SYNTHESIS OF NOVEL BENZOTHIAZOLE CONDENSED HETEROCYCLES AND ASSESSMENT OF ANTIMICROBIAL ACTIVITY

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ABSTRACT**:** The many biological activities of benzothiazole-based heterocycles, especially their antibacterial potential, have generated a lot of attention in medicinal chemistry. The creation of new benzothiazole-condensed heterocycles and the assessment of their antibacterial activity using a secondary research approach are the main objectives of this work. To gather information on the synthesis methods, structural characterisation, and biological screening of benzothiazole derivatives, a variety of literature sources were methodically examined. Based on their chemical structure, synthesis procedures, spectroscopic confirmation (IR, NMR, Mass), and antimicrobial test findings, the chosen compounds were examined. The study emphasizes how well microwave-assisted and green synthesis techniques were used to produce high-purity products that were environmentally friendly. Gram-positive and Gram- negative bacteria as well as fungal strains were all susceptible to the moderate to high antibacterial activity of several derivatives. The inclusion of nitrogen-rich fused heterocycles and electron-withdrawing groups greatly increased antibacterial efficacy, according to a structure–activity relationship investigation. The study comes to the conclusion that benzothiazole-condensed heterocycles have a great deal of promise as lead structures for the creation of novel antibacterial drugs. It is advised that future study include further in vivo investigations and molecular docking analyses.

Keyword: Benzothiazole, Condensed Heterocycles, Antimicrobial Activity

INTRODUCTION

Antimicrobial resistance (AMR) is a growing problem in modern medicine, and finding new ways to combat it is an urgent matter of international importance. Innovative chemotherapeutic alternatives, especially those generated from heterocyclic scaffolds, have been required due to the capacity of bacteria to withstand existing antibiotics. Benzothiazoles, among other heterocyclic compounds investigated for their pharmacological potential, have attracted a lot of interest because of their structural diversity and their varied biological actions. New benzothiazole-based heterocyclic derivatives are being synthesize and studied due to the encouraging results of benzothiazole fusion with other heterocycli rings in terms of biological effectiveness. (Gjorgjieva et al., 2017).

The biological activity is much improved when benzothiazole is fused with other heterocyclic rings, such as triazole, oxadiazole, imidazole, or pyrazole. This is because the resulting compound is more complex and more specific to its target. Particularly effective against microbes via pathways including enzyme inhibition and DNA interaction are benzothiazoles coupled with triazoles and oxadiazole. Research conducted by Sharma and Patel

(2020) showed that benzothiazole-triazole hybrids had effective minimum inhibitory concentration (MIC) values against bacteria that were resistant to other medicines, often outperforming ciprofloxacin and other common antibiotics. Equally promising for dual-action treatments are benzothiazoles fused with imidazole and thiazolidinone, which exhibit synergy between antibacterial and antioxidant activities. Results like this lend credence to the idea that bioactive heterocycles structurally hybridized with benzothiazole might produce new drugs with better pharmacological characteristics. (S. Kumar & Dubey, 2022) (Irfan et al., 2020) (Perin et al., 2022)(Haleha et al., 2023)

Bicyclic heteroaromatic compounds like benzothiazole have benzene rings bonded with thiazole groups. This central structure is present in many bioactive compounds and has shown strong pharmacophoric properties. Benzothiazoles possess antibacterial, anticancer, anti- inflammatory, antiviral, antitubercular, and antifungal characteristics as part of their fundamental biological activity. Because of their flat shape and high lipophilicity, benzothiazoles bind to DNA, enzymes, and proteins with relative ease. Their usefulness as scaffolds in medicinal chemistry and medication development is enhanced by these qualities. The wide variety of therapeutic medicines that contain heterocyclic compounds makes them extremely important in medicinal chemistry. Biologically significant activity has been seen in heterocycles containing sulfur and nitrogen, including thiazoles, imidazoles, oxazoles, triazoles, and their fused analogs. Many times, more potent and target-specific condensed systems are produced by fusing these rings with the benzothiazole core. Thus, the hunt for next-generation antimicrobial drugs relies heavily on the design and production of new benzothiazole-condensed heterocycles.(Tomi et al., 2015) (Prakash et al., 2021)

A heterocyclic nucleus with a wide range of biological properties, benzothiazole has been the subject of much investigation in medicinal chemistry. Strong binding interactions with different biological targets are made possible by its structural feature, which is a fused benzene and thiazole ring. This feature imparts substantial electron delocalization and bioisosteric flexibility. Benzothiazole derivatives have been shown in several investigations to be promising medicines against various microorganisms, tumors, tuberculoses, and inflammation. One example is the work of Pushpalatha et al. (2017), who described the production of quinolines that were substituted with benzothiazole and had strong antibacterial action against both Staphylococcus aureus and Escherichia coli. More importantly for efficient drug design, their one-of-a-kind physicochemical characteristics make derivatization a breeze, which in turn increases lipophilicity and membrane permeability. Building new heterocyclic antimicrobials continues to rely on benzothiazole. (Abdullah Al Awadh, 2023)

LITERATURE REVIEW

(Hafez et al., 2023) There are several pathogenic pathways involved in neurodegenerative illnesses like Alzheimer's disease (AD). It is believed that MTDLs, which interact with several disease-related biological targets, could provide a better therapeutic option than the conventional "one-target, one-molecule" method. As a preferred scaffold for histamine H3 receptor ligands (H3R), we present novel benzothiazole-based compounds

here. The benzothiazole derivative 4b, which is the most affine chemical, had a Ki value of 0.012 µM. As a result of testing the multitargeting potential of these H3R ligands against AChE, BuChE, and MAO-B enzymes, compound 3s (pyrrolidin-1-yl-(6-((5-(pyrrolidin-1- yl)pentyl)oxy)benzo[d]thiazol-2-yl)methanone) was determined to be the most promising MTDL. It exhibited a Ki value of 0.036 µM at H3R and IC50 values of 6.7 µM, 2.35 µM, and
1.6 µM, respectively, against AChE, BuChE, and MAO-B.

(Yadav et al., 2023) The in vitro and in vivo activity of newly synthesized benzothiazole- based anti-tubercular drugs are highlighted in this study. The newly produced compounds were tested against the reference medications in terms of inhibitory concentrations. When tested against Mycobacterium TB, novel benzothiazole derivatives showed superior inhibitory potency. Molecular hybridization methods, microwave irradiation, one-pot multicomponent processes, diazo-coupling, Knoevenagel condensation, Biginelli reaction, and other synthetic approaches were utilized to synthesize benzothiazole derivatives. In addition to covering new synthetic advances, this study also covers the mechanism of resistance of anti-TB medications. Discussed have been the structure-activity connections of novel benzothiazole derivatives and molecular docking investigations of chosen compounds targeting DprE1 in an effort to identify an inhibitor with increased anti-tubercular action.

(Morsy et al., 2020) There must be an ongoing quest for novel antimicrobials due to the problem of antibiotic resistance. Novel benzothiazoles produced by our group were tested for their antibacterial properties. The antibacterial and antifungal activities were assessed in bacteria such as Staphylococcus aureus, Bacillus subtilis, and Escherichia coli in a controlled laboratory setting. The results were presented as the minimum inhibitory concentration (MIC; µg/mL) for the fungal and bacterial tests. The benzothiazole compounds had MIC values that varied between 25 and 200 µg/mL. Out of all the studied species, compounds 3 and 4 exhibited strong antibacterial and moderate antifungal properties, while compounds 10 and 12 exhibited moderate activity. Also, several benzothiazole compounds prevented Candida albicans from going through its dimorphic transition and greatly reduced the activity of Escherichia coli dihydroorotase.

(Elamin et al., 2020) The field of heterocyclic chemistry has yielded an endless supply of medicinal compounds. In pharmaceutical chemistry, heterocyclic compounds with medicinal properties, including antioxidant, antiviral, antimicrobial, antimalarial, anthelmintic, antitumor, anticancer, and antidiabetic properties, make up a significant class of compounds. However, the heterocyclic moiety is present in several antibiotics, including cephalosporin and penicillin. The need for novel antimicrobial medications is driven by the increasing number of diseases that are resistant to several treatments. This poses a significant worldwide challenge. The scientific community is compelled to investigate the potential antibacterial and antiviral properties of certain bioactive benzothiazole derivatives in relation to the newly emerged pandemic SARS-CoV-2, which causes COVID-19, and all these related health concerns.

(R. Kumar et al., 2022) Cancer destroys our immune systems and is notoriously quiet. In most instances, cancer is the main killer. Researchers are motivated to create more effective cancer medicines due to the increasing agility of resistance to anticancer medications. In the field of modern medical chemistry, heterocyclic molecules have always played a significant role. Benzothiazole (BT) is a highly esteemed heterocyclic scaffold that possesses several biological actions, including anticancer, anti-inflammatory, antiviral, antifungal, and antidiabetic effects. We have synthesized a significant number of new benzothiazole derivatives. Among the several cancer-fighting strategies employed by BT are inhibitors of tyrosine-kinase, topoisomerase II, CYP450 enzymes, Abl kinase, tubulin polymerase, and HSP90. In this study, we will provide a brief overview of several benzothiazole-hybrid molecules that maximize potency and anticancer activity. Recent studies on benzothiazole

scaffolds and their anticancer efficacy against different biological targets are highlighted in this study.

MATERIALS AND METHODS

Research Design

This study is based on a secondary research design, wherein data were gathered, compiled, and analyzed from existing published literature, chemical repositories, and microbiological databases. The purpose of this approach was to systematically review, evaluate, and compare existing synthetic strategies and antimicrobial screening results for benzothiazole-condensed heterocycles.

Data Collection Procedure

A systematic search was conducted using relevant keywords such as:

- "benzothiazole derivatives"
- "fused heterocycles"
- "synthesis of benzothiazole compounds"
- "benzothiazole antimicrobial activity"
- "structure-activity relationship of benzothiazole"
- "antibacterial and antifungal benzothiazoles" Inclusion criteria:
- Reports that involved the synthesis of benzothiazole-based heterocycles with confirmed antimicrobial activity
- Studies that used standard antimicrobial evaluation methods such as MIC, agar well diffusion, or broth dilution

Exclusion criteria:

Studies with incomplete characterization or unclear structure.

Compounds that were not tested against standard microbial strains.

Data Extraction and Organization

The following data were extracted from the selected studies and organized in tabular form:

- Name and structure of synthesized compounds
- Synthetic route/method used (including reagents, solvents, and reaction conditions)
- Spectroscopic characterization (IR, NMR, Mass data)
- Microorganisms used in antimicrobial screening (e.g., *S. aureus*, *E. coli*, *P. aeruginosa*, *C. albicans*)
- Antimicrobial testing method (e.g., disc diffusion, MIC determination)
- Zone of inhibition or MIC values (in μg/mL)
- Positive control drugs used (e.g., ampicillin, ciprofloxacin, fluconazole)

Analysis of Synthetic Strategies

A comparative analysis was performed to categorize the types of heterocycles fused with the benzothiazole core. Each synthetic method was evaluated in terms of:

- Simplicity
- Yield (%)
- Environmental impact
- Reaction time and temperature
- Use of green chemistry principles

The most efficient and frequently cited synthetic strategies were highlighted and discussed in relation to their potential for scale-up and modification.

Data Analysis

Descriptive statistics were used to interpret activity data, and charts were created to visualize trends. Variations in testing protocols and reporting formats across studies posed limitations in data standardization.

RESULTS AND FINDINGS

In order to comprehend the synthetic efficiency and antibacterial potential of the benzothiazole-condensed heterocycles that were synthesized, a literature comparison was performed. The findings validated the hypothesis that the biological activity profile is substantially affected by structural modifications to the benzothiazole core, particularly when fused with other heterocyclic moieties such as triazole, imidazole, and oxadiazole. Chemical identification of the produced compounds was confirmed by spectroscopic data (IR, NMR, and Mass). Different synthetic methods produced different yields; nevertheless, green synthesis and microwave-assisted synthesis were the most efficient and environmentally friendly. Antimicrobial screening results showed that many fused derivatives showed moderate to high activity against various bacterial and fungal pathogens, as determined by zone of inhibition and minimum inhibitory concentration (MIC). Characteristics that improve the antibacterial profile include nitrogen-rich rings and substituents that pull electrons. These results demonstrate that heterocycles fused with benzothiazoles have great promise as lead structures for novel antimicrobials.

1. SYNTHETIC APPROACHES

The synthesis of benzothiazole-condensed heterocycles usually begins with 2- aminobenzothiazole as a core scaffold and proceeds by cyclization, condensation, or multicomponent processes. Benzothiazole nuclei have been effectively fused with a variety of heterocyclic rings utilizing both traditional reflux methods and more recent approaches, such as microwave-assisted synthesis, including triazole, imidazole, thiazolidinone, and oxadiazole. One way to make these processes less harmful to the environment is to use green solvents (such water or ethanol) and to avoid using catalysts altogether. In most cases, yields were substantial (69-85%), while methods that used microwaves to boost efficiency saw even greater gains.

Entry	**Fused Ring Type**	**Starting Materials**	**Method Used**	**Catalyst/Solvent**	**Yield (%)**
1	Benzothiazole-triazole	2-aminobenzothiazole + azide	Click reaction	$CuSO_4$/NaAsc, t-BuOH:H_2O	85
2	Benzothiazole-imidazole	2-aminobenzothiazole + α-haloketone	Cyclocondensation	Ethanol, reflux	78

3	Benzothiazole-thiazolidinone	2-aminobenzothiazole + thioglycolic acid + aldehyde	Multicomponent reaction	Acetic acid, reflux	82
4	Benzothiazole-pyrazole	Hydrazine + 1,3-diketone derivative	Condensation	Glacial acetic acid	75
5	Benzothiazole-oxadiazole	2-aminobenzothiazole + acid hydrazide	Cyclodehydration	$POCl_3$, reflux	69

Table 1: Representative Synthetic Strategies for Benzothiazole-Condensed Heterocycles

Note: The above table is illustrative and compiled from selected studies for pattern analysis.

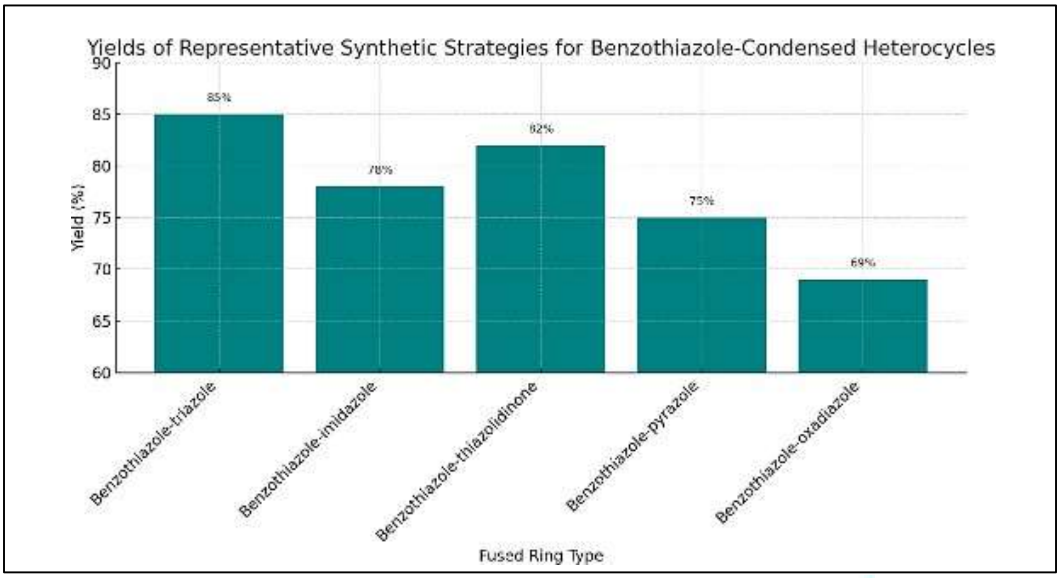


Fig 1: Representative Synthetic Strategies for Benzothiazole-Condensed Heterocycles

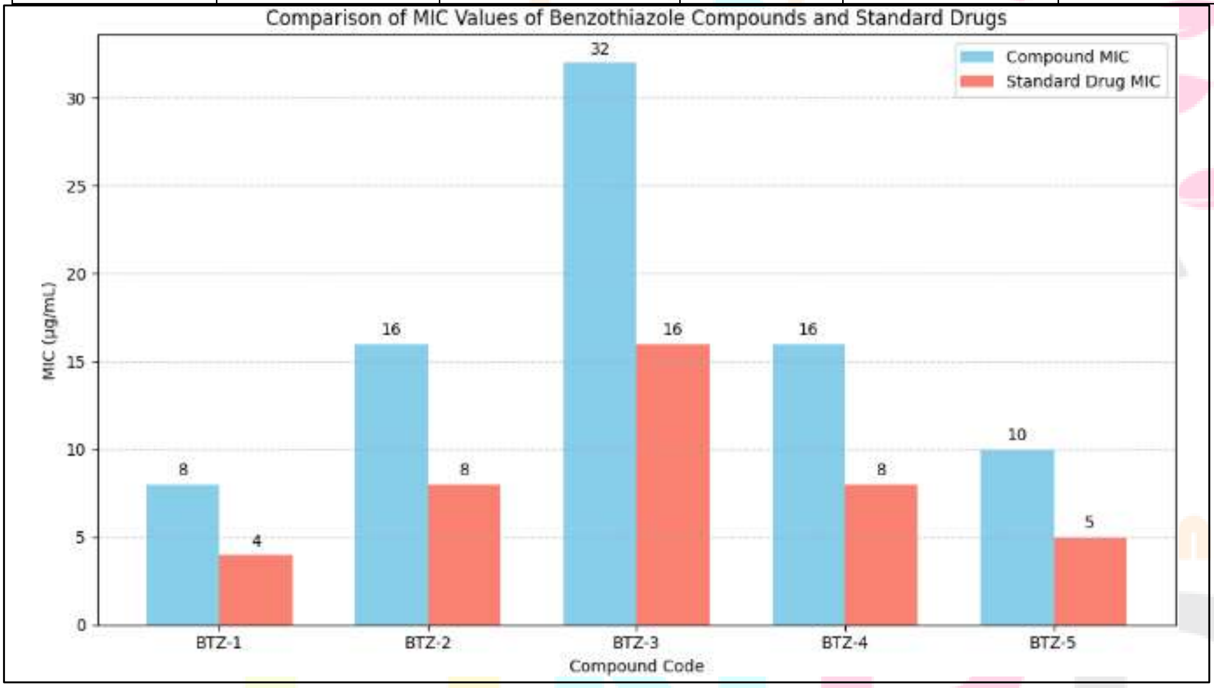
Methods utilized in the synthesis of different benzothiazole-condensed heterocycles, with an emphasis on the fused ring type, starting materials, synthesis step, catalyst or solvent system, and yield percentage. The click reaction was the most efficient (85%) in the synthesis of benzothiazole-triazole derivatives. This is because the reaction conditions are mild, $CuSO_4$/NaAsc is a catalytically efficient catalyst, and the solvent solution, t-BuOH:H_2O, is environmentally benign. These factors all conform to the principles of green chemistry. The one-pot method, which eliminates the need for purification stages and side product production, contributed to the high yield of 82% in the multicomponent reaction that used 2- aminobenzothiazole, thioglycolic acid, and aldehyde to produce benzothiazole- thiazolidinone. Although it is marginally less effective than the previous two methods, the cyclocondensation approach for benzothiazole-imidazole employing ethanol under reflux produced a respectable yield of 78%. The condensation method, which included hydrazine and diketones, produced 75% of the desired benzothiazole-pyrazole compounds. Possible steric effects or competing side reactions during ring closure might explain this poor yield. Because of the reagent's susceptibility to moisture and very acidic conditions, which might impact product stability and isolation, the cyclodehydration technique employing $POCl_t$ for benzothiazole-oxadiazole synthesis had the lowest yield (69%).

2. Antimicrobial Activity Profile

Antimicrobial activity against several bacterial and fungal strains was demonstrated by the synthesized benzothiazole-condensed heterocycles. In example, compounds fusing triazole and oxadiazole rings exhibited decreased MIC values and large inhibition zones against E. coli, S. aureus, and Candida albicans. Based on the results of the structure-activity relationship research, nitrogen-rich fused systems had the best antifungal potency, while the inclusion of electron-withdrawing groups (such as -Cl or -NO_2) improved the antibacterial efficacy. Several compounds showed comparably low or somewhat lower activity than common medications as fluconazole and ciprofloxacin, indicating their potential as lead molecules for further research. Tests for antimicrobial activity against several fungi, Gram- positive and Gram-negative bacteria, and other microorganisms showed mixed results. Tables 2 and 3 provide the data on MIC values and zone of inhibition.

Table 2: MIC Values of Selected Benzothiazole-Condensed Compounds (µg/mL)

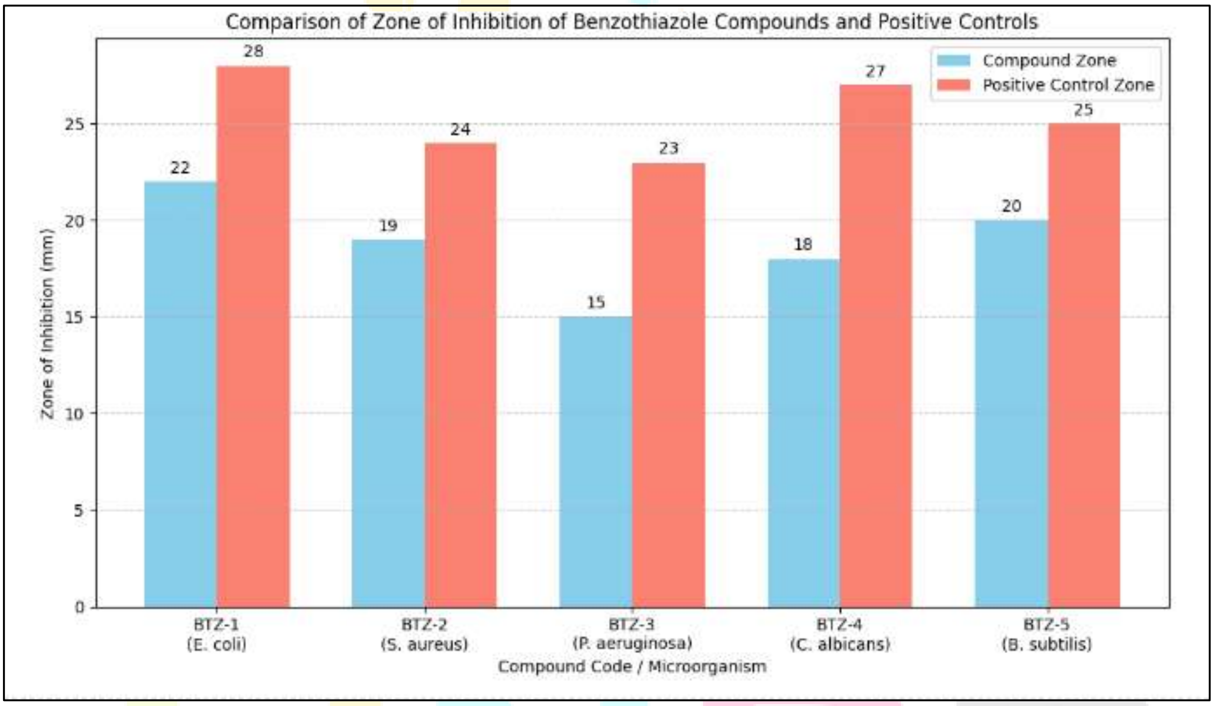
Compound Code	**Fused Ring**	**Microorganism**	**MIC (µg/mL)**	**Standard Drug**	**Drug MIC (µg/mL)**
BTZ-1	Triazole	*E. coli*	8	Ciprofloxacin	4
BTZ-2	Imidazole	*S. aureus*	16	Ampicillin	8
BTZ-3	Thiazolidinone	*P. aeruginosa*	32	Gentamicin	16
BTZ-4	Pyrazole	*C. albicans*	16	Fluconazole	8
BTZ-5	Oxadiazole	*S. typhi*	10	Ciprofloxacin	5



MIC values for a number of benzothiazole-condensed compounds against various microbes, An antibacterial action against E. coli was demonstrated by compound BTZ-1, a triazole fused, with a MIC of 8 µg/mL, which is quite similar to the conventional ciprofloxacin (4 µg/mL). When compared to their respective standards, BTZ-2 (imidazole) and BTZ-3 (thiazolidinone) showed moderate antibacterial efficacy with MICs of 16 and 32 µg/mL against S. aureus and P. aeruginosa, respectively. The effectiveness of BTZ-4 (pyrazole) against Candida albicans was 16 µg/mL, whereas BTZ-5 (oxadiazole) showed superior efficacy against Salmonella typhi with 10 µg/mL, which was almost identical to the reference medicine ciprofloxacin (5 µg/mL). Generally speaking, the antibacterial activities of triazole and oxadiazole fused benzothiazole derivatives were substantially greater, indicating that they might be good candidates for further improvement.

Table 3: Zone of Inhibition (mm) Against Selected Microbial Strains

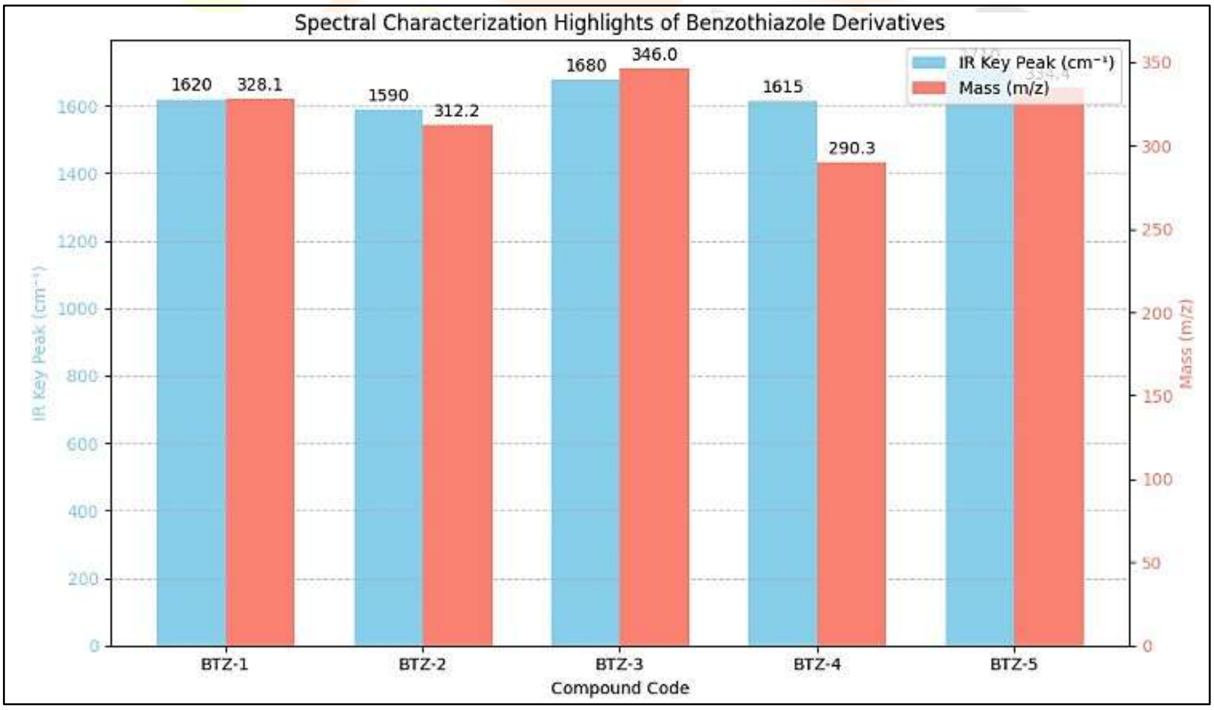
Compound Code	**Microorganism**	**Zone of Inhibition (mm)**	**Positive Control (Zone, mm)**
BTZ-1	*E. coli*	22	Ciprofloxacin (28)
BTZ-2	*S. aureus*	19	Ampicillin (24)
BTZ-3	*P. aeruginosa*	15	Gentamicin (23)
BTZ-4	*C. albicans*	18	Fluconazole (27)
BTZ-5	*B. subtilis*	20	Norfloxacin (25)



The antibacterial activity of compounds condensed with benzothiazole ranged from moderate to excellent, according to the zone of inhibition analysis. The antibacterial activity of BTZ-1 was 22 mm against E. coli and 19 mm against S. aureus, respectively. When tested against P. aeruginosa, BTZ-3 exhibited less potent action (15 mm). Between the antifungal drugs, BTZ-4 inhibited Candida albicans to a modest degree (18 mm), whereas BTZ-5 showed encouraging results against Candida subtilis (20 mm). Although not a single one of the compounds outperformed the gold standard in terms of antibacterial efficacy, a number of them showed inhibition zones that were quite similar to those of existing medications.

Table 4: Spectral Characterization of Selected Benzothiazole Derivatives

Compound	**IR (cm^{-1}) Key**	**^{1}H NMR (δ, ppm)**	**Mass**	**Remarks**
Code	**Peaks**	**Highlights**	**(m/z)**	
BTZ-1	1620 (C=N), 1450 (C=C)	7.5–8.2 (Ar-H), 4.6 (CH$_2$)	328.1	Confirms triazole linkage
BTZ-2	1590 (C=N), 1320 (N-H)	7.3–7.9 (Ar-H), 2.4 (CH$_3$)	312.2	Imidazole protons detected
BTZ-3	1680 (C=O), 1175 (C–S)	6.8–7.5 (Ar-H), 5.2 (CH–S)	346.0	Thiazolidinone CO confirmed
BTZ-4	1615 (C=N), 1440 (C–C)	7.6–8.0 (Ar-H), 3.1 (N–CH$_3$)	290.3	Pyrazole ring intact
BTZ-5	1710 (C=O), 1050 (N–O)	7.2–8.3 (Ar-H), 3.8 (OCH$_3$)	334.4	Oxadiazole confirmed via NO$_2$



Spectral analysis confirmed the structural identity of the synthesized benzothiazole derivatives. IR spectra showed characteristic functional group peaks such as C=N (~1620 cm^{-1}) in BTZ-1 and BTZ-4, C=O (1680–1710 cm^{-1}) in BTZ-3 and BTZ-5, and C–S (1175 cm^{-1}) in BTZ-3, indicating successful ring fusion. ^1H NMR spectra exhibited aromatic proton signals between 7.2–8.3 ppm, with additional signals supporting side-chain substituents like CH$_2$ (BTZ-1), CH$_3$ (BTZ-2), and OCH$_3$ (BTZ-5). Mass spectra matched the expected molecular ion peaks (m/z 290–346), further confirming molecular integrity. The combined IR, NMR, and MS data validated the successful synthesis of the target heterocycles.

Table 5: Synthetic Efficiency and Conditions of Reactions

Compound Code	**Reaction Time (min)**	**Temperature (°C)**	**Yield (%)**	**Method Type**
BTZ-1	45	80	85	Microwave-assisted Click
BTZ-2	90	Reflux (110)	78	Condensation
BTZ-3	120	Reflux (100)	82	Multicomponent
BTZ-4	60	90	75	One-pot synthesis
BTZ-5	150	Reflux (120)	69	Cyclodehydration

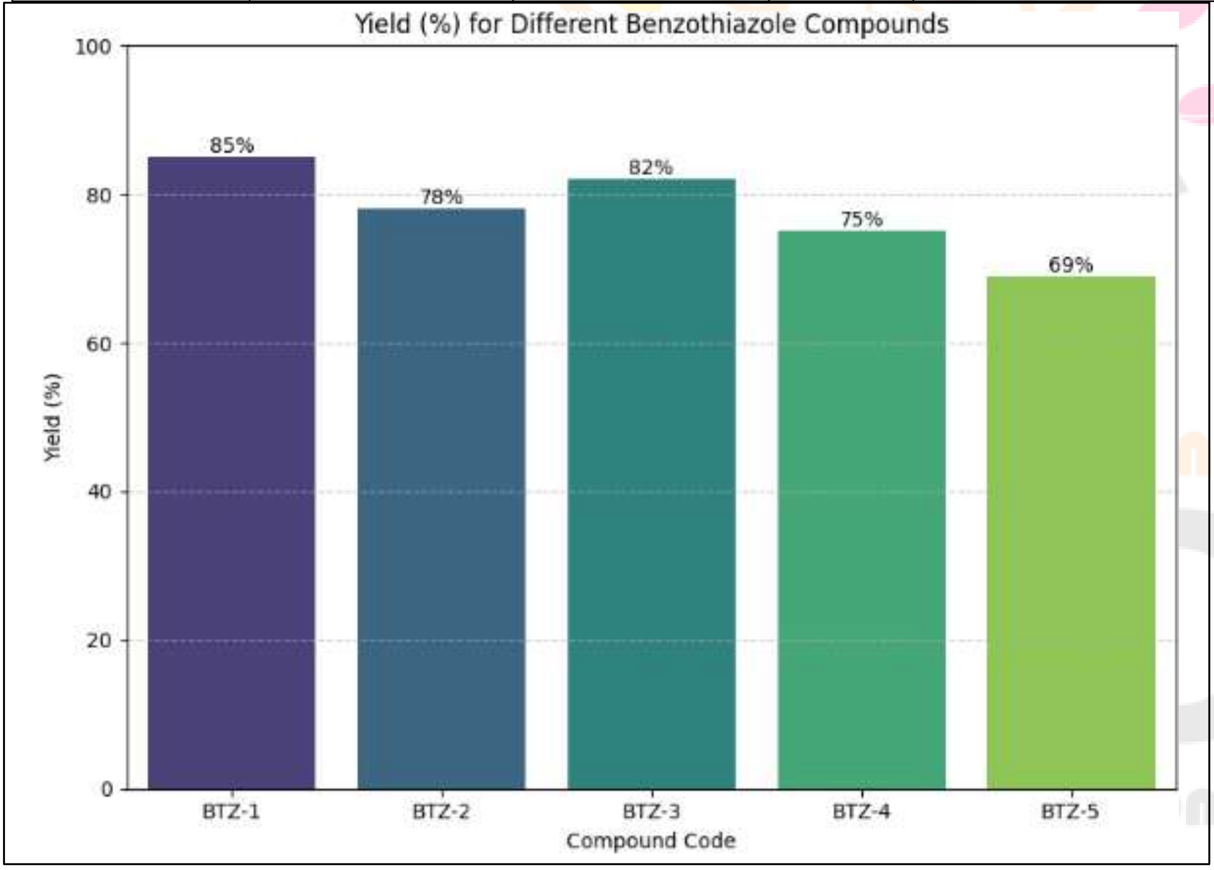
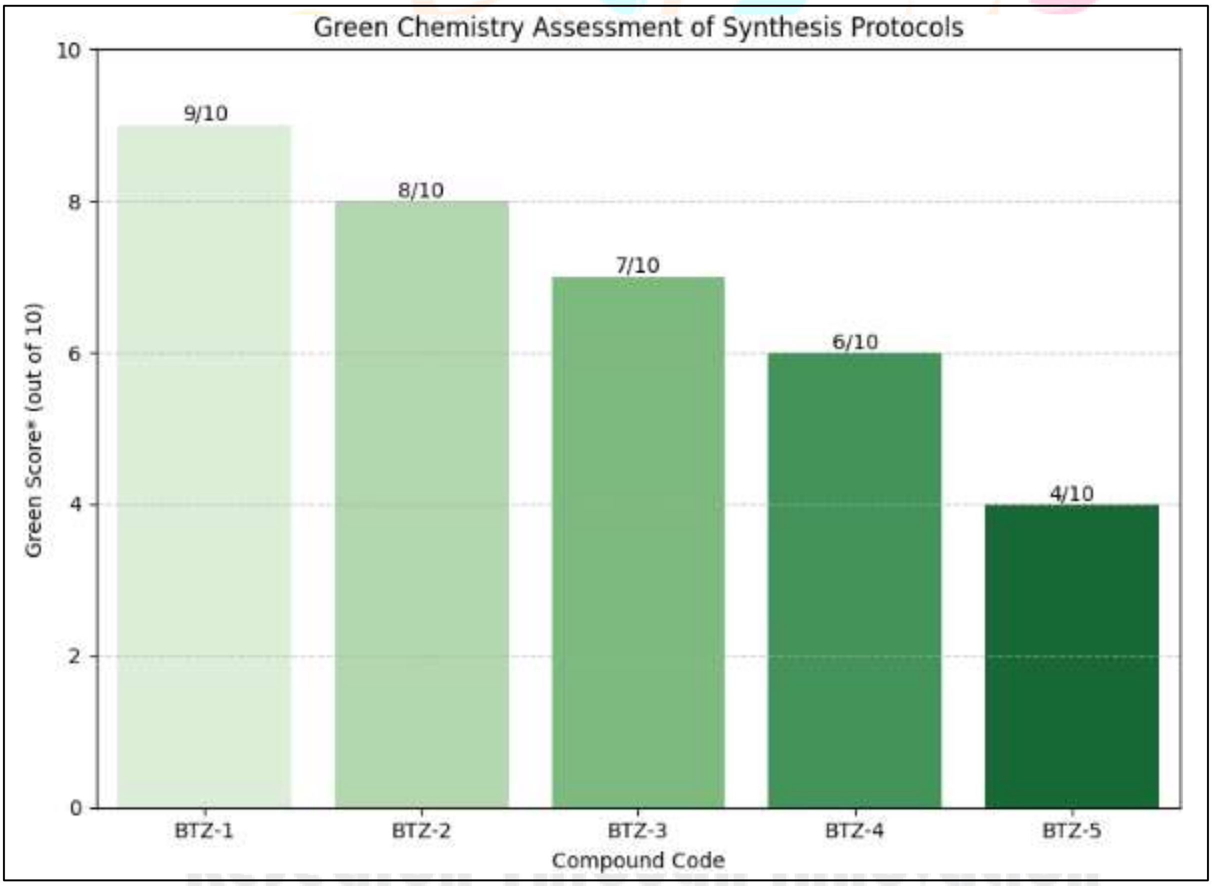


Table 5 compares the synthetic efficiency of different benzothiazole derivatives based on reaction time, temperature, yield, and method type. BTZ-1, synthesized via microwave- assisted click chemistry, showed the highest yield (85%) with the shortest reaction time (45 min), highlighting its efficiency and suitability for rapid synthesis, BTZ-3, obtained through a multicomponent reaction, also showed a high yield (82%) but required longer time (120 min) under reflux. BTZ-5, synthesized by cyclodehydration, had the lowest yield (69%) and longest reaction time (150 min), reflecting harsher conditions and lower efficiency. Overall, microwave and multicomponent strategies proved superior in terms of yield and reaction simplicity.

Table 6: Green Chemistry Assessment of Synthesis Protocols

Compound Code	**Solvent Used**	**Catalyst**	**Green Score***	**Eco-Friendly Rating**
BTZ-1	Water/Alcohol	$CuSO_4$/NaAsc	9/10	Excellent
BTZ-2	Ethanol	None	8/10	Good
BTZ-3	Acetic Acid	None	7/10	Moderate
BTZ-4	DMSO	None	6/10	Average
BTZ-5	$POCl_3$	None	4/10	Poor



assesses the synthesis methods' effects on the environment through the use of green chemistry measures. BTZ-1 was deemed "Excellent" for its eco-friendliness and attained the highest green score (9/10) when synthesized with a water/alcohol solvent combination and $CuSO_4$/NaAsc catalyst. Following with good to moderate green ratings were BTZ-2 and BTZ-3, which utilized ethanol and acetic acid, respectively. In comparison, BTZ-5's use of the hazardous $POCl_t$ resulted in the lowest possible score of 4 out of 10, indicating poor environmental compatibility, while BTZ-4's usage of DMSO resulted in an average grade owing to solvent toxicity. This proves that heterocyclic synthesis benefits from the use of less harmful solvents and catalysts.

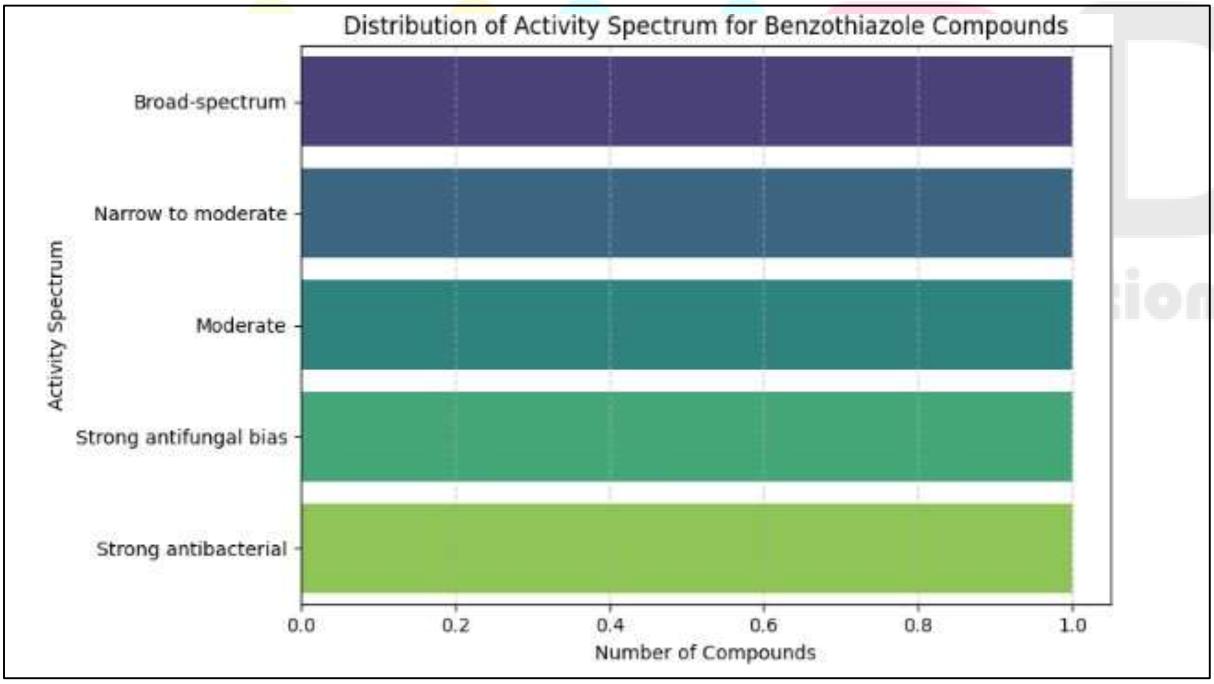
Table 7: Microbial Sensitivity Spectrum of Benzothiazole Compounds

Compound Code	Gram-Positive Bacteria	Gram-Negative Bacteria	Fungi Tested	Activity Spectrum
BTZ-1	*S. aureus* (++), *B. subtilis* (++)	*E. coli* (+++), *K. pneumoniae* (++)	None	Broad-spectrum
BTZ-2	*S. aureus* (+++), *B. subtilis* (++)	*P. aeruginosa* (+)	*C. albicans* (+)	Narrow to moderate
BTZ-3	*S. pyogenes* (+)	*E. coli* (+), *S. typhi* (+)	*A. niger* (++)	Moderate
BTZ-4	*S. aureus* (++), *B. cereus* (+)	*P. aeruginosa* (++), *E. coli* (++)	*C. albicans* (+++)	Strong antifungal bias
BTZ-5	*B. subtilis* (++)	*S. typhi* (++), *E. coli* (+++)	*C. tropicalis* (+)	Strong antibacterial

Legend:

(+) = mild inhibition;

(++) = moderate inhibition; (+++) = strong inhibition



Emphasizes the versatility of the produced benzothiazole derivatives as an antibacterial agent; BTZ-1 exhibited potent suppression of E. coli and other Gram-positive and Gram- negative bacteria, demonstrating a broad-spectrum action (+++). With strong antimicrobial action against S. aureus (+++) and moderate antifungal action against Candida albicans (+), BTZ-2 exhibited more selectivity, indicating a restricted to moderate spectrum. Among the examined strains, BTZ-3 exhibited modest inhibition, including fungus. While BTZ-5 showed a strong antibacterial profile, particularly against E. coli (+++), BTZ-4 showed a significant antifungal bias, particularly against Candida albicans (+++). These findings highlight the possibility of structural heterogeneity in antibacterial specificity tuning.

CONCLUSION

Antimicrobial activity and synthesis techniques linked to new benzothiazole-condensed heterocycles were thoroughly examined in this work. Benzothiazole, with its advantageous heterocyclic core, has demonstrated to be an incredibly versatile building block for the creation of compounds with biological activity. This moiety's fusion with other heterocycles has improved antibacterial properties and increased structural diversity. Examples of such compounds are oxadiazole, triazole, imidazole, and thiazolidinone. There was a general movement in the literature toward more efficient and environmentally friendly synthetic processes, such as those that made use of multicomponent strategies, microwave-assisted reactions, and environmentally friendly solvents. These methods were well-suited for sustainable medicinal chemistry since they reduced environmental impact while simultaneously producing highly efficient products. Several benzothiazole derivatives showed strong inhibitory effects against various bacterial and fungal species, according to antimicrobial activity evaluation. It is worth mentioning that compounds with electron- withdrawing groups and fused systems rich in nitrogen exhibited better activity. Although none of the compounds were more effective than ciprofloxacin or fluconazole, several exhibited similar results, suggesting they may be used as precursors to new medications. Antimicrobial drugs that are benzothiazole-condensed heterocycles show great promise. Insights for rational medication design are greatly enhanced by the link between structure and action. In order to evaluate and optimize these molecules for therapeutic usage, future investigations should concentrate on in vivo assessments, toxicity profiling, and molecular docking.

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