthermore, widespread clinical use of fluconazole has led to an increases is isolates of C. albicans that are resistant to the drugs.



Fluconazole

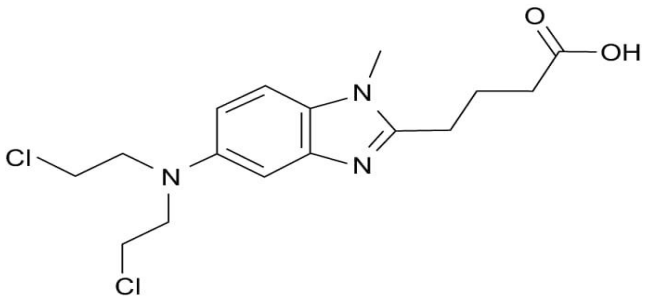
ANTIMALARIAL ACTIVITY:

[8]Every year, malaria results in 350-500 million clinical episodes and over one million death; in sub-Saharan Africa, children under the age of five account for the majority of these deaths. Malaria ranks fifth globally in terms of infectious disease-related deaths (tuberculosis, respiratory infection, HIV\AIDS and diarrheal diseases). According to the recent estimates, 3.3 billion people in 109 countries reside in areas where malaria is a risk. Malaria not only have a negative impact on the health but also severely damage the economics of endemic nations and feeds the poverty cycle that many people live in. The 1980s saw a rise in malaria mortality and morbidity as a result of several factors, including the development of humanitarian crisis situations in many

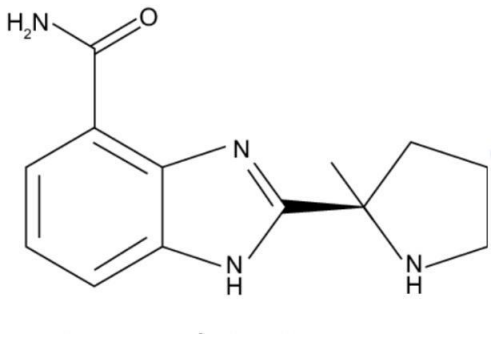
malaria-endemic areas, the weakening of traditional malaria control programs the rapid decentralization and integration into failing primary health services, and the increase in parasite and vector resistant to current anti-malarial drugs and insecticides.

ANTICANCER ACTIVITY :

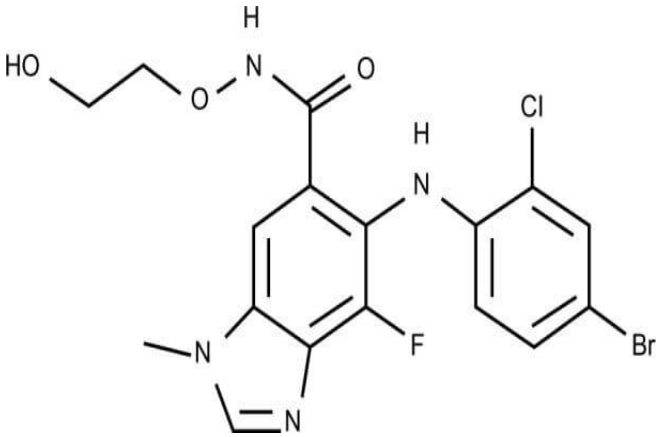
[9] As the second greatest cause of death in the US, cancer is a dangerous global public health issue.[10] 119% A class of diseases is known as cancer is defined by the unchecked development and spread of abnormal cells that have the potential to spread to other body parts. Death may result if the spread is not stopped. [11,12]Benzimidazole is one of the nitrogen-containing heterocyclic ring systems that are used to treat various types of cancer. [13]Examples of these drugs are bendamustine, which is used is to treat chronic lymphocytic leukaemia (CLL); [14]veliparbib is an anti-cancer PARP inhibitor, [15]selumetinb, an ATP-independent inhibitor nitrogen-activated protein kinase (MEK or MAPK/ERK kinase) 1 and 2; [16]galeterone, a steroidal anti-androgen, is used to treat prostate cancer; and [17]nocodazole, a synthetic tubulin-binding agent, which causes microtubule dynamics to be disrupted and prevents mitosis in tumor cells. Scientists are working to develop novel and more effective anti-cancer agents in an effort to overcome adverse toxicity, drug resistance and anti-cancer type based specificity. The benzimidazole pharmacophore is linked to potent anticancer activity, making it a promising template for the development of novel anticancer leads. The development of 2-substituted benzimidazoles as drug leads, such as 2-aryland 2-heteroaryl benzimidazoles, has received a lot of attention in current research. Additionally, it has been reported that 2-substituted bisbenzimidazoles exhibit remarkable cytotoxicity against a variety of additionally, cancer cell lines as well.

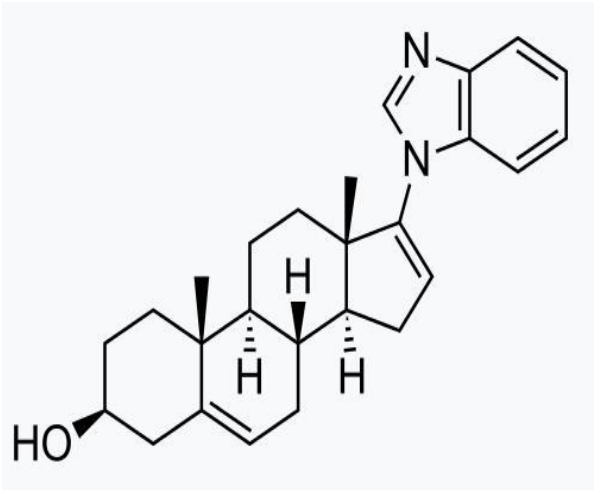


Bendamustine

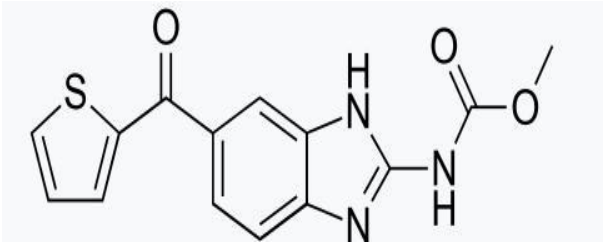


Valiparib





Galeterone



Nocodazole

ANTIPROTOZOAL ACTIVITY:

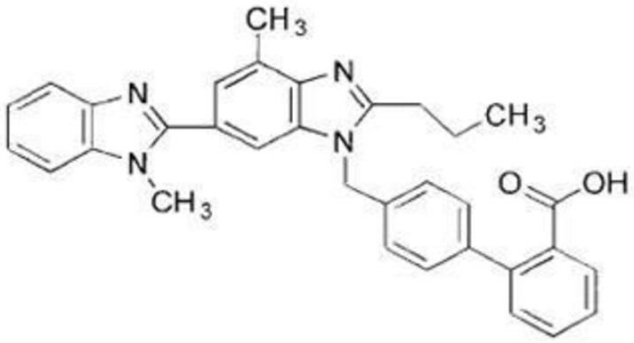
[18] There are also been reports of 5,6 dinitro and thioalkyl or thioaryl substituted compounds as benzimidazoles derivatives according to reports, these active ingredients are effective against Stenotrophomonas malhophillia. These substances work against both gram-positive and gram-negative bacteria bacteria in a manner similar to metronidazole. There have been reports to substituted 2-trifluorobenzimidazoles. [19]It has previously documented anti-giardial activity. [20,21]In a different study, a subustituted 1,2-phenylenediamine and trifluoroacetic acid are cyclocondensed by Phillips to create a series of 2-(trifluorometry0-1H-Benzimidazole derivatives. The compounds demonstrated nanomolar activities against some of the aforementioned protozoa,[22] including Giardia intestinalis, Entamoebe histolytica, Trichomonas vaginalis and Leishmania Mexicana, when tested in nematode Trichinella spiralis both in vitro and in vivo.

ANTIVIRAL ACTIVITY:

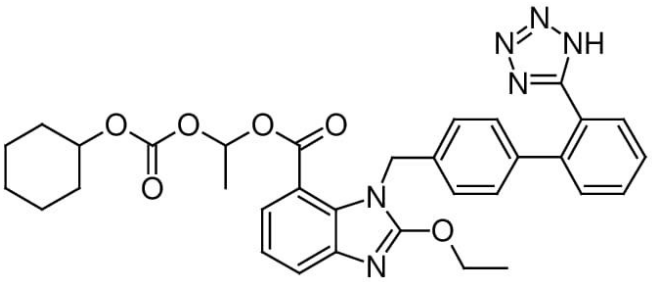
According to research, benzimidazoles have antiviral properties against Enterivirus, [23]Picornaovirus and [24]Poliovirus. Additionally, N-substituted benzimidszoles have activity against the [25]Tobacco Mosaic virus. [26]Preparing benzimidazole heterocycles with an amidino substituent at the C-5 position was another method that was mentioned. In a published study, a number of novel benzimidazole derivatives were created synthesized and tested in VERO cells for their ability to inhibit four different enterovirus. The compound that showed the greatest promise was (L)-2-(pyridin-2-yl)-N-(4-nitrophenyl)pentan-3yl)1H-benzimidazole-4-carboxamide, possessing an exceptional selectivity index and strong antiviral potency.

ANTIHYPERTENSIVE ACTIVITY:

[27]Compared to earlier related drugs, biphenylbenzimidazoles exhibit a stronger antihypertensive effect because they are more radily available when taken orally. Additionally, the 2-position of the biphenyl is critical for the activity. It has been reported that 41.5 substituted aryl or alkyl carboxamido derivatives exhibit antagonistic activity against the Angiotensin-II AT1 receptor, making them effective antihypertensive agents.



Telmesartan



Candesartan

II. CONCLUSION

On significant pharmacophore in contemporary drug discovery is the benzimidazole. The synthesis of benzimidazole derivatives has drawn more and more attention as a potential source of novel antimicrobial agents. The derivatives of benzimidazoles are useful for medical research. Numerous studies have revealed that heterocycles and substituted benzimidazoles, which are nucleotides structural isosteres and enable easy interaction with biopolymers, have pharmacological activity and lower toxicities. Currently, scientisties are drawn to creating more powerful benzimidazole derivatives with a broad range of biological activity.

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