



## BENZOTHAZOLE DERIVATIVES: EXPLORING MULTIFACETED BIOLOGICAL ACTIVITIES FOR THERAPEUTIC INNOVATIONS

**Ragini Jaiswal\***

Assistant Professor, Lucknow University Institute of Pharmaceutical Sciences, Lucknow University (U.P.).



\*Corresponding Author: Ragini Jaiswal

Assistant Professor, Lucknow University Institute of Pharmaceutical Sciences, Lucknow University (U.P.).

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### ABSTRACT

The review highlights benzothiazoles as a versatile class of organic compounds with significant bioactive and industrial relevance. Known for their diverse pharmacological properties, including antimicrobial and anti-inflammatory activities, benzothiazoles<sup>[1]</sup> also demonstrate efficacy in anthelmintic, antidiabetic, anti-tubercular, antiulcer, anti-tumor, antioxidant, analgesic, acaricidal, schistosomicidal, antileishmanial, antipsychotic, anti-convulsant, local anesthetic, anti-parkinsons, anti-parasitic, diuretic, and plant growth regulator applications.<sup>[5-6]</sup> This unique review article focuses on the distinctive contributions of benzothiazoles to the realms of anti-inflammatory and antimicrobial activities, providing a comprehensive exploration of their multifaceted biological impacts.<sup>[8]</sup>

**KEYWORDS:** Benzothiazole, Antimicrobial, Antifungal, Anti-inflammatory.

### INTRODUCTION

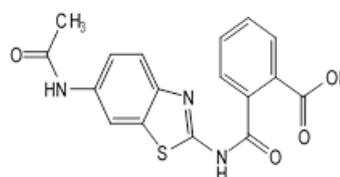
The investigation of heterocyclic molecules in the context of medicinal chemistry has been a captivating area of study, encompassing both chemical and biological aspects.<sup>[9]</sup> A heterocyclic compound is defined as a chemical compound that has a cyclic structure including a minimum of two distinct heteroatoms within the ring. The most prevalent heteroatoms include nitrogen, oxygen, and sulphur. Heterocyclic compounds exhibit a ubiquitous presence in the natural world and play crucial roles in sustaining life through several mechanisms. Benzothiazoles are a class of fused bicyclic compounds that consist of a thiazole heterocycle. The basic structure of thiazole and several pharmacologically and physiologically active chemicals is composed of sulphur and nitrogen atoms.<sup>[10-11]</sup>

During the 1950s, there was a significant focus on the extensive investigation of several 2-aminobenzothiazoles as potent central muscle relaxants. Subsequently,<sup>[12]</sup> biologists became interested in this series following the discovery of the pharmacological profile of Riluzole (6-trifluoromethoxy-2-benzothiazolamines, Rilutek), which acts as an inhibitor of Glutamate neurotransmission. Subsequently, benzothiazole derivatives have undergone comprehensive investigation,<sup>[13]</sup> revealing their wide-ranging chemical reactivity and expansive range of action. Despite their long-standing recognition for their biological activity, the many biological characteristics of these entities continue to be a subject of significant scientific intrigue.<sup>[14-15]</sup>

Furthermore, the benzothiazole ring can be found in a variety of natural substances derived from marine or terrestrial sources, exhibiting valuable biological features. In recent years, there have been reports indicating that benzothiazole, along with its bioisosters and derivatives, exhibit antimicrobial properties against various microorganisms, including Gram-negative and Gram-positive bacteria, as well as the yeast *Candida albicans*. Notably, these compounds have demonstrated significant antimicrobial activity against specific strains such as *Enterobacter*, *Pseudomonas aeruginosa*, *Escherichia coli*, and *Staphylococcus epidermidis*.<sup>[16-17]</sup>

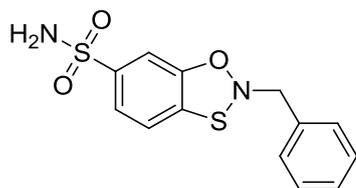
### "Benzothiazole Moiety: A Dual Role as Potent Anti-inflammatory and Antimicrobial Agents"

Abhay Kumar Verma et al conducted the Synthesis, Characterization, and evaluation of Anti-inflammatory and Analgesic activity of Benzothiazole derivatives. The synthesized derivatives demonstrated notable anti-inflammatory and analgesic activities compared to previously reported benzothiazole derivatives.<sup>[18]</sup>



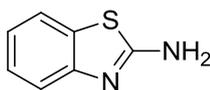
Rats' paw edema caused by carrageenan was used by Reena Mahtab et al. to synthesize novel 2-benzylbenzod

thiazole-6-sulfonamide derivatives and assess their anti-inflammatory potential. The recently created benzothiazole compounds showed strong anti-inflammatory properties.<sup>[19]</sup>



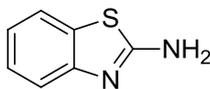
2-benzylbenzoxthiazole-6-sulfonamide

The synthesis, characterisation, biological assessment, and ADME studies of new benzothiazolyl-amides were the main areas of interest for V. S. Velingkar et al. Using a mouse paw edema model generated by carrageenan, the synthesized compounds were investigated for their anti-inflammatory properties and showed promise as non-acidic anti-inflammatory medicines. Using the  $\lambda$ -Carrageenan-induced mice paw edema method, P. Venkatesh et al. synthesized 2-amino benzothiazole derivatives with different substitutions and assessed their anti-inflammatory properties. In the benzothiazole ring system, several changes, such as chloro at position 5 and methoxy replacements at positions 4 and 6, improved anti-inflammatory action.<sup>[20]</sup>



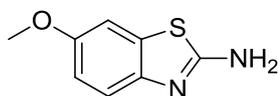
2-amino benzothiazole

5. The study conducted by Muttu C T et al. focused on the synthesis and assessment of fluoro, chloro 2 N-(substituted Schiff bases) amino benzothiazole derivatives using microwave assistance for their anti-inflammatory properties.<sup>[21]</sup>



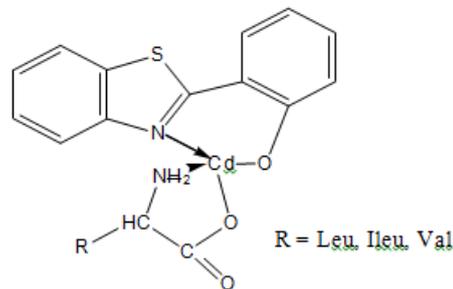
2-amino benzothiazole

In vitro anti-inflammatory activity of 2-amino-6-methoxy benzothiazole derivatives was assessed by Vrushi Patil, Ashish Asrondkar, Vishal Bhadane, A.S. Bobade, and Abhay Chowdhary, and the results were satisfactory when compared to the standard medication DFS.<sup>[22]</sup>

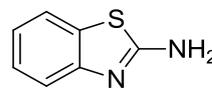


2-amino-6-methoxy benzothiazole

The anti-inflammatory effect of new derivatives of 2-amino-3-cyano-14-imino-10-methoxy-4-methylthio pyrimido 2,1-b pyrazolo 4,5-d pyrimido 2,1-b benzothiazole was evaluated by Kamlesh D. Niranjane et al. Excellent anti-inflammatory effect was demonstrated by several substances.<sup>[23]</sup>

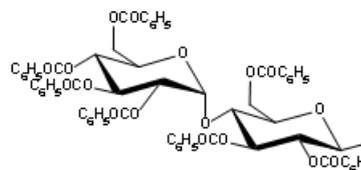


A.G. Awale et al focused on the synthesis and characterization of 2-amino-1,3-benzothiazole, Schiff bases, and Azo dyes, observing antimicrobial activity.<sup>[24]</sup>

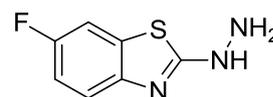


2-amino-1,3-benzothiazole

1.hepta-o-benzoyl-d-maltosyl-4-benzothiazolyl semicarbazides were synthesized and studied by Renu B. Ghayalkar and colleagues for their antibacterial and antifungal activity, demonstrating that they have both antimicrobial and antifungal properties.<sup>[25]</sup>

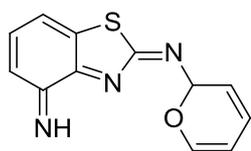


The antibacterial activity of 2-substituted hydrazino-6-fluoro-1,3-benzothiazole was investigated against a number of different bacterial species by Priyanka Yadav and colleagues.<sup>[26]</sup>



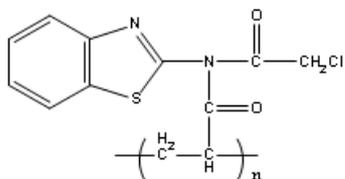
hydrazino-6-fluoro-1,3-benzothiazole

The antibacterial assessment of fused iminopyrimido benzothiazole derivatives was investigated by G. R. Shendarkar and colleagues, who discovered that these derivatives exhibited powerful antimicrobial action against harmful bacteria that were resistant to many drugs.<sup>[27]</sup>

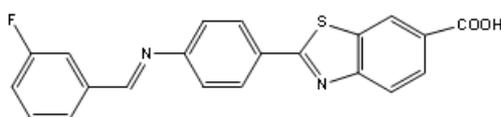


iminopyriminobenzothiazole

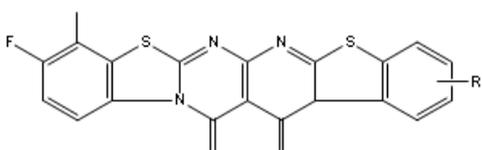
Padmavathi P. Prabhu and colleagues synthesized Schiff's Bases of novel benzothiazole compounds and evaluated their in vitro growth inhibitory efficacy against a variety of microorganisms. They found that the Schiff's Bases exhibited considerable antibacterial activity.<sup>[28]</sup>



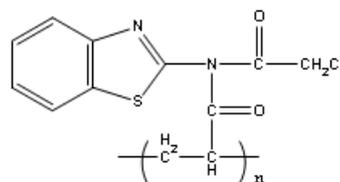
A new series of heterocyclic compounds was synthesized by P. Ravi Prasad and colleagues. These compounds include 9-chloro-10-fluoro-15-imino-14-oxo-14H-benzothiazole 2,3-b pyrimido 5,6-e pyrimido 2,3-b benzothiazole and its substituted derivatives. In addition to demonstrating antifungal efficacy against *C. rugosa*, the fused iminopyrimidobenzothiazole derivatives revealed considerable antibacterial activity against multidrug-resistant pathogenic bacteria.<sup>[29]</sup> This activity was comparable to that of the conventional Streptomycin.



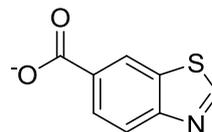
Entesar O. AL-Tamimi et al synthesized substituted and unsubstituted polyimides by reacting acryloyl chloride with different amides. The derivatives were identified as antimicrobial agents.<sup>[30]</sup>



The tube dilution approach was utilized by Vrushali Patil and colleagues in order to successfully synthesis benzothiazole derivatives and assess the anti-microbial properties of these compounds. Out of the compounds that were produced, the derivatives of compounds 5c, 5d, and 5e demonstrated powerful antibacterial properties, whereas the molecule that was not replaced exhibited only a moderate level of activity.<sup>[31]</sup>



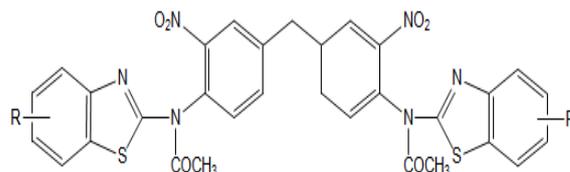
The antibacterial activity of Benzothiazole-6-carboxylate derivatives was devised, synthesized, described, and tested by Padmavathi P. Prabhu and colleagues. The antibacterial activity of some of the compounds was significantly higher than that of the standards.<sup>[32]</sup>



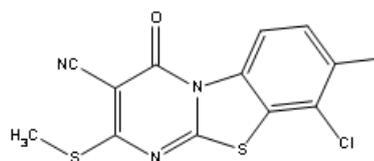
Benzothiazole-6-carboxylate

An evaluation of the biological activity of a series of \{4-(6-substituted-benzothiazol-2-yl-amino)-3-nitrobenzyl-2-nitro-phenyl\}-6-substitutedbenzothiazol-2-yl-amines was conducted by Pradip P. Deohate. These amines were tested against gram-positive and gram-negative microbes. The majority of the compounds demonstrated enhanced antibacterial and antifungal activity with their components.<sup>[33]</sup>

R = H, 4-CH<sub>3</sub>, 5CH<sub>3</sub>, 6-CH<sub>3</sub>, 4-Cl, 5-Cl, 6-Cl



An innovative series of 2-substituted aryl amine, heteryl amine, and active methylene group chemical derivatives of 9-chloro-3-cyano-8-fluoro-2-methylthio-4-oxo-4H-pyrimido 2,1-b 1,3-benzothiazole was presented by P. Ravi Prasad and colleagues. Evaluation of the compounds using the disc diffusion method and comparison with standard medications revealed that the compounds had antibacterial and antifungal activity that ranged from good to moderate.<sup>[34]</sup>



## CONCLUSION

The exhaustive examination of research and review articles unequivocally affirms that the benzothiazole scaffold stands out as a genuinely versatile and multifunctional molecule. Its therapeutic efficacy

extends across a spectrum of diseases, encompassing cancer, diabetes, and various others. Particularly noteworthy is the availability of diverse marketed preparations of benzothiazole, such as the neuroprotective drug Riluzole, diuretic drug Ethoxolamide, antiparkinson drug Pramipexole, and Alzheimer's disease medication Thioflavine. The manifold applications of benzothiazole underscore its potential as a pivotal player in medicinal chemistry, providing a promising foundation for the development of superior drugs. This body of evidence strongly advocates for sustained research efforts to unlock the full potential of benzothiazole in the pursuit of enhanced therapeutic agents.

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**Conflict Of Interest:** Authors declare no Conflict of Interest.

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