Benzimidazole: A Versatile & Multifunctional Scaffold

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Opinion

Benzimidazole is one of the oldest known nitrogen heterocycles. It is a bicyclic ring made up by fusion of benzene to 4, 5 position of imidazole and also known as benzoglyoxaline or benziminazole. It was first synthesized by Hoebrecker and afterward by Ladenberg and Wundt during 1872–1878. [1–3] and received attention since 1950s. [4-7] Heterocycles play an essential role in the field of organic and medicinal or pharmaceutical chemistry. Especially, nitrogen heterocycles display a broad range of biological activities because of similarities with many naturally occurring products such as α-amino acid histidine, purine, histamine, and biotin. These are useful scaffolds for the development of drug and active pharmaceutical ingredients (API). Such molecules can easily interact with biomolecules within the living systems because of the structural similarity and show their desired effects. [8]. Substituted benzimidazole derivatives have been used in various applications of biological interest such as anticancer agents, analgesic agents, antiulcer, and anthelmintic, anti-inflammatory, antibacterial, antifungal, antioxidant, anti-HIV, antitubercular, anticonvulsant, antileishmanial, antidiabetic, antimalarial, antihistaminic agents, topoisomerase I inhibitors [9], angiotensin II inhibitors [10], selective neuropeptide Y1 receptor antagonists [10], inhibitors of HCMV replication [11], dipeptidyl peptidase IV inhibitors [12] and inhibitors of the hepatitis C virus RNA polymerase. [13] Moreover, some benzimidazole derivatives exhibited significant activity against RNA [14], herpes (HSV-1) [15], human cytomegalovirus (HCMV) [16], and influenza. [17] There is a very long list of benzimidazole derivatives which are actively used in pharmaceutical industry and some of them are mentioned here as omeprazole (**1**), triclabendazole (**2**), pimobendan (**3**), oxfendazole (**4**), flubendazole (**5**), mebendazole (**6**), fenbendazole (**7**), albendazole (**8**), parbendazole (**9**), oxibendazole (**10**), luxabendazole (**11**), thiabendazole (**12**) and cambendazole (**13**). (Figure 1) There are various effective anticancer drugs which are used to treat several types of cancers, eg. Nocodazole, bendamustine, veliparp and carbendazim.

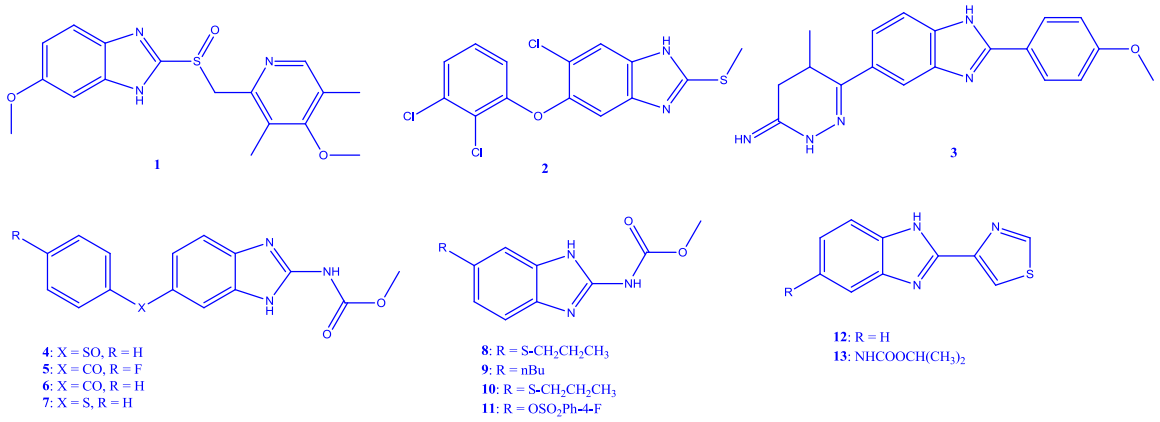

Figure 1. Some bioactive benzimidazole containing drugs.

Alzheimer's disease is a neurodegenerative disorder of the brain characterized by progressive neurodegeneration, memory loss, impairment in cognition and ultimately leading to death of the patient [18]. To tackle with this disease, it is important to design new multitarget drugs for Alzheimer's disease rather than single-target drugs. A. S. Alpan et al. reported the synthesis of Mannich bases of benzimidazole derivatives having phenolic group and evaluated for their possible *in vitro* antioxidant and AChE/BuChE inhibitory potentials. [19] Te-Mao Li et al. reported the synthesis of novel benzimidazole derivative, which induced cell apoptosis in human chondrosarcoma tumor cells. [20] Ju-Fang Liu et al. studied the anticancer effects of a new benzimidazole derivative, 2-(furanyl)-5-(piperidinyl)-(3,4,5-trimethoxybenzyl)benzimidazole which also induced

apoptosis in human chondrosarcoma cell lines (SW1353 and JJ012) and thus may prove a potential anticancer agent for the treatment of this bone tumor. [21] A. Rathore et al. synthesized new benzimidazole derivatives endowed with oxadiazole and investigated for selective cyclooxygenase (COX-2) inhibitor activity. [22] Therefore, the benzimidazole nucleus has gained attention to synthetic organic chemists for the synthesis of various bioactive compounds.

In addition of displaying a wide array of pharmaceutical properties, benzimidazole moiety has great potential of showing some other diverse properties as well such as bioimaging, water sorption, gas sorption, and electrochemical properties. Transition metal ions are essential for the normal growth and fundamental physiological processes within the body in trace quantity. But when they are taken in excess amount, they may prove fatal for the organism. For instance, excess Cu^{2+} ion concentration in the body can cause neurodegenerative diseases such as Alzheimer, Menkes, and Parkinson. [23] Hence, their detection in the living systems at lower concentration becomes very important. Several techniques such as atomic absorption spectrometry, coupled plasma atomic emission spectrometry and electrochemical method has been used to detect the metal ions [24], but they are associated with some limitations like on-site detection. Now a days, fluorescent chemosensors, mainly synthesized from benzimidazole moiety, are utilized to detect the metal ions due to their high sensitivity and selectivity, fast response, on-site monitoring, and lower cost. [25] The transition metal complexes derived from benzimidazole have also been observed to exhibit catalytic activity in various transformations. In this context, B. Cetinkaya et al. synthesized Rhodium complexes of benzimidazole and investigated the catalytic activity in the intramolecular cyclization of (*Z*)-3-methylpent-2-en-4-yn-1-ol into 2,3-dimethylfuran in good yield**.** [26] Water-soluble benzimidazole containing ionic palladium(II) complex have also been reported for rapid microwave-assisted Suzuki reaction of aryl chlorides. [27] The polyamides containing a benzimidazole moiety were reported to exhibit the water sorption properties. [28] The probe made from benzimidazole derivative can also detect water at trace level as impurity in organic solvents by colorimetric and fluorescence method. [29] Y. Cui et al. reported the gas sorption properties of porous benzimidazole-linked polymers possessing excellent applications of gas storage. [30] Similarly, R. Muhammad also synthesized an imine and benzimidazole functionalized nanoporous polymer which had good selectivity of CO_2 over N_2. [31] Benzimidazole derivatives have also been shown physical, optical and electrochemical properties e.g. the electrochemical studies of myoglobin were carried out by using benzimidazole modified silver electrode [32] and fabrication of OLED devices. [33]

Therefore, I must say that benzimidazole is an established multifunctional scaffold with their vast biological applications. The author of this article keeps engaged in drug research and has published various papers on antibacterial, antifungal, and anticancer drug discovery. The continuous R & D in the field of synthesis and pharmacological activity of benzimidazole derivatives is continuously going on. Hence, the researchers are constantly putting their endeavours to find out more effective drugs derived from benzimidazole, but their efforts are still to go miles for wellness and betterment of human life.

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