Chapter 3
Imidazothiazole: Different Synthetic Approach and their Anticancer Activity

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ABSTRACT

Recent research on cancer therapy has revealed that the emergence of malignant cells is caused by several enzyme alterations. such include kinase inhibitors of ErB4 (HER4), B-Raf kinase, and indoleamine 2,3-dioxygenase 1 (IDO1). Researchers discovered that drugs based on imidazothiazoles, and their analogues exhibit more robust anticancer action by inhibiting these enzymatic receptors. In recent times, imidazothiazole scaffold is broadly explored for its anticancer activity, which acts through various mechanisms such as EGFR, B-RAF, DHFR kinase inhibition and tubulin polymerization inhibition and other molecular mechanisms of action. Due to their feasible synthetic accessibility and promising pharmacological profile, it has attracted various medicinal chemists to explore and develop imidazothiazole derivatives as potent and safe anticancer agents. In the present book chapter, we have reviewed various potent imidazothiazole scaffold-based derivatives reported as anticancer agents, their synthetic strategies, with their future perspective.

1. INTRODUCTION

Organic molecules known as heterocyclic compounds have at least one carbon atom and at least one extra heteroatom, such as N, O, or S. All living cells' metabolism depends on heterocyclic molecules, and most of these nitrogen-containing, five-membered fused heterocyclic molecules have biological function (Jaiswal,

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2019, pp. 36-39). The fused heterocyclic compounds are one of the most important systems in medicine because of their wide range of biological activity. In the field of medicine, imidazothiazole is a crucial molecule. The fused heterocyclic molecule with a bridgehead nitrogen and sulfur atom that is physiologically active. It is made up of a five-membered thiazole ring and an imidazole ring. The imidazole is found in many synthetic and natural materials. (Shaik et al.,2017)

Imidazole is a planar five-membered ring **(Figure 1, Compd. 1)** (Guo et al.,2023) with two meta-nitrogen atoms at the first and third positions. Furthermore, since the unshared electron pair of the 1-position nitrogen atom in the structure participates in the cyclic conjugation, the electron's density decreases. A wide range of pharmacological properties is often exhibited by compounds containing imidazole rings, including antibacterial (Jaiswal & Dwivedi, 2017; Salahb et al.,2018; Senkardes et al.,2020), antifungal (Slassi et al.,2020), anticonvulsant (Jakovleva et al.,2020), antioxidant (Abdelhamid et al.,2020), anticancer (Bae et al.,2018), and antiparasitic (Adeyemi et al.,2020) properties. It has been shown that only substituents at the N- of the imidazole ring are tolerated without loss of activity in terms of druggability for the investigation of various N-substituted imidazole inhibitors of p38 mitogen-activated protein kinases, and appropriate substituents (Margutti & Laufer,2007). Furthermore, it has been documented that the compound's free nitrogen within the imidazole ring may initiate water-mediated associations with both the Arg85 side chain and the OH-4 of Globo H's GlcNAc moiety (Lal et al.,2021). Thiazole is also the five-membered, heterocyclic compound that contains nitrogen having smell like pyridine **(Figure 1, Compd. 2)**. Its chemical composition consists of one N-atom and one S-atom.

Figure 1. Imidazole and thiazole

Thiazole, meantime, serves as a crucial building block for a variety of synthetic molecules. Thiazole molecules have a wide range of biological functions and may adhere to different targets in the microbe, such as enzymes or receptors. Thiazole and bis-thiazole derivatives have been shown to have a wide range of biological actions (Borcea et al.,2021), including analgesic (Thore et al.,2013), antioxidant (Liu et al.,2021), anticancer (Wan et al.,2021; Gomha, 2017), anti-inflammatory (Pricopie et al.,2020), antibacterial (Liaras et al.,2011), and cardioprotective (Drapak