Original Article

Biological Potential of Benzothiazole Derivatives: Bench to Bed Side

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Abstract

Heterocycles played a significant contribution to the creation of pharmaceutically effective compounds in medicinal chemistry. The bulk of synthetic medicine compounds have therapeutic potential due to their heterocyclic structure. Drug molecules undergo therapeutic alterations that are connected to minor variations in the heterocyclic moiety. The pharmacological effects of benzothiazole and its analogues were strong and important. Our study's major goal is to disseminate up-to-date knowledge regarding synthesised benzothiazole analogues and related biological activity against a variety of disorders. A literature review was conducted using the terms "Benzothiazole," antimicrobial potential, anticancer potential, antitubercular activity, and "anthelmintic potential" in the datasets like ScienceDirect, MDPI, PubMed, Springer, Taylor, and Francis. This evaluation may illuminate the way for scientists who are attempting to create innovative benzothiazole derivatives with the hope of increasing their potency and security. However, more *in-vivo* and clinical research on the probable benzothiazole analogues is required.

Keywords: Benzothiazole, Bioactive, Benzothiazole pharmacophore, Therapeutic effect, Reactivity

INTRODUCTION

Beginning in the middle of the 19th century, while organic chemistry was developing, heterocycles have a extensive history. Heterocyclic compounds are an essential element of the biology and chemistry sciences. More than 75% of the top 200 drugs in the pharma industry belong to the heterocyclic family [1]. Heterocyclic compounds make up the majority of medicines and naturally occurring agrochemicals. [2, 3].

Among the heterocyclic compounds, 1, 3-benzothiazole has a weak base and a number of biological functions. Rarely do they occur naturally as a bioactive compound originating from the marine or terrestrial species. The scent of tea leaves contains benzothiazole analogues, as do flavourings made by fungi like *Aspergillus clavatus* and *Polyporous frondosus*. [4-5]. The primary structural component of benzothiazole is the benzene ring linked with thiazole at positions 4, 5, and 6. (figure 1a and 1b). Numerous pharmacological activities of benzothiazole compounds and their derivatives, including the antitumors [6], the anticonvulsants [7], antimicrobials properties [8], anthelmintics activities [9], antileishmanial activities [10], the anti-tubercular activity [11], schictosomicidal activities [12], an antifungals [13], anti-inflammatory [14] antipsychotics activities [15] and anti-diabetics activities have been discovered [16].

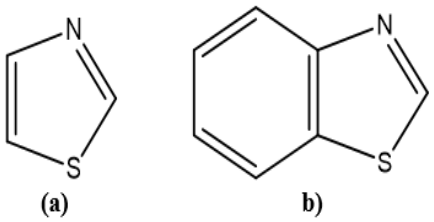
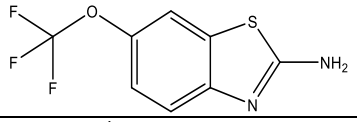
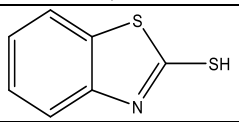
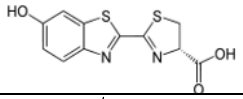
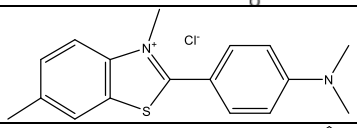
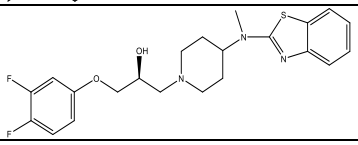
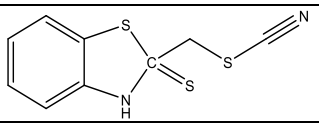
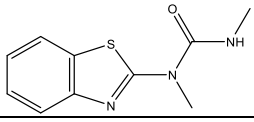


Fig. 1: (a) Thiazole (b) Benzothizole

Biological Potential of Popular Benzothiazoles Molecules

A series of 2-amino benzothiazoles had been heavily researched as central muscle relaxants in the 1950s. Biologists became interested in this series after learning about Rilutek's (2-Amino-6-(trifluoromethoxy)benzothiazole) pharmacological profile like a Glutamate receptor antagonist was identified. Following thereafter, benzothiazole moiety were widely synthesised, investigated for a diverse range of pharmacological activity (Table 1), and the benzothiazole moiety was discovered to have a broad range of activity and a variety of chemical reactivity.

Table 1: Popular Benzothiazole Molecules [17-19]

S. No.	Molecules	Biological Potential	Structure
1	Riluzole	Amyotrophiclateral sclerosis (ALS)	
2	2-Mercaptobenzothiazoles	polymer chemistry, pigments, medications, as a accelerating agent in vulcanization process, and protective coatings	
3	Luciferin	Bioluminescent compound	
4	Thioflavin T	Visualizing and measurement of the conformational changes of protein content	
5	Lubeluzole	Neuroprotective and indirectly N-Methyl D-Aspartate receptor antagonist (NMDAR)	
6	2-Thiocyano-methyl-thiobenzothiazole	Treatment of field crop soil and seeds for various diseases	
7	Methabenzthiazuron	As herbicides	

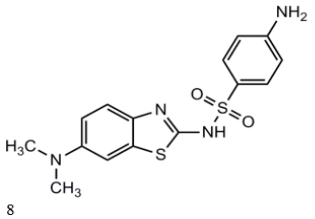
Pharmacological activities of the Benzothiazole analogs

Benzothiazole as Antimicrobial agent

Scientists are concerned about some types of microbes that can infect animals and cause a number of illnesses, including AIDS, malaria, respiratory infections, coughing, typhoid, and amoebiasis. Benzothiazole derivatives continue to be one of the key molecules against bacteria throughout the development of medicinal chemistry, despite numerous attempts to create innovative models for the creation of more potent antimicrobials. [20].

Sutoris *et al*. **(1977)** generated the 2- and 2, 6-disubstituted thiobenzothiazoles, which showed good antibacterial efficacy against mycobacteria, pathogenic fungi, and non-specific bacterial flora. Derivatives of 2-allylbenzothiazole, 2-allyl-6-nitrobenzothiazole, and 2-allyl, 6-nitrobenzothiazole were shown to have the outstanding activity. [21].

Sreenivas *et al*. **(1998)** produced several 6-fluoro,7-substituted sulfonamide-benzothiazole analogues and underwent for antimicrobial evaluation. The bulk of the compounds showed modest efficacy against *S. aureus*, *S. albus*, and *C. ablicans*. [22].



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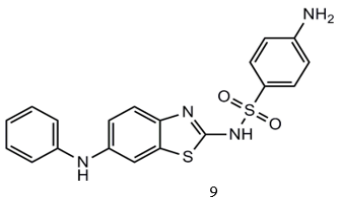

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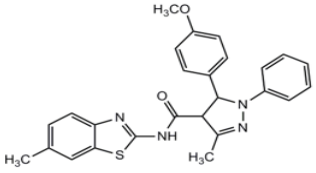
The compounds of benzothiazolyl-carboxamido-pyrazoline were reported by Gopkumar *et al*. **(2001)**. The generated compounds had their anti-microbial properties evaluated. Compounds with 4-methoxyphenyl and methyl groups scored for the effectiveness over *S. aureus*, *E. coli*, *P. aeruginosa*, *K. pneumonia*, and *P. mirabilis*, according to SAR analyses. Compounds with Cl and 4-methoxy phenyl groups also exhibited significant activity for *S. Aureus*. [23].



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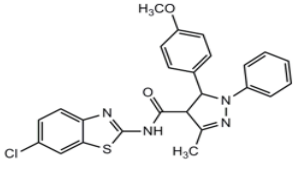

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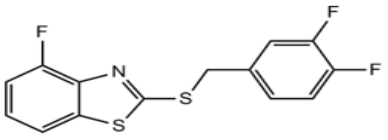
In a series of polyfluorinated2-benzylthiobenzothiazoles, Huang *et al*. **(2006)** reported 2-(3, 4-difluorobenzyl sulfanyl)-4-fluorobenzothiazole, which showed excellent antifungal potential against *R. solani*, *B. cinereapers*, and *D. gregaria*. [24].



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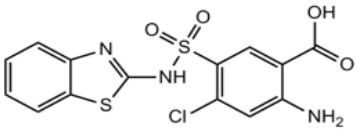
Bhusari et al. **(2008)** developed the benzothiazole compounds that are linked to benzoenesulfonamide as antibacterial and anti-TB medicines. The compounds selected to combat *B. subtilis* and *E. coli* microbiological growth contain Cl and carboxyl substitutions.



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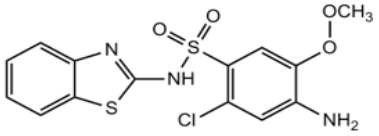

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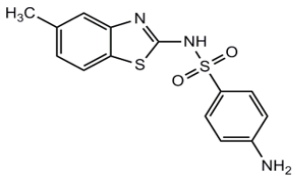
The substances with chlorine and methoxy substitutions worked as antifungal agents towards *C. albicans*. For anti-TB actions, the agents with the chloro and bromo groups were much more effective than the molecule with the nitro group. [25].

Benzothiazole was prepared by Argyropoulou *et al*. **(2009)** utilizing phenyl sulfonamide at the C-2 position and evaluated for its *in-vitro* antibacterial effectiveness for some of the microbes, shown exceptional antibacterial potential over gram positive bacteria and revealed the MIC scores between and including 0.3-100 g/mL. *Bacillus subtilis* was here particularly susceptible to synthetic chemicals. The strongest compounds in this class were benzothiazole sulfonamides containing nitro- and amino-groups in the aromatic ring's 4th position. [26].



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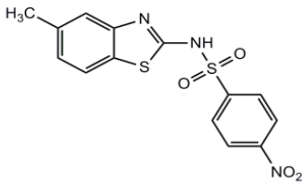

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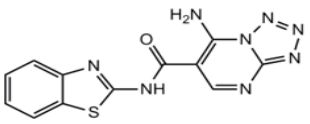
Heterocycles like pyrazole, isoxazole, and pyridine derivatives having benzothiazole moiety were prepared by Bondock *et al*. **(2009)** and the resulting analogues were examined for Gram-positive, Gram-negative, and fungal strains *in-vitro* antibacterial activities. In this instance, the bulk of the analogues had good to exceptional activity, with MICs ranging from 3.125 to 100 g/mL. Increased action against gram-positive bacteria is produced when benzothiazole is added to pyrimidine derivatives via acid amine coupling. When compared to the norm, a few of the pyrazole linked benzothiazole derivatives also demonstrated outstanding activity. [27].



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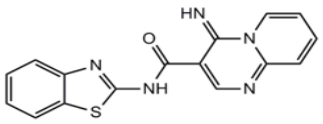

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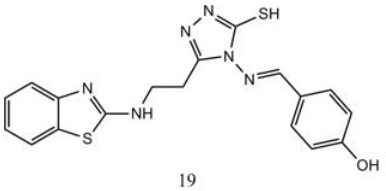
Soni *et al*. **(2010)** produced benzothiazole linked with triazole moiety and evaluated towards a variety of bacteria. The findings show that, among the produced compounds, those containing *p*-hydroxy, *p*-dimethyl amino, and *m, p*-dimethoxy groups on aromatic ring shown superior antimicrobial properties. The *o*-nitro, *m*-nitro, and *o*-chloro groups on the aromatic ring cause the activity to continue declining. In other terms, groups that donate electrons in the para position exhibit increased activity while groups that pull electrons exhibit decreased activity [28].



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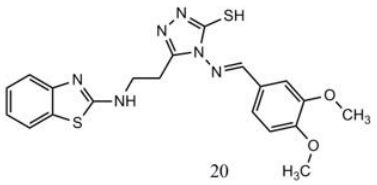

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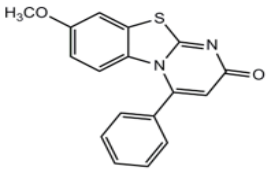
Sharma *et al*. **(2010)** developed the benzothiazole-pyramidino derivatives and evaluated them towards various bacterial strains.



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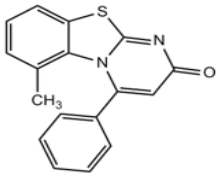

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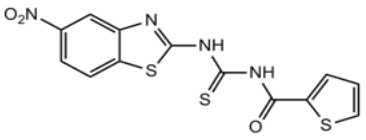
Benzothiazole and pyrimidine were combined to create heterocyclic systems, which were highly effective against the bacteria *B. coagulans*, *P. aeruginosa*, and *S. aureus*. 6-methoxy substituted analogues from the produced compounds showed enhanced efficacy at MIC levels of 25 g/mL.[29].

The benzothiazole thiourea analogues were produced by Saeed *et al*. **(2010)** and tested for their ability to fight cancer and bacteria. For the studied microorganisms, the produced compounds displayed a wide variety of activities, with some of them having better effects on fungi than on bacteria. The nitro group in the fifth position of benzothiazole gives it corresponding MIC concentrations of 10 and 5 g/mL towards bacteria and fungus respectively. According to a SAR investigation, benzothiazole compounds with thiophene and morpholine conjugation have higher activity than derivatives without replacement. Additionally, it was shown that the benzothiazole's incorporation of electron-withdrawing groups enhances activity in the current situation.

The effectiveness of these compounds atoards MCF-7 and HeLa cells was also assessed using MTT-based cytotoxicity tests; their IC50 values ranged from 18 to 46 µM. [30].



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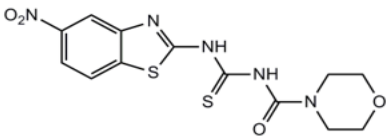

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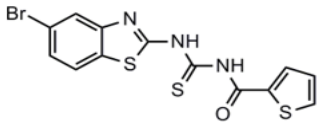

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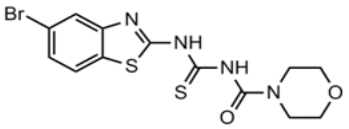

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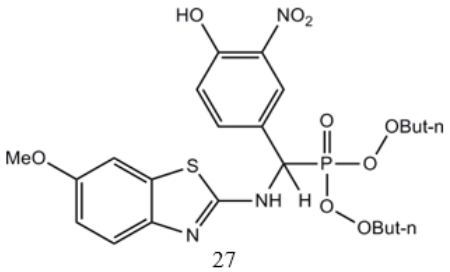
As an antibacterial and antioxidant agent, Rao *et al*. **(2010)** created 6-methoxy-2-amino benzothiazole-phosphonate analogues through a one-pot, microwave-assisted synthesis. In comparison to the regular Penicillin, nitro and bromo substitution on phenyl group phosphonates demonstrated more action.



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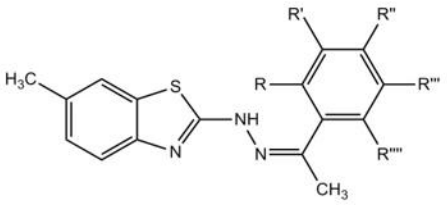
The lowest activity was obtained by the chemicals thiophene and n-butyl phosphonate. The ferric thiocyanate technique was used to assess the compounds' antioxidant properties, and the bulk of the derivatives showed outstanding activity. The IC50 values were obtained in concentration from 86 g/mL to 96.8 g/mL. [31].

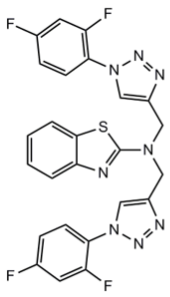
A few benzothiazole compounds that had been substituted with hydrazine at second position (Alanget *et al*., **2010**) showed better antifungal properties, and ortho substituted halogen derivatives displayed the enhanced activity, whereas the activity diminished with para substituted methoxy group. [32].



R = F, R"= NO_2, R'''= OCH_3, R''''= CH_3

28

A number of triazole fused benzothiazole compounds were created and their antibacterial properties were assessed by Singh *et al*. in **(2013)**. Compound 29 demonstrated maximum effectiveness over all strains of bacteria with MIC values of 1.56-12.56µg/mL, resulting in a two-fold increase in efficacy over the common antibiotic Ciprofloxacin (MIC6.25 g/mL). The fungal species where Compound 30 was very effective had MIC values between 1.56 and 12.5 g/mL. [33].



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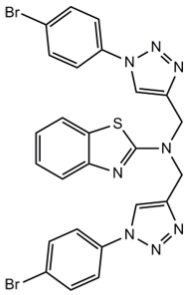

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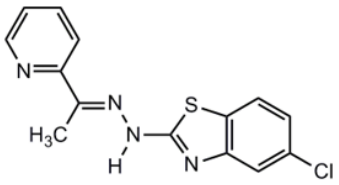
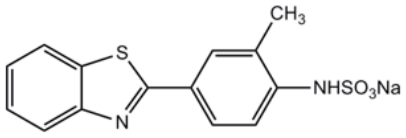
Benzothiazole as anticancer agent

In order to explore the antiproliferation action of benzothiazolyl-hydrazones analogues made from acetyl pyridines, Easmon *et al*. **(1997)** synthesized the compounds. They then screened them for a number of cell lines. These substances demonstrated outstanding action for Burkitt's lymphoma cells and reasonable amount of activity for tested cell lines. [34].



31

Shi *et al*. **(2001)** reported the sulfamate salt of 2-(4-aminophenyl)benzothiazole and revealed that In *in vitro* experiments, salts are less potent towards MCF-7 and MDA-468 cell lines than their parental amines. [35]. Additionally, they found that highly acidic environments cause the amine to decline. The IC50 values for the aforementioned compounds' free amines were between 0.0001-0.001 M and 0.42-9.0 M, respectively [36]. Activity was highest for methyl substitution.



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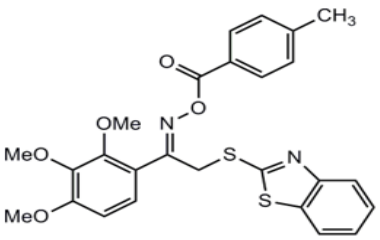
Hutchinson *et al*. **(2002)** created a number of L-lysyl- and L-alanyl-amide prodrugs of 2-(4-aminophenyl)benzothiazoles that are water soluble and examined for anticancer action on mice and dogs. From the group, 2-(4-amino-3-methylphenyl)-5-fluorobenzothiazole (NSC710305, also known as Phortress), was chosen for phase 1 clinical testing as a more potent option for antitumor illness [37]. Regardless of the presence or absence of the oestrogen receptor, this drug has demonstrated efficacy against breast, ovarian, kidney, lung, and colon cancers.

Drug Development Group granted authorization for a clinical candidate, synthesis, formulation, and pharmacokinetics investigation for the aforementioned chemical in the same year. Phase I clinical examinations for the chemical are still ongoing in the UK after Pharminox acquired the rights to develop it in 2004. [38].

A set of 2, 3, 4-trimethoxyacetophenoxime linked benzothiazoles were created by Song *et al*. **(2005)** through the reaction of oxime with acylchloride in an alkaline medium. When the synthetic compounds were examined using an *in-vitro* MTT assay, the bioassay revealed a moderate level of activity. At a concentration of 10 g/mL, the antiproliferative effects of the p-methyl substituted compounds on PC3 and A431 cells were 71.3 percent and 69.9 percent, respectively. [39].



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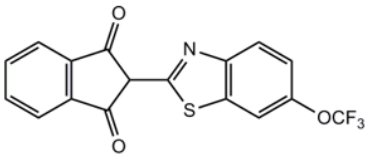
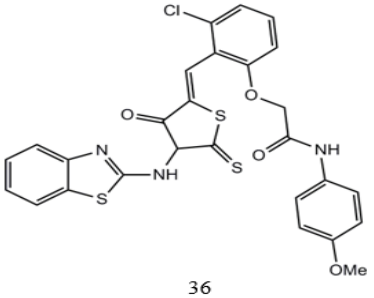
Phthalamide analogues of the benzothiazole were produced by Kok *et al*. **(2008)** utilising a one-pot condensation method and tested them on human cancer cell lines for in-vitro cytotoxicity. After 48 hours of research, it was discovered that these substances were lowering the intracellular adenosine triphosphate (ATP) level by 50%, which was found to be at a concentration of about 25 g/mL. [40].



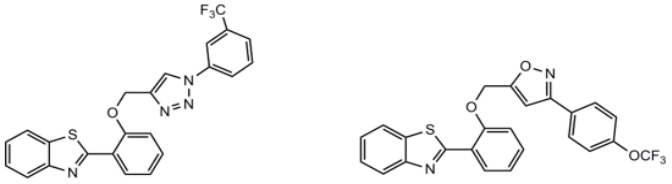
35

The 4-thiazolidinone linked benzothiazole was made by Havrylyuka *et al*. **(2010)** via the Knoevenagel condensation method. Two of the synthesised compounds demonstrated activity for leukaemia, lungs, colorectal, melanoma, CNS, kidney, ovarian, prostate, and breast cancer celllines when they were tested for in-vitro anticancer activity. Here compound 36, which had log TGI value and log GI 50 value of -4.45 and -5.38, was a good candidate for anti-cancer action. [41].



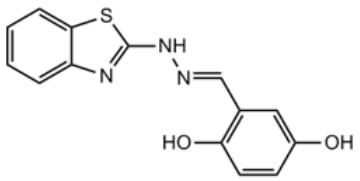
36

Kumbhare *et al*. **(2012)** established a set of triazoles/isoxazole-linked 2-phenyl benzothiazole and used the MTT assay to test for anticancer activity in the MCF10A, A549, colo-205, and MCF-7 cell lines. The target triazole molecule's cytotoxic activity was increased by the addition of fluorine atoms, particularly CF_3, in the third position, according to the SAR investigation. The isoxazole moiety with the trifluoromethoxy substituted compound also shown good activity. The IC50 (µM) values for compound 37 were determined using the cell lines MCF-7, Colo205, A549, and MCF10A, and they were 18.94, 10.78, 11.07, and 31.07 and for compound 38 they were 26.62, 19.87, 23.87 and 43.87 respectively. [42].



37 38

In a 2014 study, Lindgren *et al*. prepared (*E*)-2-benzothiazole hydrazones and tested them for *in vitro* antitumor potential against HL-60, MDAMB-435, and HCT-8 cell lines. By using both theoretical and practical techniques, they investigated the anticancer potential of the produced chemicals. The molecule with electron-donating groups demonstrated increased activity in comparison to electron-withdrawing groups theoretically (Gaussian 09W programme). Dihydroxy group-containing substances displayed impressive activity for cell lines in MTT assay, having IC50 values varying between 0.59 and 11.18 mM. [43].



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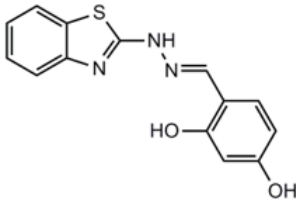
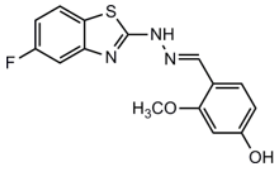


40

Moustafa *et al*. **(2016)** reported a number of 6-fluoro-2-substituted Schiff's bases, investigated simulation molecular modelling using the ATP binding sites. The IC50 (µMol/L) values for compound 41 were determined using the cell lines HeLa, and COS7, they were 2.41 and 4.31 and for compound 42, they were 22 and 45.6 respectively.



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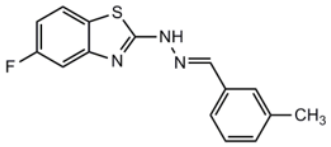
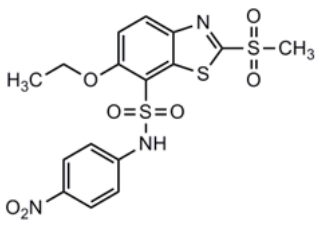


42

The SAR study revealed that changes in the locations of the hydroxy and methoxy groups likewise diminished activity, as did substituting the 4-hydroxy group with the 4-methoxy group. Due to the hydrophobic contact with the receptor, the inclusion of 2-(3-methyl benzylidene) hydrazino group also demonstrated higher activity. [44].

Lad *et al*. **(2017)** discovered a new class of methylsulfonyl-benzothiazole derivatives with 4 and 5 substituents. and examined them for their ability to fight cancer and bacteria. Some of the substances displayed MIC values between 4 and 50 g/mL. These antimicrobial substances were tested on HeLa cell lines for their ability to cause cancer. The computed IG50 values ranged from 0.2 to 0.6 M. [45].



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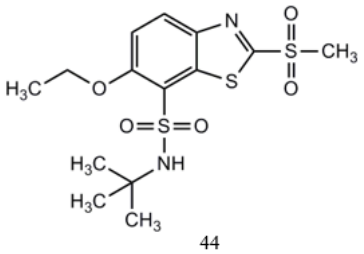
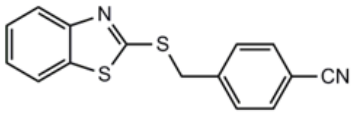


44

Benzothiazole as anti-tubercular agent

Koci *et al*. **(2002)** produced a set of 2-benzylsulfanyl linked benzothiazoles and examined their *in-vitro* anti-tubercular efficacy. Dinitrobenzyl replacements exhibited excellent Mtb MIC values in the series (2 mol/L), whereas pera-cyano, *o*-nitro and benzyl group substitutions reduced activity. [46].



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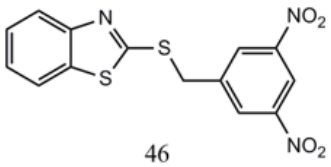
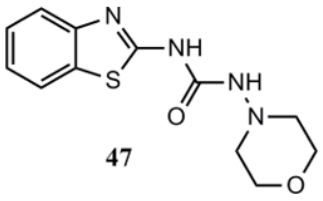


46

Vicini *et al*. **(2003)** synthesised Benzoisothiazole and Benzothiazole Schiff's bases and tested them using the MTT method for the presence of anti-Mycobacterium tuberculosis activity. However, the compound did not demonstrate the noteworthy activity but did exhibit antibacterial, cytotoxic, and HIV-1 properties instead. [47].

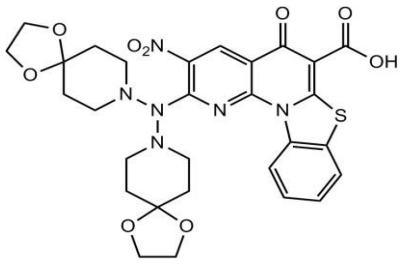
Rahman *et al*. **(2007)** produced urea analogues of benzothiazol and assessed their antibacterial propertie towards *M. tuberculosis*. The most cytotoxic analogue, morpholine-thiourea derivative of benzothiazole (47), reduced the growth of mycobacterium strain H37Rvstrain by 37 percent at a 6.25 g/mL concentration while lowering the growth of the MCF-7 celllines by 76 percent. [48].



47

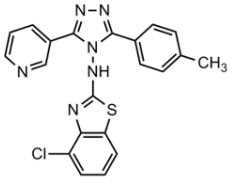
The synthesis of benzothiazole-isoxazole-carboxamide analogues was published by Huang *et al.* **(2009)**, who also tested the compounds against the Mycobacterium TB H37Rv strain. MIC values for some of the substances ranged from 1.4 to 1.9 M concentrations, and they suppress Mtb proliferation at micromolar doses. Different substitutions at the amide position, for effective anti-TB action, were well matched for improving the activity. [49].

Anti-TB activity was shown by benzothiazol linked naphthyridone carboxylic acids against the multidrug-resistant and H37Rv strains of *Mycobacterium tuberculosis* (MDR-TB) *in-vitro* and *in vivo*. Compound 48 shown the highest level of activity against M. tuberculosis and Multi - drug resistant, exhibiting Minimum inhibitory concentration (MIC of 0.19 M and 0.04 M, respectively. in a number of *in-vitro* investigations, outperforming the conventional drugs gatifloxacin and isoniazid. A 50 mg/kg dosage of these compounds was used in an *in vivo* animal investigation to show their efficacy and revealed a MIC value for lungs and spleen tissues of 2.81 M. Conjugation of piperidine demonstrated excellent anti-TB and cytotoxic effects. [50].



48

Patel *et al*. **(2010)** prepared benzothiazole-triazole linked pyridine compounds and tested their anti-TB efficacy towards H37Rv strain using Lowenstein-Jensen media. 6-methoxy benzothiazole (50)-containing synthetic compounds shown better anti-MTB efficacy (50 g/mL). The compound with the chloro group (49) had a minimum inhibitory concentration value of 25 g/mL due to the mesomeric impact. [51].



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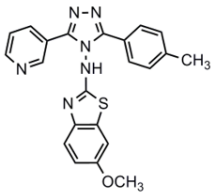
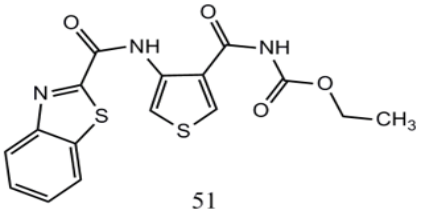


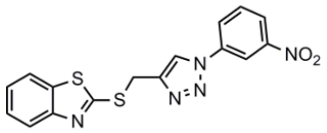
50

In order to prevent the Mtb H37Rv strain from forming biofilms, Wang *et al*. **(2013)** reported benzothiazole linked with thiophene at second position with amide as linker. This compound also demonstrated inhibitory action, and the minimum inhibitory concentration value was determined to be 0.01 g/mL. [52].



51

Fauzia *et al*. **(2014)** made a set of 1, 2, and 3 triazole derivates of mercapto-benzothiazole, and their antitubercular activity was assessed using the *in-vitro* broth dilution method against the *Mycobacterium tuberculosis* H37Rv strain. Triazole conjugated series from the produced compounds were more active than amide linkage moiety.



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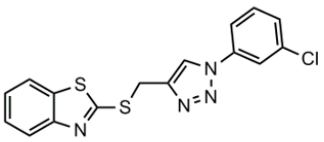
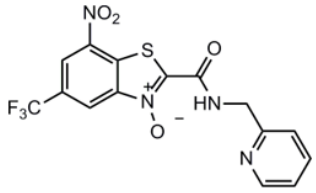


53

Compounds having changes to the aromatic rings for chlorine and nitrogen, demonstrated promising activity and had a minimum inhibitory concentration of 8 g/mL. The above compounds appeared to behave as DprE1 inhibitors according to the docking tests. The compounds' bactericidal activity demonstrated the benzothiazole moiety's potential as a powerful ligand against tuberculosis. [53].

According to Landge *et al*. **(2015)**, 2-substituted benzothiazole was prepared, examined for anti-TB activity, and the derivatives were found to have powerful anti-mycobacterial action by specifically inhibiting decaprenylphosphoryl-D-ribose 2'-oxidase (DprE1). Utilizing co-crystallization and mass spectrometry, they also determined the manner of binding and particular target linkage. [54].



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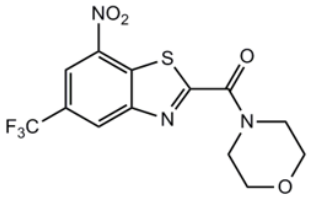
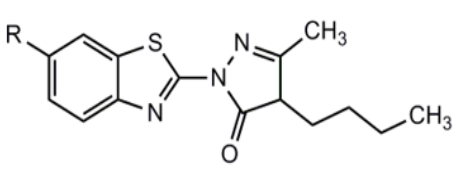


55

Anti-inflammatory activity of Benzothiazoles

The (2-dimethylpyrazole)-6-substitutedbenzothiazoles were prepared by Singh *et al*. **(1986)** and were found to have a mild anti-inflammatory effect [55]. Sawhney *et al*. **(1987)** developed a set of 2-aryl substituted 6-hydroxybenzothiazoles, and these compounds had low to moderate activity. [56].



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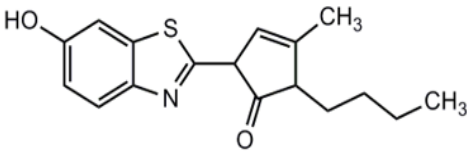
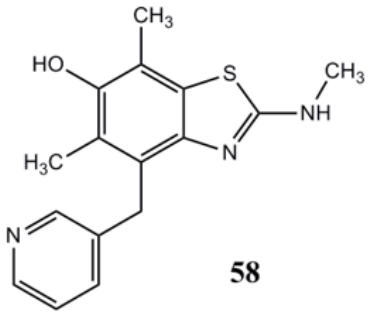
R = H, Cl, F, CH_3, OCH_3



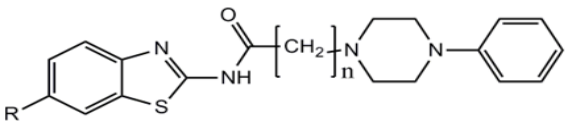
57

Hibi *et al*. **(1994)** produced 2-amino-6-hydroxy benzothiazoles with a substitution of pyridylmethyl at 2nd position and anti-inflammatory properties were noted. Synthesized substances have a dual inhibitory effect on thromboxane A2 and leukotriene B4. These substances block the effects of their direct inhibition of TXA2 synthase and 5-lipoxygenase. Here, the activity was greatly influenced by the location of the 3-pyridylmethyl group. The most active compound was 6-hydroxy-5,7-dimethyl-2-(methyl amino)-4-(3-pyridyl methyl) benzothiazole. [57].



58

The 4-phenyl-piperazine benzothiazolyl amide analogues were created by Papadopoulu *et al*. **(2005)** and investigated for their ability to reduce inflammation. Using a mouse paw oedema model caused by carrageenan, the efficacy of the produced compounds to decrease inflammation was assessed. The compounds inhibited inflammation by 44–74.1%. [58].

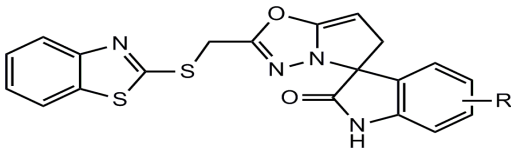


R = H, F, OC_2H_5 n = 1, 2

59

Kaur *et al*. **(2010)** synthesised benzothiazole linked spiroindole compounds and tested them for in-vitro anti-inflammatory and analgesics properties. A number of compounds were created, At a dose of 100 mg/kg, 5-chloroindolyl-benzothiazole showed significant anti-inflammatory activity reduction (72%) and at the same dose, 7-chloroindolyl-benzothiazole showed strong analgesic action (69.2%).

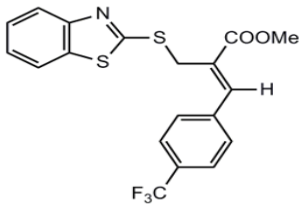
According to Structure Activity Relationship of compounds, the incorporation of the oxadiazole ring (60) improved the activity of the Br- and Cl- analogues, which was active well. [59].



60

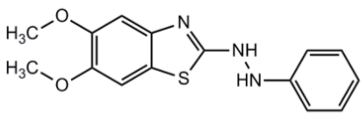
A COX test and carrageenan-induced hind paw oedema were used by Shafi *et al*. **(2012)** to calculate the anti-inflammatory and anti-nociceptive properties of 2-mercapto benzothiazole based bis-heterocycles. On substituted aromatic rings, electron-withdrawing groups in the *p* and *o*- locations had elevated activity, whereas electron donating groups shown lower activity. [60].

Under neat conditions at rt, the Bylis-Hillman bromides approach was used to create a number of benzothiazolethio substituted analogues. By using a calorimetric cyclooxygenase inhibition screening method, synthetic substances were assessed for their capacity to inhibit. The activity was improved by electron withdrawing groups, and the compound containing the benzothiazole unit had greater inhibition capacity than the benzoxazole and pyramidine units. At a dose of 100 mg, the benzothiazoletrifluoro compound showed a 77% inhibition and an IC50 value of 2.93 micromolar doses. [61].



61

Abbas *et al*. **(2015)** produced a number of benzothiazole coupled with heterocycles. The compounds' ability to reduce inflammation was examined using the carrageenan rat paw edoema model, and it was found that they had more activity than expected and much longer duration of effect. With percentage inhibitions of 95.16% for 2-phenylhydrazine benzothiazole analogues and 84.54% for 2-substituted hydrazino Schiff's base, respectively, these compounds were quite active. These substances also demonstrated anti-neoceptive properties; the most effective of the group is 2-substituted hydrazine Schiff's base. [62].



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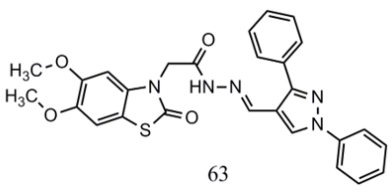
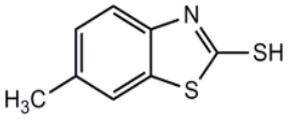


63

Benzothiazole as antioxidant agent

Cressier *et al*. **(2009)** produced a series of 6-substituted benzothiazoles, and the DPPH and ABTS assays were used to assess their in-vitro antioxidant ability. Thiol analogues of benzothiazole in this instance had an IC50 value of 0.046 mM, while aminothiole analogues of benzothiazole had an IC50 value of 1.39 mM. [63].



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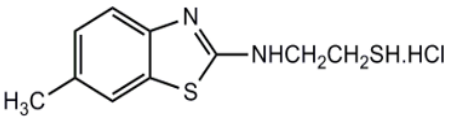
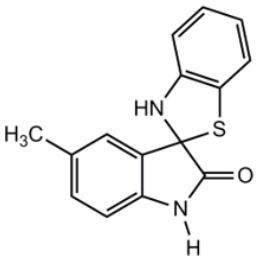


65

Karali *et al*. **(2010)** By suppressing lipid peroxidation and demonstrating excellent radical scavenging activities against the DPPH and ABTS assay techniques, all derivatives were found to be active. Some compounds are capable of reducing ferric ions and have an IC50 value of 1.30 mM. The compounds with methyl substitution show the increased activity. [64].



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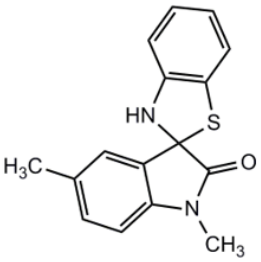
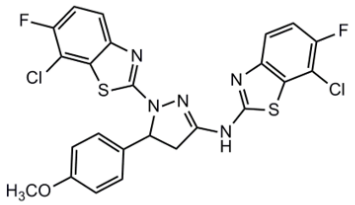


67

IC50 DPPH for 66: 1.30 mM, 1.02 mM ABTS, and 1.36 mM Reducing Power
IC50 DPPH for 67: 0.98 mM, 0.98 mM ABTS, and 0.70 mM Reducing Power

The *p*-OCH3 and *p*-OH modified fluorobenzopyarazoline derivatives made by Using DPPH methods, Hazra *et al*. **(2011)** demonstrated antioxidant potential at 0.01 mM concentration (68). At doses of 2-4 mM, the same compounds exhibited ferric ion reduction capability. Here, the activity was boosted by using pyrazoline bridged benzothiazole derivatives. The activity was elevated by replacing with electron-donating groups in the fourth positions. [65].



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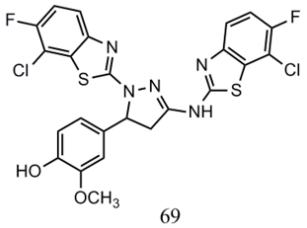
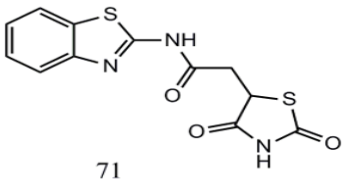


69

By using the DPPH scavenging and Fenton reaction methods, a set of benzothiazole isothiourea analogues had evaluated for antioxidant potential (Lauraetal.,2016).(E)-5-[(benzothiazol-2-ylimino) (methylthio)methylamino]-2-hydroxyben zoic acid (70) was tested for an ex-vivo acetaminophen-induced hepatotoxicity model because it outperformed the benchmark by 37% at 0.013 mM concentration in terms of scavenging, demonstrating greater activity. These substances showed that they could lower levels of malondialdehyde and glutathione as well as cytochrome P450, providing a reactive intermediate by scavenging free radicals. [66].

The scavenging of DPPH radicals, superoxide anion ions, lipid peroxidation, and hemolysis inhibition were tested using benzothiazole thiazolidinedione-2-acetamides that had been produced. The EC50 values for DPPH radical scavenging varied from 20 to 60 M, which were higher than the benchmark (ascorbic acid, 40.28 M). Compounds containing benzothiazole-2-amine shown strong antioxidant DPPH, LPI, and EHI potential. The 6-methylbenzothiazole-2-amine derivative showed exceptionally good IL-1 suppression effectiveness, having IC50 value of 6.38 M. Methoxy- and nitro-substituted derivatives of benzothiazoles displayed high antioxidant activity. [67].



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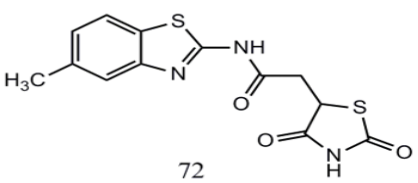

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CONCLUSION AND FUTURE PERSPECTIVES

Various studies have shown that the benzothiazole is a flexible, versatile molecule with the ability to treat both bacterial and cancerous strains. Researchers in medicinal chemistry who are developing new molecules with benzothiazole scaffolds may find this review to be a novel field of study. Numerous derivatives with strong biological activity have been created by researchers, however further clinical research on these substances is still needed.

FUNIDNG STATUS

Nil.

CONFLICT OF INTEREST

None conflict of interest has been declared by the authors.

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