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Review Article

A Review on Emerging Benzothiazoles: Biological Aspects

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Abstract

Due to its beneficial natural and pharmacological properties, heterocyclic element analogues and derivatives have recently received a lot of attention. One of the frequently occurring heterocyclic nuclei in both marine and natural grow solutions is benzothiazole. A favoured bicyclist band method with numerous utilizations is benzothiazole. It is well known for exhibiting a broad variety of beneficial natural activities, including those that are anticancer, antiviral, anti-inflammatory, anticonvulsant, and antidiabetic, antimicrobial, and antitubercular. The benzothiazole nucleus is used in the synthesis of many therapeutic agents. We have seen a few surprising developments in the natural functions of benzothiazole derivatives over the past few years. Due to their extraordinary pharmacological potential, these components are only relevant in the context of therapeutic hormones. This evaluation primarily aims to demonstrate recent systematic research on the various natural functions of benzothiazole compounds that has been conducted.

Keywords: Benzothiazole, Anticancer activity, antimicrobial activity, Heterocyclic element analogues, Benzothiazole derivatives

Introduction

A special bicycle ring structure with numerous uses is benzothiazole. Several 2-aminobenzothiazoles were heavily researched as gastrointestinal tranquillizers in the 1950s. Since that time, this molecular group has not piqued the curiosity of medical chemists. The pharmaceutical characteristic of riluzole was identified, which attracted the attention of scientists to this class. In biochemical, electrophysiological, and behavioural studies, riluzole was discovered to inhibit glutamate neurotransmission. After then, benzothiazole derivatives underwent substantial research, and it was discovered that they have a wide range of chemical reactivity and bioactivity[1,2].

Benzothiazole, a heterocyclic compound, in research, it is utilised as a building block for the creation of complex particles, typically biologically active components. Due of its scent, it is relatively. Colorless and relatively viscous, benzothiazole has a boiling temperature of 227–228°C and a melting temperature of 2°C. Benzothiazole has a density of 1.24 g/mL and a molecular weight of 135.19 gmol'1. Benzothiazole cannot be consumed at home. It is used in research and the market.

The benzothiazole nucleus is used in the synthesis of many therapeutic agents. There were some fascinating developed in the natural functions of derivatives of benzothiazole over the past several years. These substances hold a special importance in the therapeutic hormones due to their extraordinary therapeutic potential[2].

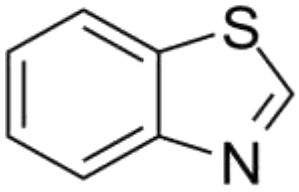

Figure 1: Benzothiazole Nucleus[3]

The benzothiazole nucleus is used to manufacture a significant range of medicinal medicines. There were some intriguing changes in the bioactivity of benzothiazole derivative products in current history. These substances' exceptional pharmacological potentials give them a distinct place in the area of biomedical sciences[4].

Biological Aspects

Anticancer Activity[5]:

Nearly 7 million individuals die from cancer each year, making it a huge threat to global health and a major obstacle for medical science. The creation of new effective anticancer drugs and the identification of new molecular receptors are the main focuses of the worldwide research projects in this subject[6].

The focus of current research initiatives in this area is split equally between the creation of new works and potent anti-cancer agents and the identification of fresh natural objectives. Wang et al. produced novel benzothiazole-2-thiol derivatives and tested the antiproliferative effects of these compounds on MCF-7 and HepG2 cells. Numerous substances showed effects that inhibited cellular growth, and some of them were superior to cisplatin. Numerous synthetic compounds have been tested for cytotoxicity using two monocytic human cell lines and a mouse melanoma cell collection. By using Mannich type addition for an ionic fluid press, -Aminophosphonates(3) may be produced by Jin et al. with a high yield and quick turnaround time. The in vitro anticancer effects of the recently synthesised compounds on PC3, A375, A431, and Bcap37 cells were evaluated using the MTT assay. Five thiourea derivatives were successfully synthesised by Saeed et al., four of which include a benzothiazole moiety, and their antibacterial and anticancer properties were evaluated. Havrylyuk et al. have evaluated a number of new 4-thiazolidinones with benzothiazole moiety for their ability to combat cancer (five). The National Cancer Institute assessed the in vitro anticancer activities of synthetic compounds. Several among them have demonstrated their ability to treat anemia, carcinoma, and lung disease, prostate, renal, ovarian, CNS, colon, as well as breast cancer cellular collections[7].

Solomon et al. designed and synthesised isatin benzothiazole analogues (six) to examine their antibreast cancer activity. They did this using a crossbreed pharmacophore method. Three different man-made breast carcinoma cell lines, as well as two normal breast epithelial cell lines, 184B5 and MCF10A, were used to test the cytotoxicity of the various substances. Kamal et al. prepared seven benzothiazole-linked pyrrolobenzodiazepine conjugates that were connected using various alkane or even alkylamine spacers. Their anticancer activity has been investigated by DNA winter denaturation tests, restriction endonuclease digestion assays, and flow cytometric analysis in a man's melanoma cell collection. The QSAR situation was started using a correlation analysis and a stepwise regression analysis. Mortimer et al. constructed a number of brand-new 2-phenylbenzothiazoles on the basis of the finding of the selective and strong in vitro anticancer properties of 2-(3,4-dimethoxyphenyl)-5-fluorobenzothiazole. Oanh et al. created two sequences of benzothiazole-containing analogues of SAHA in order to find novel modest particles that would concentrate on Class I and Class II histone deacetylase (HDAC) enzymes (twelve). In addition to showing strong cytotoxicity against five cancer cell collections with typical IC50 values of around 0.81 g/mL, nearly equal to SAHA, it was discovered that some ingredients with a 6C-bridge connecting the benzothiazole moiety and hydroxamic functional organisations exhibited excellent inhibition from HDAC and HDAC3 four. Kok et al. [13] studied the "one pot" condensation reaction of the phthalic imide derivative synthesis, demonstrating in vitro cytotoxic potential on man cancer cellular collections. They further showed how our new benzothiazole, which contains phthalimide, caused apoptosis on cancer cells via both caspase-independent and caspase-dependent methods.

Antimicrobial Activity[8]

Since harmful microorganisms and fungi are increasingly developing resistant to current antimicrobial medications, the development of novel chemicals to combat resistant bacteria and fungus has emerged as one of the most crucial fields of antibiotic and antifungal studies.

The search for brand-newly components to combat resist bacterial and fungal is currently the very useful aspects of antifungal and antibacterial research because Resistance of harmful bacteria and fungi to commonly used antimicrobials medicines is quickly developing into a significant issue everywhere. As a result, finding new and effective antibacterial and antifungal agents has become increasingly difficult for chemists and pharmacists these days. As well as examining their antibacterial activities against Staphylococcus aureus, Pseudomonas aeruginosa, and Providencia rettegeri, among other gram-positive and gram-negative organisms.

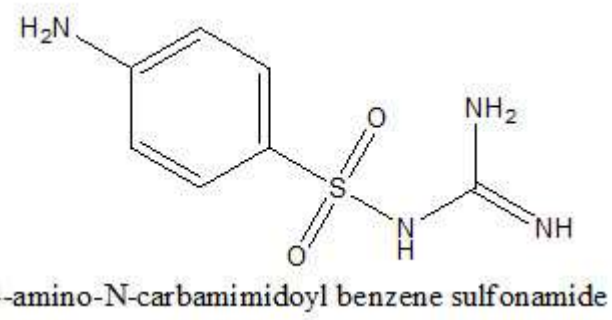

Figure 2: 4-amino-N-carbamimidoyl benzene sulfonamide [9]

In, Asundaria and Patel describe it and assess its antibacterial efficacy against various significant Gram positive and Gram negative bacteria. Bolelli et al. synthesised a new class of substituted benzamido/phenylacetamido)phenyl] benzothiazole derivatives and tested them against drug-resistant isolates of Candida albicans, Staphylococcus aureus, and Escherichia coli in order to discover if they had any antibacterial or antifungal properties[10]. Sharma By combining the two-aminebenzothiazole reaction with an alkyne, 4-phenyl-2H-pyrimido[2,1-] has been synthesised by et al. in quantifiable yields of b]benzothiazol-2-ones. When tested against Bacillus coagulans and other bacterial species, the synthesised compounds were found to have antibacterial characteristics. S. aureus, P. aeruginosa, and B. subtilis are also included[11]. N-Myristoyltransferase It has been demonstrated as a possible new target by innovative antifungal medications with a novel method of action to date. Examples of 3D-QSAR approaches include molecular docking and 3D quantitative structure activity relationships. Sheng et al. used CoMFA and CoMSIA in their investigation[12].

There are now known benzothiazole CaNmt (CaNmt) inhibitors that are antifungal. Compounds modes of binding to the active site of CaNmt were investigated. materials that repel water utilising the flexible docking technique It was found that interactions between the enzyme and benzothiazole inhibitors involved hydrogen-bonding. a fiction novel Schiff bases series with benzothiazole derivatives Synthesised by Soni et al.[13] Every single created antimicrobial compound underwent testing. 4Hpyrimido[2,1-b] One-pot synthesis of benzothiazole derivatives of curcumin: a quick and simple process. microwave ovens with and without solvents High yield synthesis is done by Sahu et al. a combination of several elements Investigated were the antibacterial qualities of several substances. antibiotics with gram positive and gram negative bacterial resistance, Several typical pathogens, such as the following, are present in the food supply: Typhi, Providencia rettgeri, and Bacillus cereus the capacity to fight against Aspergillus and other fungi Three Aspergillus species are A. fumigates, A. flavus, and A. niger. Tomi's buddies two By al., new five-member heterocyclic compounds comprising benzothiazole and oxazole have been discovered. Syllables echo. This study concentrated on microbial communities. Different levels of activity exist in two distinct kinds of heterocyclic rings with five members. We looked at the antibacterial properties of the substances. Pseudomonas in nutritive agar media was utilised to show activity against E.

coli, S. aureus, and C. difficile for the exploration of antifungal activity in Sabouraud's dextrose agar medium against Aspergillus niger and Candida albicans. A variety of 2-(1, 3-) benzothiazol-2-yl)-5-(diethylamino)phenol (23) and its derivatives were used as new antibacterial agents during the expedition. Padalkar et al. [23] synthesised derivatives and examined them in vitro for antibacterial activity against Escherichia coli, as well as antifungal activity against Candida albicans and A. niger after successively dilution of the solution. A number of novel thiazolidin4one and azetidin-2-ones were synthesised from the N-(6-)thiazolidin4ones and azetidin-2-ones. benzothiazole class hydrazine carboxamides containing chlorobenzo[d] thiazol-2-yl Gilani's ability to kill microorganisms was investigated in its derivatives. S. aureus), three gram-negatives (Klebsiella pneumoniae, Escherichia coli, and Staphylococcus aureus), and five additional microorganisms. By using the serial inoculation method of plate dilution, it is possible to grow a variety of mushrooms, including Penicillium citrinum, Aspergillus flavus, and Candida albicans[14, 15].

Epilepsy Inhibitory Activity [16, 17]

A short return of symptoms or signs is what the Campaign Against Seizure and the International Bureau of Epilepsy refer to as an epilepsy, in accordance with the International Organization for Standardization (ISO). The brain's neuronal activity and abnormally excessive or asynchronous symptoms go hand in hand. This has only been demonstrated in a small number of investigations. Patients (20–30%) are responding to the existing therapeutic drugs in their treatment. However, there is still a chance that it will work. a clinical requirement for new antiepileptic medications, or the pharmacokinetics, toxicity, or AEDs on the market nowadays aren't always up to par. The N-Series has returned! Two substituted acetates (25) Additionally, 6-(6-chlorobenzthiazo-2-yl)-2-(substituted-benzylidene) hydrazine carbothioamides (26) [25] and acute anticonvulsant in vivo were created by Amir et al. All of the synthetic compounds have undergone testing for toxicity. been executed Additionally, 3D four-point pharmacophore studies were performed on compounds to make sure they were well-known anticonvulsants. Kumar and others, A series of 2-[2-(substituted)hydrazonyl] and (2-(1,3-benzothiazole) benzothiazol-2-ylsulfanyl)-N-(substituted)acetohydrazide was created and synthesised. Titled substances were evaluated for their ability to prevent psychomotor seizures at a frequency of 6 Hz. Navale et al activity's "A substituents benzo[d]thiazol-2-yl carbamates production and anticonvulsant assessment"[18].

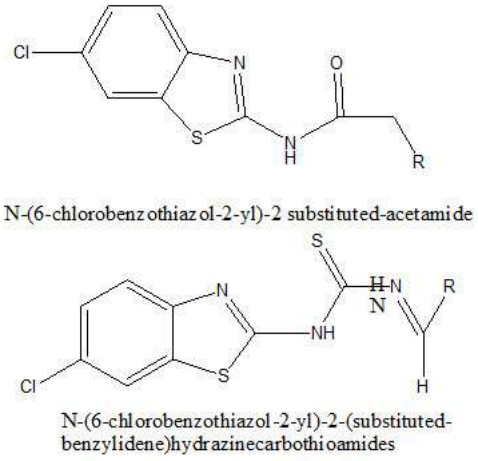

Figure 3: N-(6-chlorobenzothiazol-2-yl)-2 substituted-acetamide[19]

Diabetes prevention strategies [20, 21]

Type 2 diabetes is a hallmark of diabetes mellitus, which is one of a number of metabolic diseases with many etiologies. There are now 171 million diabetics worldwide, and according to projections from the year 2010, this number will rise to 366 million by the year 2030. As a result, the demand for efficient treatments to achieve ideal glucose control in the treatment of diabetes is increasing.

Type 2 diabetes belongs to a large category of metabolic illnesses with a wide range of potential causes and is characterised by persistently increased blood glucose levels. According to recent estimates from 2010, Around 171 million people have diabetes globally, and by 2030, that figure is expected to reach 366 million. To obtain the best glycemic control possible when managing diabetes, innovative and powerful medicines are needed. The in vivo antidiabetic activity of N-substituted 1,3 benzothiazol-2-yl benzenesulfonamide derivatives, which were synthesised and assessed by Moreno-D'az et al., was tested in a non-insulin-dependent diabetes mellitus rat model. In order to test for their anti-diabetic efficacy, Patil et al. created and produced a new series of substituted (E)- 3-(Benzo[d]thiazol-2-ylamino) phenylprop-2-en-1-ones (41). Selective 11betahydroxysteroid dehydrogenase type 1 inhibitors can be used to treat diabetes mellitus type 2 and obesity (11-HSD1). New benzothiazole derivatives (42) were found and synthesised, and [37, 38] reported on their radioimmunoassay-measured inhibitory effects against 11-HSD1 from human hepatic microsomes. Jeon et al. [22] synthesised a new class of thiazolidinone benzothiazole compounds and examined them for PPAR subtype activity and an inhibitory effect on NO generation in LPS stimulated macrophages. The majority of the compounds were discovered to show promise as potential diabetes medication candidates as PPAR agonists. A series of synthetic phenylsulfonamides were tested in vitro by GW7647 agonists against them, and the findings revealed that the most effective drugs had a dose-dependent antagonistic profile, which inhibited PPARa activation[23, 24].

When the compounds' hypoglycemic action was examined in vivo, both the oral glucose tolerance test and the acute normoglycemic model revealed significant drops in plasma glucose concentration, which are comparable to the effects of the hypoglycemic medication glibenclamide [25].

Antitubercular activity [26, 27]

Two novel 2-(2-thienyl)benzothiazole—BTT (46) metal complexes were synthesised, characterised, and investigated using DFT simulation and biological tests. Each complicated behaved wonderfully when tested against the pathogen Mycobacterium tuberulosis. Telvekar et al. developed and synthesised many fundamentally similar unique substituted 2-hydrazinobenzothiazole derivatives with the use of atomic hybrids. All the synthetic components demonstrated remarkable activity (MIC 1.5-29.00 g/mL) against M. tuberculosis H37Rv. Katz has synthesised antituberculous substances using derivatives of the 2-hydrazinobenzothiazole. HisG is an ATPphosphoribosyl transferase, which completes the initial step in the biosynthesis of histidine. Among the enzymes in this system, only HisG is a possible target for anti-tuberculosis medications. Virtual screening was performed to hunt for substances that might docking into to the structurally and functionally loops, and graphitic studies supported this binding process, according to Cho et al. in order to uncover more potent and diverse inhibitors.

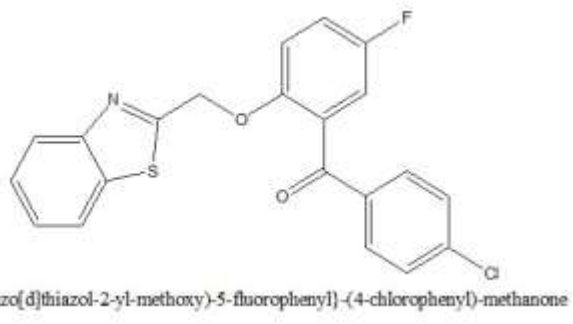

Figure 4: Structure that shows antibacterial activity [28]

Section 2.6 of Antiviral Activity By replacing the t-butylurea moiety for the benzothiazole sulfonamide (50) at the protease enzyme's cleavage site, which the inhibitors contained in a variety of isosteres, including hydroxyethylurea, it may be possible to create protease inhibitors with increased potency and antiviral action. Some of the compounds were discovered to have a high Rats' mouth half-life and availability. They were motivated to investigate other heterocyclic compounds by the benzothiazole derivatives. During their research, a two-step method for producing benzothiazole-6-sulfonic acid from sulfanilamide was also created.

Properties of Analgesics and Anti-Inflammation: [29, 30]

Shafi and colleagues synthesised new bis-heterocycles that include 2-mercaptobenzathiazole (51) via click chemistry. The anti-inflammatory abilities of the synthesised compounds have been tested using a model of carrageenan-induced hind paw edoema. Geronikaki et al. synthesised a number of novel thiazolyl/thiazolinyl/benzothiazolyl Schiff bases. The article's reference to lipoxygenase inhibitors has been associated with inflammation and psoriasis.

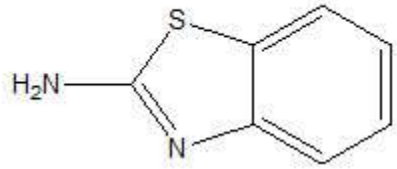

Figure 5: [31]

An antioxidant activity: [32]

Tzanova et al. successfully synthesised three novel 1,3-thiazol-modified benzophenones [49]. (54). Researchers examined the antioxidant potential of these meals using three different cell lines. An analogue of this substance, 5-(2,5-dihydroxybenzoyl)-2(3H)-benzothiazolone, shown considerable phenolic property, minimal cytotoxicity, and the capacity to inhibit the generation of reactive oxygen species when coupled with tert-butyl hydroperoxide (tBHP).

According to Cressier and colleagues [50], novel compounds have been synthesised and characterised using benzothiazoles and thiadiazoles. (55). Additionally, mice were employed to test the radioprotective qualities. Some of these substances might be helpful in the area of radiation protection.

Conclusion

As seen in this review, the benzothiazole moiety is being employed as a model for the creation of novel medicinal medicines. Due to its nucleus, it has anticancer, antidiabetic, anti-inflammatory, and antibacterial activities[33]. Designing and synthesising novel benzothiazole compounds with suitable design and structure-activity connection investigations can result in a variety of biological functions[34].

Conflict of Interest

The authors have no conflict of interest.

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