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Benzimidazole Derivatives and Its Biological Importance

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Abstract

Benzimidazole is a special type of molecule made from benzene and imidazole, containing various elements like nitrogen, oxygen, and sulfur. It's important because it has a wide range of uses in medicine and other areas. Benzimidazole and its derivatives are known for their ability to do many things, like fighting microbes, viruses, and cancer, as well as having anti-inflammatory and other helpful effects. People are always trying to make new benzimidazole compounds for different purposes, especially in medicine. These compounds can have a positive impact on our health and well-being.

Keywords: Benzimidazole, Anticancer activity, Antiviral activity, Antibacterial activity.

INTRODUCTION

A heterocyclic aromatic organic chemical is benzimidazole. This bicyclic substance is created when imidazole and benzene combine. It is effects in the body, like fighting off microbes, providing antioxidant properties, helping combat cancer, managing diabetes, dealing with parasites, and more. These compounds have diverse biological activities and can be used in various ways to treat different health conditions Benzimidazoles have various important uses. They can inhibit smooth muscle fiber propagation, potentially treat urinary tract infections, and function as antineoplastic agents in cancer treatment [1]. Additionally, they can act as thyroid receptor agonists, gonadotropin-releasing hormone In the 1950s, scientists got really interested in something called the benzimidazole ring. They found that this ring is a part of vitamin B12, which is super important for our bodies. This got them thinking that benzimidazole might be useful for treating diseases caused by parasites. One important discovery in this area was a drug called thiabendazole, which was found in 1951. This discovery motivated chemists and researchers to look more into benzimidazole and its potential for helping people with parasitic diseases [2].

Benzimidazole-based compounds are interesting because they have a wide range of different receptor antagonists, and non-nucleoside HIV-1 reverse transcriptase inhibitors. Some benzimidazole derivatives may also modulate metabotropic glutamate receptors, making them valuable in different areas of chemistry and medicine [3]. In this review, we're going to talk about the latest ways to make imidazole, benzimidazole, and similar compounds. We'll also discuss how these compounds can be used to fight against bacteria, fungi, viruses.

HISTORY OF BENZIMIDAZOLE

One important discovery in this area was a drug called thiabendazole, which was found in 1951. This discovery motivated chemists and researchers to look more into benzimidazole and its potential for helping people with parasitic diseases &Benzimidazole is a heterocyclic aromatic organic compound. Its history dates back to the early 20th century, with the first synthesis reported in 1903 by the German chemist Emil Fischer. It gained prominence in the pharmaceutical industry due to its diverse biological activities and therapeutic potential. Over the years, various derivatives of benzimidazole have been synthesized and studied for their pharmacological properties, leading to the development of numerous drugs targeting different medical conditions. These include anti-parasitic agents, anti-ulcer drugs, antifungal medications, and several other therapeutic agents [4,5]. Researchers continue to explore the diverse applications of benzimidazole derivatives in medicinal chemistry and drug development.

Benzimidazole structure and properties

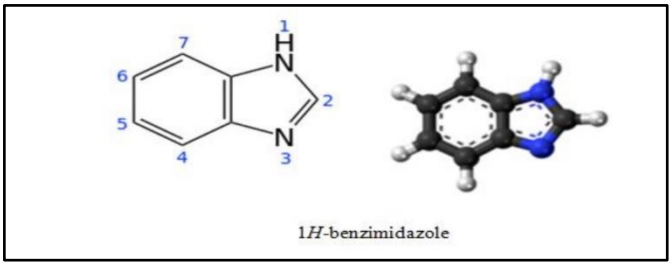

Figure 1: General Structure of Benzimidazole

Table 1: Chemical Properties of Benzimidazole

Chemical formula	$C_7H_6N_2$
Molar mass	118.139 g·mol^{-1}
Melting point	170 to 172 °C (338 to 342 °F; 443 to 445 K)
Acidity (pK_a)	12.8 (for benzimidazole) and 5.6 (for the conjugate acid)

SYNTHESIS OF BENIMDAZOLE

1) Benz imidazoles obtained from natural sources

Studying natural substances is essential for finding new compounds that can be used as models for creating new drugs. One important group of compounds is benzimidazoles, which are found in nature and have various uses [6,7]. Vitamin B12 contains a molecule with a benzimidazole core, which has sparked interest in this area of research. Some natural compounds, like (+)-CC-1065 and (+)-duocarmycin SA, have strong effects on cells and were discovered in bacteria. They can interact with DNA. Another example is makaluvamines, which were found in a type of sponge in Fiji. These compounds can kill certain types of cells and affect DNA in a test tube [8]. These natural compounds have unique structures that are interesting to scientists and can have potential uses in medicine

2) Imidazole and Imidazole N-Oxide

The synthesis of imidazole and imidazole N-oxide derivatives has been thoroughly reviewed. There are many ways to make imidazole derivatives, but only a few have widespread use. Here, innovative methods for creating highly functionalized imidazole derivatives and raising reaction yields are discussed. A method has recently been discovered for producing multikilogram quantities of 2,4-disubstituted imidazole's. These compounds were produced with high yield by condensing amidines and a-halo ketones.

From the perspective of medicinal chemistry, it is also crucial to swiftly generate imidazole's with a variety of functionalities. The imidazole has since been successfully synthesized using methods such solid-phase synthesis, one-pot synthesis, and microwave-assisted chemistry [4].

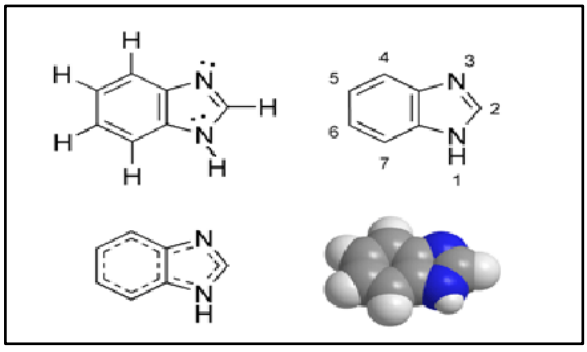

Figure 2: Structure of benzimidazole

BIOLOGICAL ACTIVITIES

1) Antiulcer Activity

This is important in managing conditions like peptic ulcers and related digestive problems. Scientists have been working to create even better compounds to make these drugs more effective for treating these issues. In 1991, they made some new benzimidazole versions with different chemical changes, and these showed promise in treating ulcers. Omeprazole (racemic mixture) 59, lansoprazole 60, rabeprazole 61, pantoprazole 62 and esomeprazole (absolute (S) configuration) 63 are the well-known antiulcer agents having benzimidazole nucleus. Kosaka have synthesized compounds with substitution of dimethyl imidazopyridine at 6-position of benzimidazole showing strong antisecretory activity. Introduction of rigid ring with benzimidazole and their conversion to biological active sulfonamide in acidic media has been verified by Yamada et al. in 1994. Yamada have substituted pyridine by triazole 3-yl, 1,3-dithiane and reported promising results when biologically evaluated against H. pylori. Other approach was also applied to reduce the basicity of ring nitrogen of pyridine and to reduce the irreversibility of compound with enzyme by using pyrimidine as ring substituent by Hiroshi in 1995. Ung et al. have reported the synthesis of leminiprazole by replacing pyridine with phenylisobutylmethylamine in 1996 which shows potent proton pump inhibitory activity. have replaced pyridine by 2,2-dimethyl pyrranopyridine ring. Jain et al. have synthesized 2-dimethylaminothiazo cyclobenzene benzimidazole showed good proton pump inhibitory activity. have replaced pyridine with pyrrolobenzimidazolyl moiety, which showed proton pump inhibitory activity. Yong et al. have synthesized esomeprazole by asymmetric oxidation of parochial sulphide of omeprazole which showed potent antiulcer activity [5].

2) Anticancer Activity:

Cancer is a major health issue that affects a large portion of the global population. Anticancer agents, also known as antitumor, antiproliferative, and antineoplastic agents, are drugs designed to treat different types of cancer by working in various ways to hinder the growth and spread of cancer cells. One significant problem with these anticancer drugs is that they can harm normal, healthy cells in addition to their intended effect on cancer cells. This unintended damage to healthy cells is known as cytotoxicity, and it's a major drawback of many anticancer treatments, leading to side effects that can be quite severe. Certainly! In simple terms, the information you provided is talking about different chemical compounds and their activities, mainly in the context of their effects on enzymes and cells. Here's a simplified summary: Compound 111 has a ketone group and maintains its activity when introduced Compound 112, which has a methyl ester substitution, is effective at killing Taxol-resistant HL60/TX1000 cells. An indolepyridoimidazole compound is very potent, about 10 times more effective than similar compounds. A 3,4-methylenedioxy analog is a strong inhibitor of FTase, a specific enzyme, and is highly selective for this enzyme over others. It's also orally bioavailable in rats. Compounds with an ether linkage are effective Ftase inhibitors, with the highest selectivity seen in compound 113. It's potent, selective, and has reasonable bioavailability. These compounds are being studied for their potential in various medical or scientific applications [5].

3) Antimicrobial Activity

Certainly! In simpler terms, researchers have been working on creating new medicines from a particular chemical called benzimidazole. These medicines can fight different types of germs like bacteria, fungi, and so on. They've tested various compounds and found that some of them work well against these germs. This research is important for developing new drugs to combat infections [2].

4) Miscellaneous Activities

Certainly! In simple terms, Bayer Yakuhin has been creating different types of chemical compounds that belong to a group called benzimidazoles. These compounds are designed to affect certain

hormones in the body, particularly ones related to reproduction. Some of these compounds have shown the ability to counteract the effects of specific hormones that play a role in the reproductive system. This research is significant because it might lead to the development of new drugs that could help regulate or control certain aspects of fertility and reproduction in both men and women. Certainly! In simple terms, scientists have created some new substances by adding different small structures to a particular chemical template. Among these, two compounds, 238 and 239, have been found to be effective in the lab when tested on a specific receptor. They showed good results, with compound 238 having an IC_{50} value of 7 nanometers (nM) and compound 239 having an IC_{50} value of 18 nM. This means they were able to inhibit the target receptor at very low concentrations. Compound 244 is a man-made chemical with a change in its structure. It has been found to effectively block the activity of Rho kinase at very low doses, but it doesn't affect other protein kinases until much higher doses are used [5].

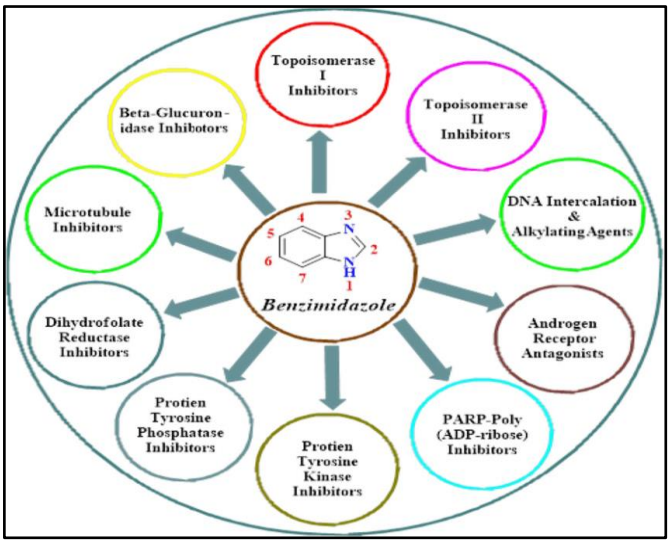

Figure 3: Different targets of benzimidazole as anticancer agents

CONCLUSION

In simple terms, this review shows that the Benz imidazole nucleus is a crucial part of many important medical compounds. These compounds are used to treat various diseases, including cancer, viruses, high blood pressure, and more. Scientists are working on creating even better versions of these compounds for more effective treatments.

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Conflict of Interest

None declared.

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