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# BENZOTHIAZOLE: A MOLECULE WITH BROAD SPECTRUM OF ANTIMICROBIAL ACTIVITY

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## ABSTRACT

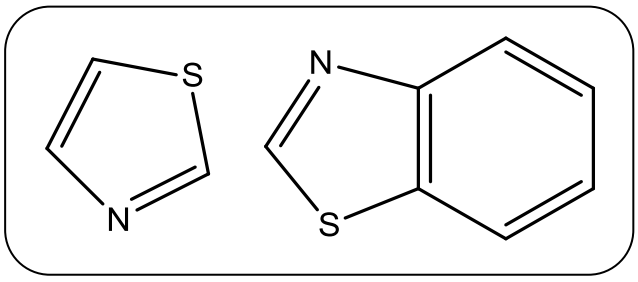
Benzothiazoles are the important pharmacophore and privileged sub-structures in medicinal chemistry owing to their involvement as a key component for various biological activities. The high profile of biological applications displayed by compounds associated with these nuclei have prompted wide studies for their synthesis a large number of efforts were made to synthesize different heterocyclic compounds a nd their derivatives in the past decade and were found to posses promising antimicrobial activity. Extensive biochemical and pharmacological studies have confirmed that benzothiazole derivatives are effective against various strains of microorganisms. Although benzothiazole moiety is very small but is fascinated by scientists becau se of the due to the structural similarity with purine, antibacterial ability of these compounds manifested their competition with purines resulting in the distinct inhibition of the synthesis of nucleic acids and proteins inside the bacterial cell wall. This review is mainly an attempt to present the research work reported in the recent scientific literature on antimicrobial activitity of benzothiazole compounds.

**KEY WORDS:** Benzothiazole, Antibacterial activity, Antifungal activity.

## INTRODUCTION[1-7]

Benzothiazole is a heterocyclic compound, weak base, is made from thiazole ring fused with benzene ring, having various biological activities and still of great scientific interest now a days. Benzothiazole and its derivatives are the most important heterocyclic compounds, which are common and integral feature of a variety of natural products and pharmaceutical agents. The broad spectrum of pharmacological activity in individual benzothiazole derivative indicates that, this series of compounds is of an undoubted interest. The related research and developments in benzothiazole-based medicinal chemistry have become a rapidly developing and increasingly active topic.

Heterocycles bearing nitrogen and sulphur atom constitute the core structure of a number of biologically interesting compounds viz. thiadiazine, thiazole and benzothiazole. Among all sulphur and nitrogen containing heteronucles, benzothiazoles found to be most interesting nucleus regarding research because it used as a starting material for the synthesis of larger, usually bioactive structures. Modifications on the benzothiazole nucleus have resulted in a large number of compounds having diverse pharmacological activities. Thus, synthesis and biological activities of benzothiazole derivatives have long been focused for interest of research in the field of medicine.The basic structure of benzothiazole consist of benzene ring fused with 4, 5 position of thiazole.



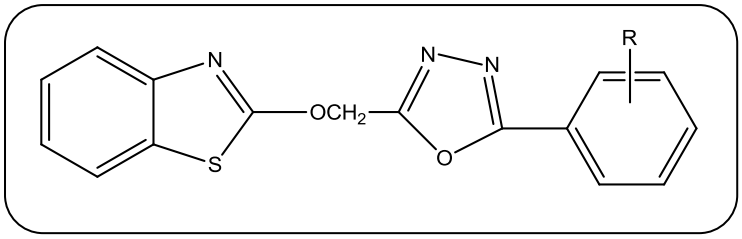

Benzothiazole ring is present in various marine or terrestrial natural compounds, which have useful biological properties. In last few years it was reported that benzothiazole, its bioisosters and derivatives had antimicrobial activity against gram-negative as well as gram-positive bacteria and the yeast candida albicans and antimicrobial activity especially against enterobacter, pseudomonas aeruginosa, e.coli, and staphylococcus epidermidis.

Bacterial diseases can result in serious or life threatening complications such as kidney failure, severe dehydration, septicemia (which is life threatening blood infection),toxic

shock syndrome, coma, shortness of breath, high fever, seizure. The current antibacterial therapy suffers from drug related toxicity, severe drug resistance, non optimal pharmacokinetics, and serious drug-drug interactions. Therefore, there is an emergent need to develop novel antimicrobial drugs with higher efficiency, broader spectrum, and lower toxicity. Benzothiazole are remarkably effective compounds both with respect to its inhibitory activity and its favorable selectivity ratio. Extensive biochemical and pharmacological studies have confirmed that benzothiazole molecule are effective against various strains of microorganisms. So, benzothiazole are regarded as a promising class of bioactive heterocyclic compounds that exhibit a range of biological activities. Given below is a brief account of various alterations conducted on benzothiazole ring and its antimicrobial activity.

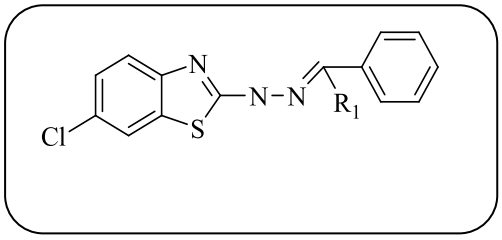
## ANTIMICROBIAL ACTIVITY OF BENZOTHIAZOLE

- Taher P. *et al*[8] have reported Synthesis and antibacterial activity of novel benzothiazole based 1,3,4-oxadiazole derivatives against *Staphylococcus aureus, Escherichia coli.*




| R= | -Cl |
|---|---|
| | $-NH_2$ |
| | $-CH_3$ |
| | -H |

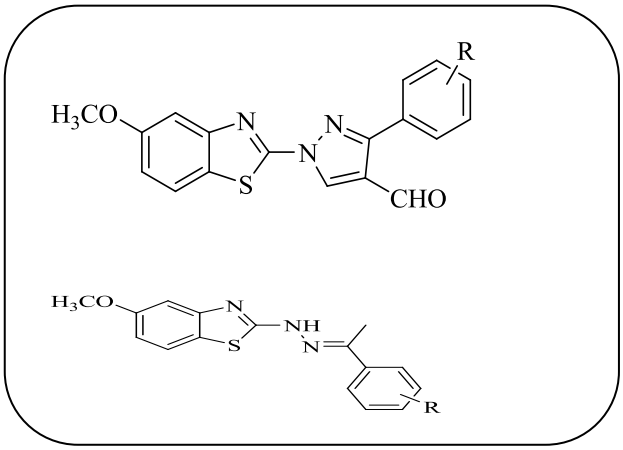
- Nitendra K.S. *et al*[9] have reported Synthesis, characterization and antimicrobial evaluation of some 1,3-benzothiazole-2-ylhydrazonederivatives against the four pathogenic bacterial strains *Bacillus subtilis, Escherichia coli, Klebsiella pneumoniae* and *Pseudomonas alkaligenes* and three fungal strains *Aspergillus niger, Rhizopus oryzae and Candida albicans.*




| $R_1$ | $R_2$ |
|---|---|
| -H | $-CH_3$ |
| $-CH_3$ | $-OCH_3$ |
| $-CH_3$ | $-NO_2$ |
| $-C_6H_5$ | -H |

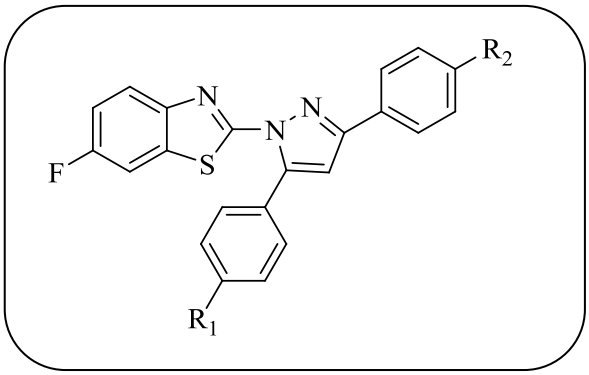
- Deepa C. *et al*[10] have reported synthesis and antimicrobial evaluation of some new substituted benzothiazole derivatives and evaluate antimicrobial activity against

*Staphylococcus aureus, Escherichia coli, Klebsiella pneumonia and Pseudomonas aeruginosa* types of bacteria and some fungus species.



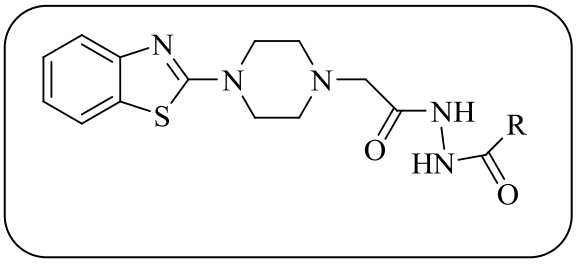

| R= | 2-OH |
|---|---|
| | 4-OH |
| | 2,5-diOH |
| | 2-$OCH_3$ |
| | 4-$OCH_3$ |

- Balaji P.N. *et al*[11] et al reported synthesis of some heterocyclic pyrazole and its derivatives from fluoro substituted hydrazino benzothiazole and evaluated anthelmintic activity as well as antimicrobial activity against *Staphylococcus aureus, Escherichia coli* type of bacteria.



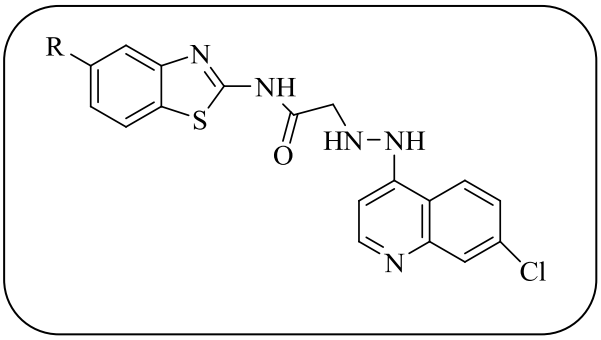

| $R_1$ | $R_2$ |
|---|---|
| -Cl | -OH |
| -$OCH_3$ | -$NO_2$ |
| -Furan | -$OCH_3$ |

- Mahmoud A.T *et al*[12] have reported synthesis and evaluation of new benzothiazole derivatives as antimicrobial agent against *Staphylococcus aureus, Escherichia coli, and Candida albicans* types of bacteria.



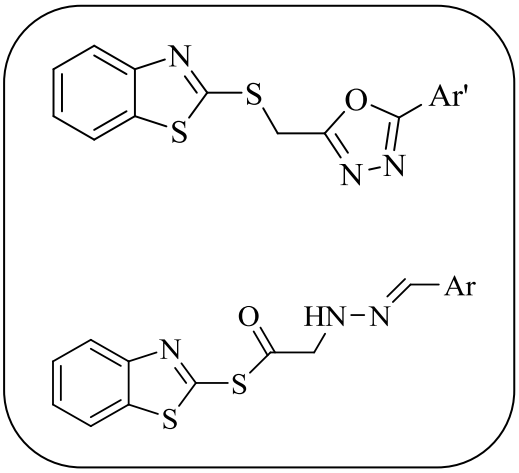

| R | $C_6H_5$ |
|---|---|
| | 3-$OCH_3C_6H_4$ |

- Manoj N.B. *et al*[13] *et al* have reported synthesis of novel N-(benzo[d]thiazol-2-yl)-2-(2-(6-chloroquinolin-4-yl)hydrazinyl)acetamide derivatives containing quinoline linkage as potent antibacterial activity against *Escherichia coli*, *Micrococcus luteus*, *Bacillus cereus.*



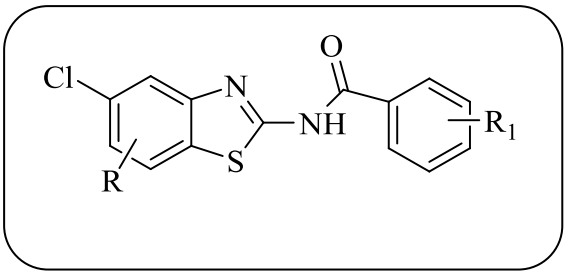

| R= | H |
|---|---|
| | $CH_3$ |
| | $OCH_3$ |
| | $NO_2$ |
| | F |

- Manju P. *et al*[14] have reported Design, synthesis and molecular docking study of benzothiazole derivatives and evaluated for antimicrobial activity against *Escherichia coli*, *Staphylococcus aureus*, *Candida albicans.*



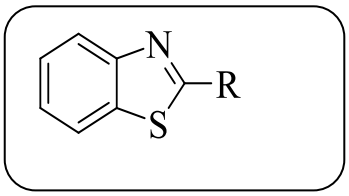

| Ar’ | Ar |
|---|---|
| 4-$ClC_6H_5$ | 2-OH-6-$ClC_6H_5$ |
| 4-$NH_2$ | 2-$OHC_6H_4$ |
| $C_6H_5$ | -$C_4H_3O$ |

- Domenico A. *et al*[15] have reported Synthesis and antimicrobial evaluation of a new series of *N*-1,3-benzothiazol-2-ylbenzamides against *Enterococcus faecalis*, *Escherichia coli*, *Staphylococcus aureus.*



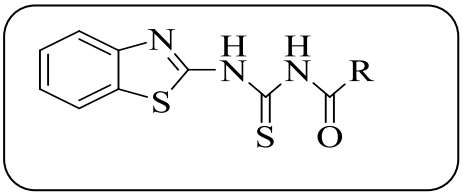

| R | $R_1$ |
|---|---|
| 4-F | 2,3-$F_2$ |
| 5-F | 2,5-$F_2$ |
| | 3.5-$F_2$ |

- Kaushik M. P. *et al*[16] have reported Exploration of in vitro time point quantitative evaluation of newly synthesized benzimidazole and benzothiazole derivatives as potential antibacterial agents against Gram-positive bacteria *Staphylococcus aureus, Bacillus cereus*, and Gram-negative bacteria *Vibrio cholerae,Shigella dysenteriae* and *Escherichia coli.*



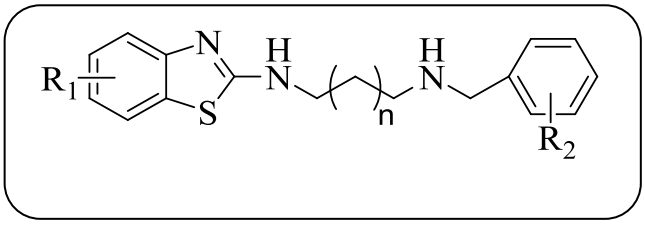
| R | 2-Et$C_6H_4$ |
|---|---|
| | 4-$NO_2C_6H_4$ |
| | 4-$OHC_6H_4$ |

- Sohail S. *et al*[17] have reported Synthesis, characterization and biological evaluation of some thiourea derivatives bearing benzothiazole moiety as potential antimicrobial and anticancer agents. Antimicrobial activity evaluate against various gram positive and gram negative bacterial and various strains of fungus.



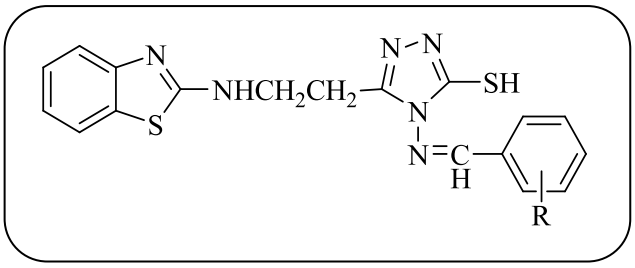
| R | 4-nitrophenyl |
|---|---|
| | n-butyl |
| | phenyl |

- Gu He. *et al*[18] have reported Preparation, antibacterial evaluation and preliminary structure–activity relationship (SAR) study of benzothiazole and benzoxazol-2-amine derivatives against methicillin-resistant *Staphylococcus aureus* (MRSA) or vancomycin-resistant *Enterococcus faecalis* (VRE) as well as *Escherichia coli.*



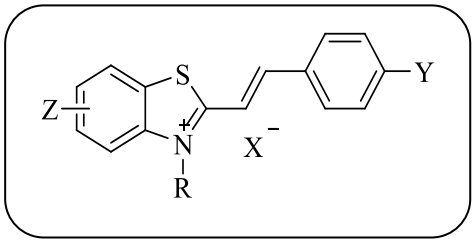
| **$R_1$** | **$R_2$** |
|---|---|
| H | 4-OMe |
| 6-Cl | 3,4-diCl |
| 5-F | 3,4-diCl |

- Balram S. *et al*[19] have reported Synthesis and evaluation of some new benzothiazole derivatives as potential antimicrobial agents against fungus strains *Candida albicans* and *Aspergillus niger* and bacterial strains *Streptomyces griseus, Escherichia coli, Bacillus subtilis.*



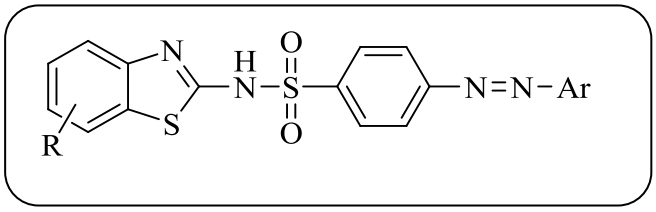
| R | H |
|---|---|
| | 2-$NO_2$ |
| | 3-$NO_2$ |
| | 2-Cl |

❖ Peter M. *et al*[20] have reported Synthesis and study of new antimicrobial benzothiazoles substituted on heterocyclic ring and evaluate activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Micrococcus luteus* and *Enterococcus faecalis.*



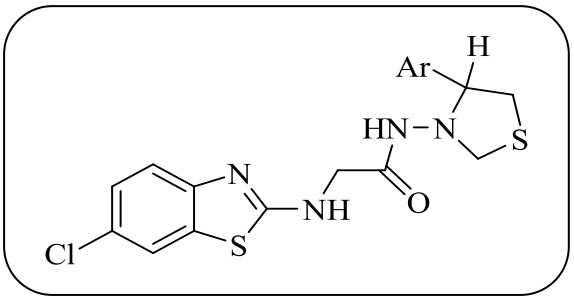
| Z | R | Y | X |
|---|---|---|---|
| 5-$NO_2$ | Methyl | -$N(CH_3)_2$ | I |
| 6-$NO_2$ | Methyl | -OH | Br |
| 5-NH-Ac | Allyl | -$N(CH_3)_2$ | I |
| 6-NH-Ac | Propgyl | N-piperidinyl | Br |

❖ Pritesh P. *et al*[21] have reported Design, synthesis and characterization of novel molecules comprising benzothiazole and sulphonamide linked to substituted aryl group via azo link as potent antimicrobial agents evaluated for their antibacterial activity against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli*, *Pseudomonas aeruginosa.*



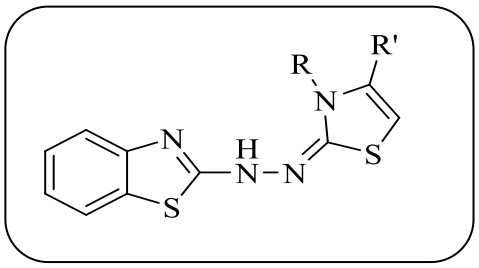
| R | Ar |
|---|---|
| 6- chloro | (4-hydroxynaphthalen-1-yl) diazenyl |
| 6-methyl | (2-hydroxynaphthalen-1-yl)diazenyl |
| 7-chloro-6-fluro | (4-hydroxyphenyl)diazenyl |

- Saarangi R. *et al*[22] have reported Synthesis, Characterization and Antimicrobial studies of new novel derivatives of 2-amino-6-chlorobenzothiazole against *Klebsiella pneumoniae, Proteus vulgaris, Bacillus subtilis.*



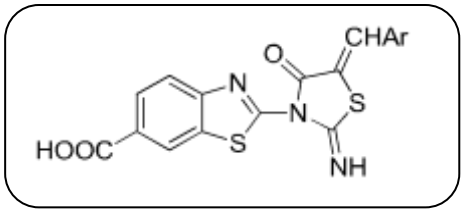
| **Ar** |
|---|
| -$C_6H_4$-4-Cl |
| -$C_6H_4$-3-$NO_2$ |
| -$C_6H_4$ |

- Mahran M.A. *et al*[23] have reported Synthesis of some new benzothiazole derivatives as potential antimicrobial and antiparasitic agents as well as antimicrobial activity was evaluated against *Staphylococcus aeurus, Escherichia coli and Candida albicans.*



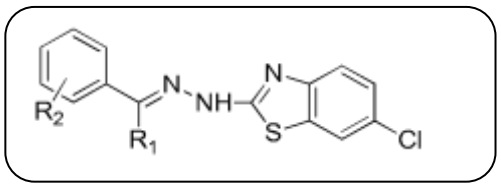
| R | R’ |
|---|---|
| 4-$C_6H_4$(Cl) | 4- $C_6H_4(NO_2)$ |
| -$C_2H_5$ | 4- $C_6H_4(NO_2)$ |

- Chavan A. A. *et al*[24] have reported synthesis of a series of 2-[5-(arylidene)-2-imino-4-oxo-thiazolidin-3-yl] benzothiazole-6-carboxylic acid. These series of compounds were screened for their antibacterial as well as antifungal activity.



| Ar = | 2-$ClC_6H_4$ | $C_6H_5$ | 4-$NO_2C_6H_4$ | 4-$ClC_6H_4$ |
|---|---|---|---|---|
| | 4-$OHC_6H_4$ | 3-$BrC_6H_4$ | 4-$OCH_3C_6H_4$ | 3-$NO_2C_6H_4$ |

- V. Asati. *et al*[25] have reported synthesis and antibacterial, antifungal as well as antimicrobial activity of a series of 1,3-benzothiazole-2-yl-hydrazone derivatives**.**



| $R_1$ = | $CH_3$ | $C_6H_5$ | H |
|---|---|---|---|
| $R_2$ = | $NO_2$ | Br | $NH_2$ |
| | F | OH | $CH_3$ |

Apart from antibacterial activity, benzothiazole nucleus also possess a wide spectrum of biological activity such as anti-inflammatory[26], anticancer[27], antiepileptic[28], antiviral[29], antitumor[29] and antiurease activities[30].

## CONCLUSION

From the above literature review concluded that the benzothiazoles and their derivatives have shown a wide spectrum of antimicrobial activity. It is a versatile nucleus in the field of medicinal chemistry. Hence this unique molecule must serve as future therapeutic leads of developing various biological agents. The biological profiles of this new generation of benzothiazoles represent much progress with regard to the older compounds.

## ACKNOWLEDGEMENTS

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