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Synthesis and Evaluation of Substituted 1,5-Benzothiazepine Derivatives For Antifungal Activity

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ABSTRACT:

The emergence of antimicrobial resistance and the increasing incidence of invasive fungal infections have created a significant demand for the development of novel therapeutic agents with improved efficacy and safety. Among various heterocyclic compounds, 1,5-benzothiazepine derivatives have attracted considerable attention due to their diverse pharmacological activities and potential applications in medicinal chemistry. In the present study, a series of substituted 1,5-benzothiazepine derivatives were synthesized through the cyclization of chalcone intermediates with 2-aminothiophenol. The synthesized compounds were designed by incorporating different substituents, including halogens, hydroxyl, nitrile, and alkyl groups, to enhance their biological activity. The synthesized derivatives were characterized using physicochemical and spectroscopic techniques such as melting point determination, thin-layer chromatography (TLC), Fourier Transform Infrared Spectroscopy (FT-IR), Proton Nuclear Magnetic Resonance Spectroscopy (¹H-NMR), and Mass Spectrometry. The characterization data confirmed the successful formation of the benzothiazepine ring system with satisfactory purity and yields ranging from 60–75%. The synthesized compounds were further evaluated for their antibacterial and antifungal activities using liquid dilution and agar diffusion methods. The compounds demonstrated notable antimicrobial activity against selected bacterial strains and Candida albicans. The minimum inhibitory concentration (MIC) of the synthesized compounds was found to be 30 µg/mL, while the minimum fungicidal concentration (MFC) was observed at 20 µg/mL. The findings of this study indicate that substituted 1,5-benzothiazepine derivatives possess promising antimicrobial potential and may serve as valuable lead molecules for the development of new antifungal

and antibacterial agents.

INTRODUCTION:

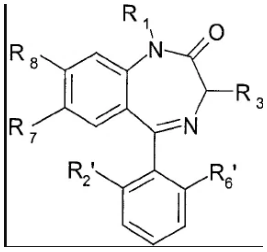
Fungal infections represent a major global health concern and are associated with significant morbidity and mortality, particularly among immunocompromised individuals. These infections are caused by various pathogenic fungi, including yeasts and molds, which can affect superficial tissues such as the skin, nails, and mucous membranes, or invade deeper organs and systemic circulation. The increasing prevalence of opportunistic fungal infections has become a serious challenge in modern healthcare systems. Members of the genus Candida, particularly Candida albicans, are among the most common fungal pathogens responsible for opportunistic infections in humans. Although Candida species normally exist as part of the human microbiota, they can cause severe infections when host immune defenses are compromised. Patients with HIV/AIDS, cancer, diabetes, organ transplantation, or those receiving immunosuppressive therapy are particularly vulnerable to invasive candidiasis and related fungal diseases. In addition to Candida species, several fungal pathogens including Aspergillus, Cryptococcus, Fusarium, Mucorales, Histoplasma, Blastomyces, and Coccidioides contribute significantly to healthcare-associated and systemic infections. These infections may occur through direct contact, inhalation of fungal spores, or traumatic implantation into tissues. Delayed diagnosis and limited therapeutic options often result in poor clinical outcomes and increased mortality. The growing incidence of fungal infections has been accompanied by the emergence of antifungal drug resistance. Prolonged and inappropriate use of antifungal agents has led to the development of resistant fungal strains, reducing the effectiveness of currently available therapies. Resistance mechanisms such as alterations in drug targets, efflux pump overexpression, and biofilm formation have been reported in several pathogenic fungi. Consequently, there is an urgent need to identify and develop novel antifungal agents with improved therapeutic profiles. Heterocyclic compounds play a central role in medicinal chemistry due to their broad spectrum of biological activities. The presence of heteroatoms such as nitrogen, sulfur, and oxygen within heterocyclic frameworks contributes significantly to their pharmacological properties. Among these compounds, benzothiazepines have emerged as an important class of biologically active molecules possessing diverse therapeutic applications. Benzothiazepines consist of a benzene ring fused with a seven-membered thiazepine ring containing sulfur and nitrogen atoms. Depending on the position of these heteroatoms, benzothiazepines are classified into several structural types, including 1,2-, 1,3-, 1,4-, and 1,5-benzothiazepines. These compounds have attracted considerable interest because of their wide range of pharmacological activities, including anticancer, anti-inflammatory, antiviral, antidiabetic, anticonvulsant, antiplatelet, antimicrobial, and calcium channel blocking properties. Several clinically important drugs contain the benzothiazepine scaffold. The biological versatility of this nucleus has encouraged researchers to synthesize novel substituted derivatives with enhanced therapeutic efficacy. Structural modification through the introduction of different pharmacophoric groups has been shown to improve biological activity and optimize pharmacokinetic properties. Chalcones represent an important class of α,β-unsaturated ketones widely employed as synthetic intermediates in heterocyclic chemistry. Structurally, chalcones consist of two aromatic rings connected through a three-carbon α,β-unsaturated carbonyl system. Their highly reactive enone moiety serves as a versatile precursor for the synthesis of various heterocyclic compounds exhibiting significant biological activities. The cyclization of chalcones with 2-aminothiophenol provides an efficient route for the synthesis of 1,5-benzothiazepine derivatives. This synthetic strategy offers operational simplicity, good product yields, and structural diversity. Furthermore, the introduction of biologically active substituents into the chalcone framework may enhance the pharmacological potential of the resulting benzothiazepine derivatives. Considering the therapeutic significance of benzothiazepines and the increasing demand for new antifungal agents, the present study was undertaken to synthesize and characterize novel substituted 1,5-benzothiazepine derivatives using chalcone intermediates. The synthesized compounds were subsequently evaluated for their antibacterial and antifungal activities to investigate their potential as promising antimicrobial candidates.

Research Gap:

Despite the extensive pharmacological potential of benzothiazepine derivatives, their application as antimicrobial and antifungal agents remains insufficiently explored. A review of the available literature indicates that many reported benzothiazepine derivatives have primarily been investigated for cardiovascular, anticonvulsant, anti-inflammatory, and anticancer activities. Comparatively fewer studies have focused on developing novel substituted 1,5-benzothiazepine derivatives as potential antifungal agents. Furthermore, several reported synthetic procedures involve multistep reactions, harsh reaction conditions, expensive reagents, or lengthy purification processes, which may limit their practical applicability. In many cases, the synthesized compounds have shown moderate yields and variable purity, creating a need for improved synthetic approaches capable of producing

structurally diverse derivatives with better efficiency.

The increasing prevalence of antimicrobial resistance and the emergence of resistant fungal pathogens further highlight the necessity for discovering new chemical entities with enhanced biological activity. Therefore, the synthesis of novel substituted 1,5-benzothiazepine derivatives possessing improved antimicrobial potential remains an important area of pharmaceutical research.



Rationale of the Study:
The design and development of new heterocyclic compounds continue to play a vital role in modern medicinal chemistry. Among various heterocyclic scaffolds, benzothiazepines have attracted considerable attention because of their broad spectrum of biological activities and favorable pharmacological properties. The presence of sulfur and nitrogen atoms within the benzothiazepine nucleus contributes significantly to its biological activity. Previous studies have demonstrated that structural modification of the benzothiazepine framework through the incorporation of suitable substituents can improve its therapeutic potential and expand its range of biological applications. Chalcones were selected as key synthetic intermediates in the present work due to their versatile reactivity and well-established role in heterocyclic synthesis. Structurally, chalcones are α,β-unsaturated ketones containing a reactive carbonyl system capable of undergoing cyclization reactions to generate various biologically active heterocyclic compounds. Their synthetic flexibility allows the introduction of diverse substituents that may enhance antimicrobial activity.

The cyclization of substituted chalcones with 2-aminothiophenol provides an efficient route for constructing the 1,5-benzothiazepine ring system. This approach offers a convenient synthetic pathway for generating structurally diverse derivatives while maintaining satisfactory yields and purity. Based on these considerations, the present study was designed to synthesize novel substituted 1,5-benzothiazepine derivatives and evaluate their antimicrobial potential against selected microbial strains, including Candida albicans.

Need of Research:
The continuous emergence of drug-resistant microbial pathogens has become a major challenge in healthcare worldwide. The effectiveness of many currently available antimicrobial agents has been reduced due to the development of resistance mechanisms, resulting in increased treatment failures and mortality rates. Fungal infections caused by opportunistic pathogens such as Candida albicans have shown a significant increase in recent years, particularly among immunocompromised patients. Although several antifungal drugs are available, their long-term use is often associated with resistance, toxicity, limited spectrum of activity, and adverse effects. Therefore, there is an urgent need to develop novel antimicrobial compounds with improved efficacy and safety profiles. Benzothiazepine derivatives have demonstrated considerable biological potential and represent promising candidates for further investigation. The present research was undertaken to address this need by synthesizing new substituted 1,5-benzothiazepine derivatives through a simple and economical synthetic route. The study aims to generate compounds with good yield, acceptable purity, and enhanced antimicrobial activity that may serve as potential lead molecules for future drug development.

Objectives of the Study:
The specific objectives of the present investigation were:
1. To synthesize substituted chalcone derivatives using appropriate substituted aldehydes and acetophenone derivatives.
2. To prepare novel substituted 1,5-benzothiazepine derivatives through cyclization of chalcone intermediates with 2-aminothiophenol.
3. To purify and isolate the synthesized compounds using suitable laboratory techniques.

4. To characterize the synthesized compounds by physicochemical and spectroscopic methods, including:
- Melting point determination
- Thin-layer chromatography (TLC)
- Fourier Transform Infrared Spectroscopy (FT-IR)
- Proton Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR)
- Mass Spectrometry
5. To evaluate the antibacterial activity of the synthesized compounds using the liquid dilution method and determine their minimum inhibitory concentration (MIC).
6. To evaluate the antifungal activity of the synthesized compounds against Candida albicans using the agar diffusion method and determine their minimum fungicidal concentration (MFC).
7. To investigate the relationship between structural modifications and observed antimicrobial activity.

Materials:
All chemicals and reagents used in the present study were of analytical reagent (AR) grade and were used without further purification. Substituted acetophenones, substituted aromatic aldehydes, 2-aminothiophenol, potassium hydroxide (KOH), ethanol, methanol, benzene, ethyl acetate, dimethyl sulfoxide (DMSO), and other solvents were procured from standard commercial suppliers. The microbial strains used for antibacterial and antifungal studies were obtained from a recognized microbiological laboratory and maintained under appropriate laboratory conditions throughout the study.

Instrumentation:
The synthesized compounds were characterized using the instruments listed below.

Sr. No.	Instrument	Make/Model
1	Melting Point Apparatus	Bubble Point Apparatus
2	FT-IR Spectrophotometer	Jasco FTIR-4100
3	NMR Spectrometer	Bruker Avance 300
4	Mass Spectrometer	Quadrupole Mass Spectrometer

Synthetic Scheme
The synthesis of substituted 1,5-benzothiazepine derivatives was accomplished through a two-step synthetic pathway.

Step I: Synthesis of Substituted Chalcones
Substituted chalcones were synthesized by Claisen–Schmidt condensation between substituted acetophenone derivatives and substituted aromatic aldehydes in the presence of alcoholic potassium hydroxide. The appropriate substituted acetophenone and substituted aromatic aldehyde were dissolved in ethanol. Alcoholic potassium hydroxide solution was added slowly with continuous stirring. The reaction mixture was stirred at room temperature until completion of the reaction, as monitored by thin-layer chromatography (TLC). After completion, the reaction mixture was poured into ice-cold water and acidified when required. The precipitated chalcone derivatives were filtered, washed with distilled water, dried, and recrystallized using suitable solvents to obtain pure chalcone intermediates.

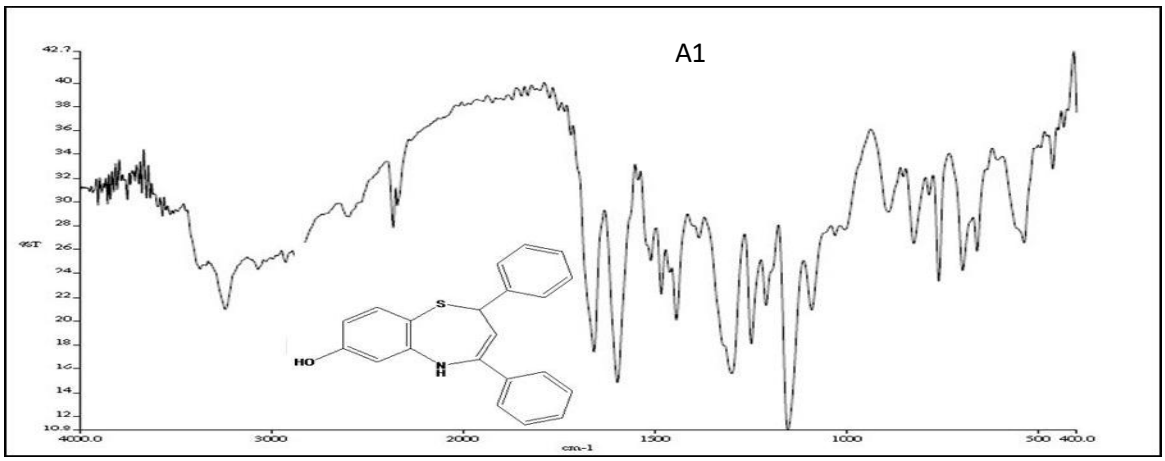
Step II: Synthesis of Substituted 1,5-Benzothiazepine Derivatives
The synthesized chalcone derivatives were reacted with substituted 2-aminothiophenol derivatives under suitable reaction conditions to obtain the target 1,5-benzothiazepine compounds.
An equimolar quantity of chalcone derivative and substituted 2-aminothiophenol was dissolved in ethanol and refluxed for an appropriate duration. The progress of the reaction was monitored by TLC. Upon completion, the reaction mixture was cooled to room temperature and poured into crushed ice. The solid product obtained was filtered, washed thoroughly with water, dried, and recrystallized from a suitable solvent system to yield pure substituted 1,5-benzothiazepine derivatives. The synthetic route enabled the incorporation of different substituents such as hydroxyl, halogen, nitrile, and alkyl groups into the benzothiazepine nucleus.

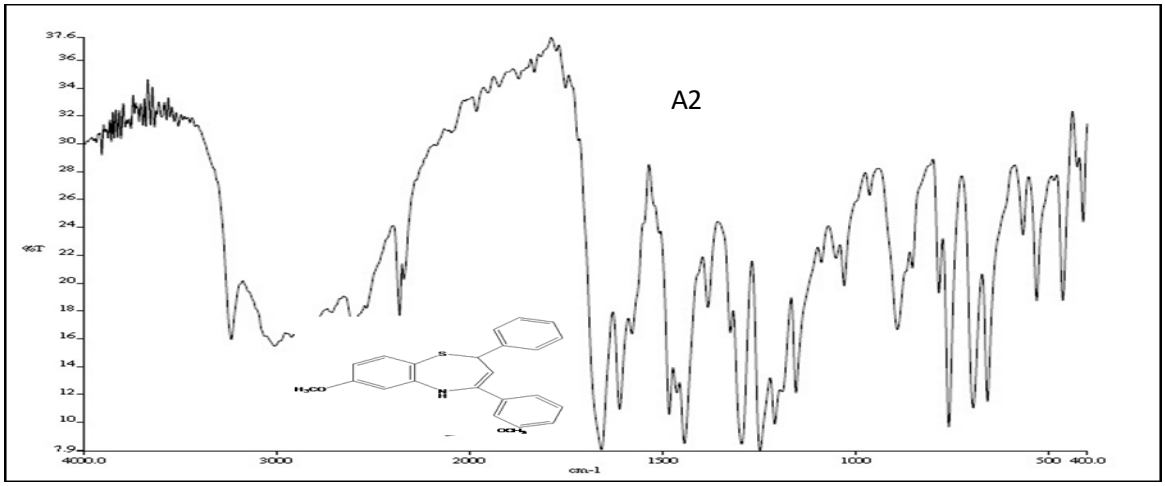
Identification and Characterization of Synthesized Compounds
The synthesized compounds were characterized using physicochemical and spectroscopic techniques to confirm their purity and structural identity. Melting Point Determination The melting points of all synthesized compounds were determined by the open capillary tube method using a Bubble Point Apparatus.

Melting point determination serves as an important parameter for assessing the purity of organic compounds. Pure crystalline compounds exhibit sharp and characteristic melting points, whereas the presence of impurities generally causes melting point depression and broadening of the melting range.

Thin-Layer Chromatography (TLC)
Thin-layer chromatography was employed to monitor reaction progress and assess compound purity. Silica Gel-G was used as the stationary phase, while benzene and ethyl acetate in different proportions were employed as the mobile phase. The chromatographic plates were visualized under appropriate conditions, and Rf values were calculated for all synthesized compounds. The appearance of a single spot with a characteristic Rf value indicated satisfactory purity of the synthesized compounds.

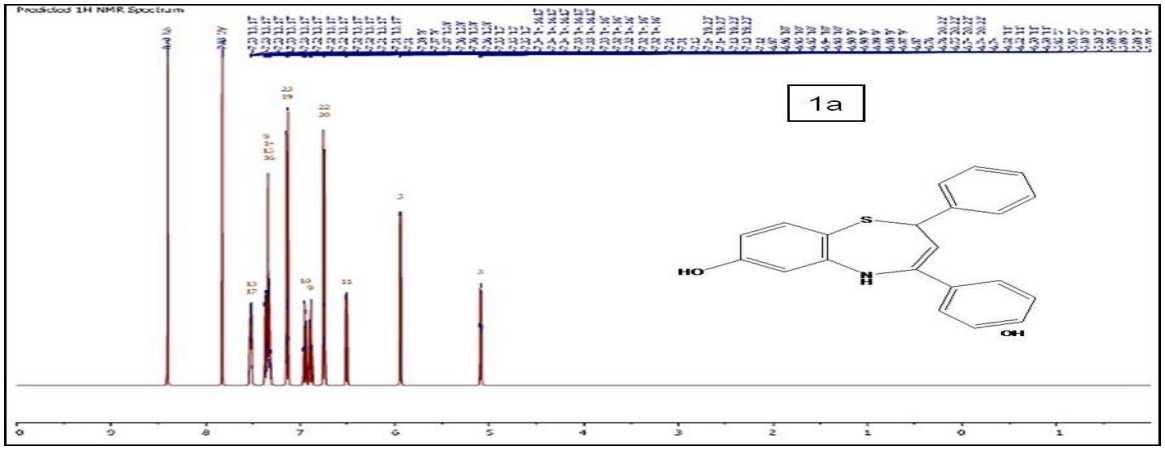
Fourier Transform Infrared Spectroscopy (FT-IR) FT-IR spectroscopy was performed to identify characteristic functional groups present in the synthesized compounds. Spectra were recorded within the range of 4000–400 cm^{-1}. The absorption frequencies corresponding to various functional groups such as O–H, N–H, C=C, C–N, C–S, and aromatic ring vibrations were analysed. The disappearance of characteristic chalcone carbonyl absorption bands and the appearance of new absorption bands corresponding to benzothiazepine ring formation confirmed successful cyclization.

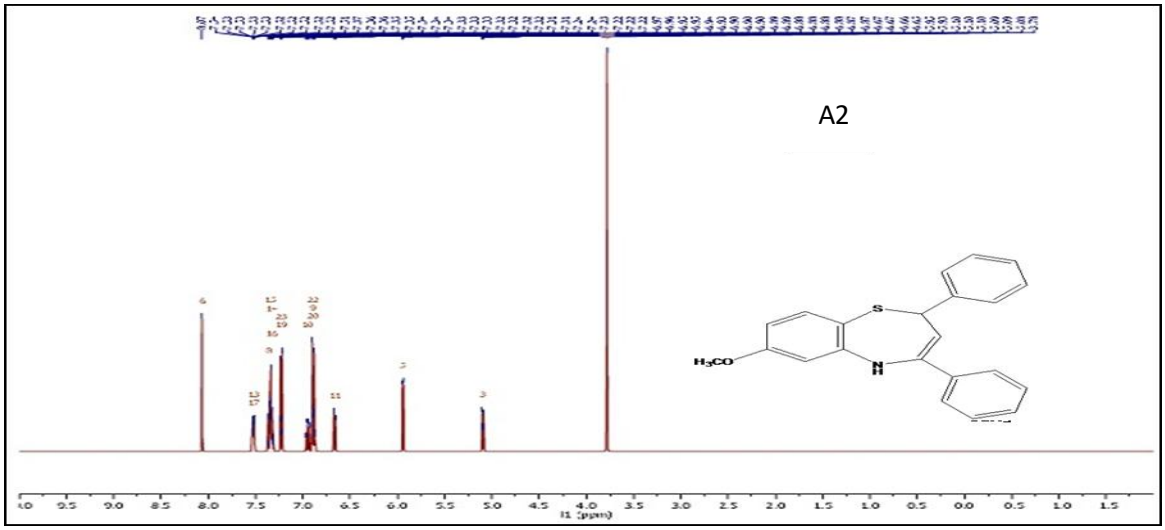




Proton Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR)
The ^{1}H-NMR spectra of the synthesized compounds were recorded using a Bruker Avance 300 NMR spectrometer. DMSO was used as the solvent, and tetramethyl silane (TMS) served as the internal standard. Chemical shifts were expressed in parts per million (ppm). The spectra provided information regarding the proton

environment within the synthesized molecules and confirmed the formation of the benzothiazepine ring through characteristic aromatic and heterocyclic proton signals.





Mass Spectrometry

Mass spectrometric analysis was performed to determine the molecular masses of the synthesized compounds. The molecular ion peaks (M^+ or $[M+H]^+$) observed in the mass spectra corresponded to the calculated molecular weights of the synthesized compounds, thereby confirming their molecular structures.

Antibacterial Activity

Determination of Minimum Inhibitory Concentration (MIC) The antibacterial activity of the synthesized compounds was evaluated using the liquid dilution method. A series of test tubes containing double-strength nutrient medium were prepared. The first tube served as the uninoculated control to verify the sterility of the medium. The second tube served as the growth control and contained microbial inoculum without the test compound. The remaining tubes contained varying concentrations of the synthesized compounds. Sterile distilled water was added to maintain a constant final volume. The microbial inoculum was introduced into all tubes except the uninoculated control. The test tubes were incubated at 37°C for 48–72 hours. Following incubation, the tubes were examined visually for microbial growth based on turbidity. The minimum inhibitory concentration (MIC) was defined as the lowest concentration of the compound that completely inhibited visible microbial growth.

MIC Observation

The standard drug (Azithromycin) exhibited complete inhibition of bacterial growth at 10 ppm. The synthesized compound exhibited complete inhibition of bacterial growth at 30 ppm.

MIC Values

Sample	MIC
Standard Drug (Azithromycin)	10 ppm
Synthesized Compound	30 ppm

Antifungal Activity

Agar Diffusion Method

The antifungal activity of the synthesized compounds was evaluated against Candida albicans using the cup-plate agar diffusion technique. Sterile agar medium was inoculated with a standardized suspension of Candida albicans and poured into sterile Petri plates. After solidification, wells were prepared in the agar medium. Solutions of synthesized compounds at different concentrations were introduced into the wells. Fluconazole was used as the reference standard. The plates were incubated under suitable conditions, and the diameters of the zones of inhibition were measured after completion of incubation. The antifungal activity was assessed by comparing the inhibition zones produced by the synthesized compounds with those produced by the standard drug.

Determination of Minimum Fungicidal Concentration (MFC)

The minimum fungicidal concentration (MFC) was determined as the lowest concentration capable of producing complete fungicidal activity against Candida Alicante synthesized compounds demonstrated antifungal activity within the tested concentration range of 0.5–50 µg/milk

MFC Values

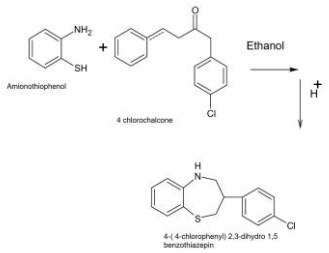
Drug	MFC
Fluconazole (Standard)	10 µg/mL
Synthesized Compound	20 µg/mL

Statistical Presentation of Experimental Data

All experimental observations were recorded carefully and analysed based on the obtained physicochemical and biological results. The synthesized compounds were evaluated for purity, structural confirmation, antibacterial activity, and antifungal activity. The generated data were subsequently used for interpretation of structure–activity relationships and assessment of antimicrobial potential.

Synthesis

The synthetic approach employed in the present study involved a two-step reaction sequence for the preparation of substituted 1,5-benzothiazepine derivatives. In the first step, substituted chalcones were synthesized through Claisen–Schmidt condensation between appropriately substituted acetophenone derivatives and substituted aromatic aldehydes in the presence of an alkaline catalyst. The reaction resulted in the formation of α, β-unsaturated ketone intermediates containing a conjugated carbonyl system. In the second step, the synthesized chalcones were subjected to cyclization with substituted 2-aminothiophenol derivatives under suitable reaction conditions. The nucleophilic addition followed by intramolecular cyclization led to the formation of the desired 1,5-benzothiazepine ring system. The overall synthetic pathway enabled the incorporation of different functional groups such as hydroxyl, halogen, nitrile, and alkyl substituents into the final benzothiazepine framework. These structural modifications were introduced with the objective of improving the antimicrobial properties of the synthesized compounds. The synthesized derivatives were subsequently characterized and evaluated for their antibacterial and antifungal activities to determine their potential as novel antimicrobial agents.



RESULTS AND DISCUSSION

Synthesis of Substituted 1,5-Benzothiazepine Derivatives A series of substituted 1,5-benzothiazepine derivatives

were successfully synthesized through a two-step synthetic route involving the formation of chalcone intermediates followed by cyclization with 2-aminothiophenol. The adopted synthetic method was found to be simple, economical, and reproducible. The chalcone intermediates were obtained through Claisen–Schmidt condensation between substituted acetophenones and substituted aromatic aldehydes. Subsequent cyclization of these chalcones resulted in the formation of the desired benzothiazepine derivatives.

The synthesized compounds were obtained as crystalline solids with colours varying from white to yellowish-green. The observed colour variation may be attributed to differences in the electronic effects of the incorporated substituents and the degree of conjugation present within the molecular framework. The overall reaction yielded the target compounds in satisfactory amounts, demonstrating the suitability of the selected synthetic methodology for the preparation of substituted benzothiazepines.

Physicochemical Characterization

The synthesized compounds were subjected to preliminary physicochemical evaluation, including determination of percentage yield, melting point, and thin-layer chromatographic analysis. The percentage yields of the synthesized compounds ranged from 60–75%, indicating efficient conversion of starting materials into the desired products. The relatively high yields suggest that the cyclization reaction proceeded successfully under the selected experimental conditions. Melting point analysis revealed values ranging from 200°C to 290°C. The compounds exhibited sharp melting ranges, indicating a high degree of purity and crystallinity. The absence of significant melting point depression further suggested minimal contamination by impurities or unreacted starting materials. Thin-layer chromatography confirmed the completion of the reactions and provided evidence of product purity. The observed Rf values ranged from 0.46 to 0.85, depending on the nature of the substituents present in the molecular structure. Single, well-defined spots were obtained for the purified compounds, indicating successful isolation of individual products.

Physicochemical Characteristics of Synthesized Compounds

Parameter	Observation
Physical State	Crystalline Solid
Colour	White to Yellowish-Green
Yield	60–75%
Melting Point	200–290°C
Rf Value	0.46–0.85

FT-IR Spectral Analysis

FT-IR spectroscopy was employed to identify characteristic functional groups and confirm the successful formation of the benzothiazepine ring system. The chalcone intermediates exhibited characteristic carbonyl (C=O) stretching vibrations associated with the α, β-unsaturated ketone moiety. Following cyclization, these characteristic chalcone absorption bands showed significant changes, indicating conversion into benzothiazepine derivatives. The synthesized compounds exhibited characteristic absorption bands corresponding to aromatic C=C stretching vibrations, C–N stretching, C–S stretching, and other functional groups introduced through substitution. The appearance of absorption bands associated with the benzothiazepine ring and the disappearance of characteristic chalcone signals provided strong evidence for successful cyclization.

^{1}H-NMR Spectral Analysis

The structures of the synthesized compounds were further confirmed through proton nuclear magnetic resonance (^{1}H-NMR) spectroscopy. The aromatic protons of the benzene rings appeared in the expected chemical shift region and exhibited characteristic multiple patterns. Signals corresponding to protons associated with the benzothiazepine ring were also observed.

A notable observation was the disappearance of the characteristic vinyl proton signals associated with the chalcone framework. This finding provided direct evidence for cyclization and formation of the seven-membered benzothiazepine ring. The chemical shift values and splitting patterns obtained from the spectra were consistent with the proposed molecular structures of the synthesized compounds. Overall, the ^{1}H-NMR spectra provided strong confirmation of successful ring closure and structural integrity of the synthesized derivatives.

Mass Spectral Analysis

Mass spectrometric analysis was carried out to determine the molecular masses of the synthesized compounds and verify their molecular identities. The spectra exhibited molecular ion peaks corresponding to the expected molecular weights of the synthesized derivatives. The observed molecular ion peaks were in agreement with the calculated molecular masses based on the proposed structures. The mass spectral data therefore confirmed the successful synthesis of the target compounds and supported the structural assignments established through FT-IR and ^{1}H-NMR analyses. The combined spectroscopic findings conclusively demonstrated the successful formation of substituted 1,5-benzothiazepine derivatives.

Antibacterial Activity

The synthesized compounds were evaluated for antibacterial activity using the liquid dilution method. The antimicrobial potential was assessed by determining the minimum inhibitory concentration (MIC), defined as the lowest concentration capable of preventing visible microbial growth. The control tube exhibited heavy turbidity, confirming the viability of the test microorganism and the suitability of the growth medium. At lower concentrations, partial inhibition was observed; however, complete inhibition of microbial growth occurred at higher concentrations. The standard drug, Azithromycin, demonstrated complete inhibition at a concentration of 10 ppm. In comparison, the synthesized benzothiazepine derivative showed complete inhibition at 30 ppm.

Minimum Inhibitory Concentration (MIC)

Sample	Observation	MIC
Control	Heavy Turbidity	Growth Observed
Azithromycin	Clear Solution	10 ppm
Synthesized Compound	Clear Solution	30 ppm

These findings indicate that the synthesized benzothiazepine derivatives possess appreciable antibacterial activity. Although the activity was lower than that of the standard drug, the observed inhibitory effect suggests that the benzothiazepine scaffold contributes significantly to antimicrobial action.

The presence of electron-withdrawing substituents such as halogens and nitrile groups may have enhanced the interaction of the compounds with microbial targets, thereby improving antibacterial efficacy.

Structure–Activity Relationship (SAR)

Preliminary structure–activity relationship analysis suggests that the biological activity of the synthesized compounds is influenced by the nature and position of substituents attached to the benzothiazepine nucleus. The incorporation of halogen substituents may enhance lipophilicity, facilitating improved penetration through microbial cell membranes. Similarly, nitrile-containing derivatives may contribute to stronger molecular interactions with biological targets. Hydroxyl groups may improve hydrogen-bonding interactions, while alkyl substituents can influence electronic distribution and steric characteristics of the molecules. The combined presence of these functional groups within the benzothiazepine scaffold likely contributes to the observed antimicrobial activity. Further studies involving a larger number of derivatives and detailed molecular investigations are required to establish a comprehensive structure–activity relationship.

DISCUSSION

The present investigation successfully demonstrated the synthesis of novel substituted 1,5-benzothiazepine derivatives using chalcone intermediates through a convenient cyclization approach. The synthesized compounds were obtained in satisfactory yields and were successfully characterized by physicochemical and spectroscopic techniques. FT-IR, ^{1}H-NMR, and mass spectral analyses confirmed the formation of the desired benzothiazepine ring system. Biological evaluation revealed that the synthesized compounds exhibited both antibacterial and antifungal activities. The MIC value of 30 µg/mL and MFC value of 20 µg/mL indicate promising antimicrobial potential. The observed biological activity may be attributed to the synergistic contribution of the benzothiazepine nucleus and the incorporated functional substituents. These findings are consistent with previous reports demonstrating the antimicrobial potential of benzothiazepine derivatives. Overall, the results suggest that substituted 1,5-benzothiazepines represent promising pharmacophores for the development of future antimicrobial agents and warrant further optimization and biological investigation.

CONCLUSION

The present study successfully achieved the synthesis, characterization, and antimicrobial evaluation of a new series of substituted 1,5-benzothiazepine derivatives. The compounds were synthesized through a convenient and

economical synthetic route involving the preparation of chalcone intermediates followed by cyclization with 2-aminothiophenol. The synthesized derivatives were obtained in satisfactory yields ranging from 60–75% and exhibited good physicochemical characteristics. The purity and structural identity of the compounds were confirmed through melting point determination, thin-layer chromatography (TLC), Fourier Transform Infrared Spectroscopy (FT-IR), Proton Nuclear Magnetic Resonance Spectroscopy (^{1}H-NMR), and Mass Spectrometry. The spectral data confirmed the successful formation of the benzothiazepine ring system and validated the proposed molecular structures.

Biological evaluation demonstrated that the synthesized compounds possess noteworthy antimicrobial activity. The antibacterial studies performed using the liquid dilution method revealed a minimum inhibitory concentration (MIC) of 30 µg/mL for the synthesized compounds, whereas the reference drug Azithromycin exhibited an MIC of 10 µg/milk Similarly, antifungal evaluation against Candida albicans showed a minimum fungicidal concentration (MFC) of 20 µg/mL for the synthesized derivatives, while Fluconazole demonstrated an MFC of 10 µg/mL. The observed antimicrobial activity may be attributed to the presence of biologically active functional groups such as halogens, hydroxyl, nitrile, and alkyl substituents incorporated into the benzothiazepine framework. These structural modifications are likely to influence the physicochemical properties and biological interactions of the synthesized molecules, thereby contributing to their antimicrobial effects. Overall, the results of the present investigation indicate that substituted 1,5-benzothiazepine derivatives constitute a promising class of heterocyclic compounds with potential applications in antimicrobial drug discovery. The findings support the continued exploration of benzothiazepine-based molecules as lead candidates for the development of novel therapeutic agents against microbial infections.

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