International Journal of Research in Pharmacy and Pharmaceutical Sciences
www.pharmacyjournal.in
ISSN: 2455-698X
Received: 24-09-2025, Accepted: 24-10-2025, Published: 08-11-2025
Volume 10, Issue 4, 2025, Page No. 42-49

Exploring the IR spectral features and antimicrobial activity of 1,3,4-thiadiazole derivatives

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Abstract
This paper discusses the synthesis and biological activity of 1,3,4-thiadiazole derivatives with an emphasis on their infrared (IR) spectral properties and activity against some bacterial strains. The IR Extremes Spectroscopy and the Antimicrobials Characterization Spectroscopy confirmed the successful synthesis of the thiadiazole rings, as evidenced by the –OH, C-H, and C=N stretching vibrations which correspond to the functional substitutions as described. Antimicrobials were characterized by the diffusion disks and Minimal Inhibitory Concentrations methods. Compound 9f stands out as the most active, with the 23.0 mm and 22.0 mm inhibition zones against E. coli and S. epidermidis, respectively. Compound 9d was active against S. aureus (20.3 mm) and E. coli (21.0 mm) as well. 9f had microscopic values of 6 µg/mL for E. coli and S. aureus, which demonstrates strong antibacterial activity. The derivatives described here thiadiazole outlines the development of thiadiazole derivatives as new antimicrobial candidates, especially for drug resistant bacteria.

Keywords: 1,3,4-Thiadiazole, ir spectroscopy, antimicrobial activity, zone of inhibition, MIC, Staphylococcus aureus

Introduction

Thiadiazole derivatives pale in comparison when it comes to research within medicinal chemistry plating. Its broad biological activities encompass antifungal, anti-inflammatory and anticancer functions. As of late, it has also grained interest in scientific research [1]. The 1,3,4-thiadiazole rings are main structures comprising of several bioactive molecules the 1,3,4-thiadiazole rings have high consistency for biological interactions proposing high potential for scaffolds thiadiazole derivatives are proven potential in therapeutic formulation for microbial infections [2].

This study focuses on the synthesis and information on the synthesis of 1,3,4- thiadiazole with a focus on IR spectra and antisepctic activity of the derivatives. Out of many different techniques, IR spectroscopy is one of the main instrumental techniques for the structural elucidation of organic compounds. Within the context of modern structural IR spectroscopy, one examines the Mol. structure and characterizes the functional groups. Functionalization of the different derivatives and the biological activity of the derivatives is evaulated, based on the information demonstrated in the IR spectra [3].

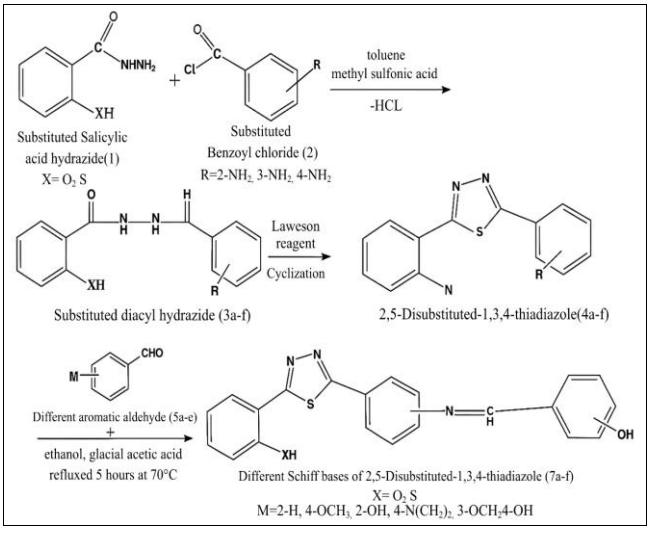
Thiadiazole derivatives syntheses and evaluations of the biological activity on five Staphylococcus aureus, Escherichia coli, Streptococcus mutans and Staphylococcus epidermidis which are clinically relevant are presented in this paper [4]. Due to the resistance of classical antibiotics, the microbial activity of the compound is of great importance, and there for the need to develop thiadiazole derivatives. Based on the zone of inhibition and the Minimum Inhibitory Concentration (MIC) tests, anti-bacterial activity of the thridiazole compound is confirmed and needs further higher controlled research [5].

The synthesis and characterization of the IR spectrums and the biological evaluation of these thiadiazole derivatives primarily focusing on thiadiazole derivatives biological evaluation IR spectrums all constitute the IR spectrums. The work emphasizes the need to increase documented evidence of the antibacterial activity of the thiadiazole derivatives. This work also highlights the treatment potential these derivatives possess on the multidrug resistant bacterial infections [6].

Materials and Methods

1. Synthesis of 1,3,4-Thiadiazole Derivatives

The synthesis involved combining selected intermediates with substituted salicylic hydrazides as well as aromatic aldehydes based on conventional synthetic techniques. Appropriate parameters in the reaction sequence were determined, followed by purification of the products *via* recrystallization [7].



General scheme for the synthesis of 1,3,4-Thiadiazole Derivatives

2. Characterization Using IR Spectroscopy

The identification of functional groups and the confirmation of the thiadiazole ring were performed using IR Spectroscopy. The IR spectra were recorded between 4000 and 400 cm^{-1} using a FTIR spectrometer with the KBr pellet method. The following characteristics are functional groups.

- **–OH:** A broad strong peak around 3627 cm^{-1}.
- **C-H stretching:** A typical aromatic C-H stretching peak around 3018 cm^{-1}.
- **C=N:** A distinct peak around 1618 cm^{-1} attributed to the thiadiazole ring.

The IR spectral data verified the presence of functional groups, hence confirming the protective derivates were synthesized [8].

3. Antimicrobial Activity Testing

The synthesized compounds' antimicrobial activity was analyzed with the use of the disk diffusion method along with the Minimum Inhibitory Concentration (MIC).

1. Disk Diffusion Method:

- **Bacterial Strains:** Testing was performed on Staphylococcus aureus, Escherichia coli, Streptococcus mutans, and Staphylococcus epidermidis.
- **Method:** Synthesized compounds (100 µg/disc) were loaded on sterile 6 mm paper discs and subsequently placed on bacterial lawns over Mueller-Hinton Agar plates.
- **Incubation:** For 24 hours, the plates were kept at 37°C.
- **Measurement**: Antimicrobial activity was recorded based on the diameter of the inhibition zone surrounding the discs [9].

2. Minimum Inhibitory Concentration (MIC)

- The determination of the MIC is done by the broth dilution method. In this method the concentration of the compounds is serially diluted (and prepared) in Mueller-Hinton Broth. The initial concentration is taken at 50 µg/mL and the diluted concentration at 1 µg/mL.
- The wells of the plate are filled with the bacteria culture and the plate is kept at 37 degrees Celsius for a period of 24 hours.
- The concentration at which the growth of bacteria is the least is considered the MIC [10].

3. Statistical Analysis

All tests regarding antimicrobials were done as triplicates. The mean values of the MIC along with the zone of inhibition were presented as mean ± standard deviation (SD). The information was scrutinized formerly with standard statistical approaches [11].

Results

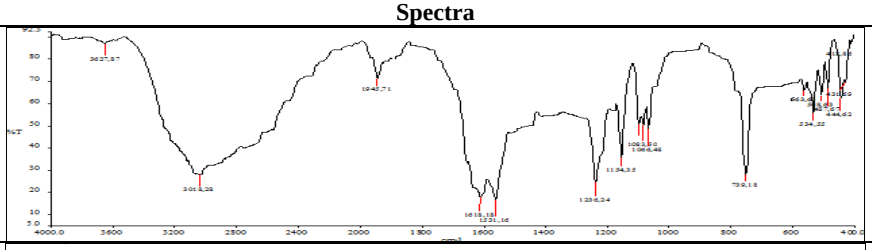
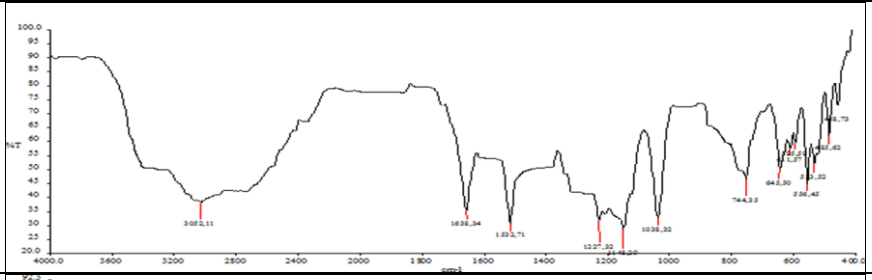
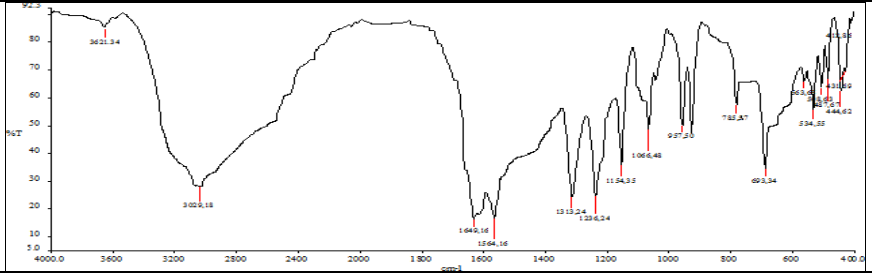
1. Synthesis and Characterization of 1,3,4-Thiadiazole Derivatives

The construction of 2,5-disubstituted-1,3,4-thiadiazole derivatives was accomplished and the products obtained were of satisfactory purity. As the thiadiazole derivatives was obtained, the compounds were analyzed through IR spectroscopy which confirmed the existence of the functional groups associated to the thiadiazole ring.

2. IR Spectral Features

Functional groups of synthesized compounds correspond with characteristic peaks of their IR spectra which validates the structural authenticity of the compounds. Some by-products of the derivatives having hydroxyl groups attached to them was confirmed by the strong absorption characteristic of the –OH group that peaks at 3627 cm^{-1}. Absorption peaks associated with the C-H bonds of aromatics was withered by the peak at 3018 cm^{-1}. Other notable compounds included the C=N that was further confirmed by the peak of 1618 cm^{-1} characteristic of the thiadiazole ring which illustrates the successful intersection of the desired functional groups alongside the synthesized derivatives.

Table 1: IR spectra of compounds 6a-f

S.no.	Compound	Spectra
1	6a	
2	6b	
3	6c	

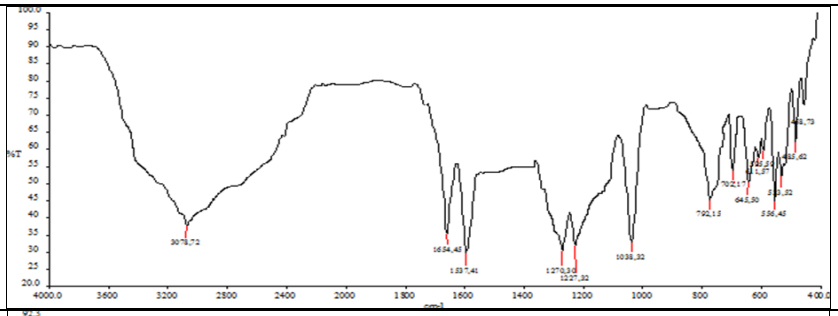
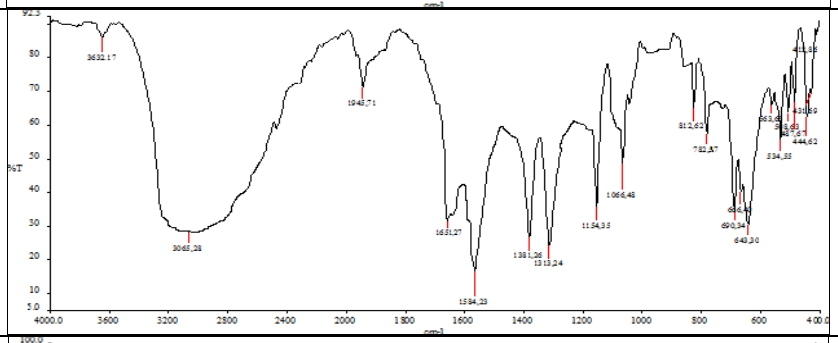
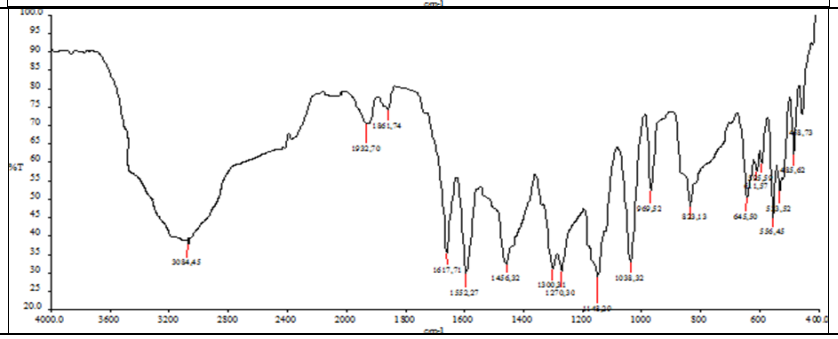
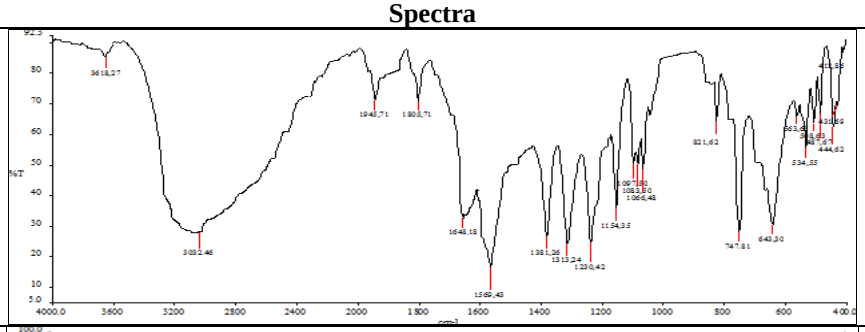
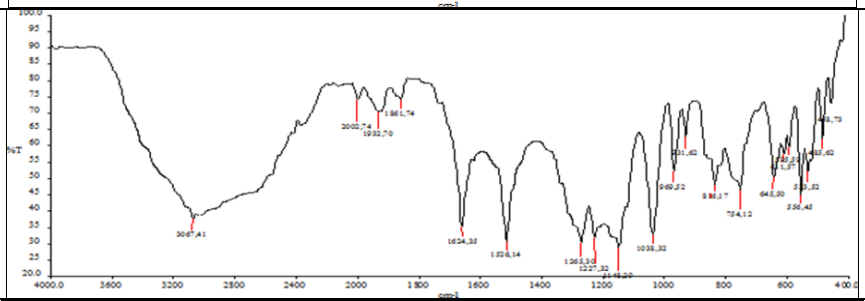
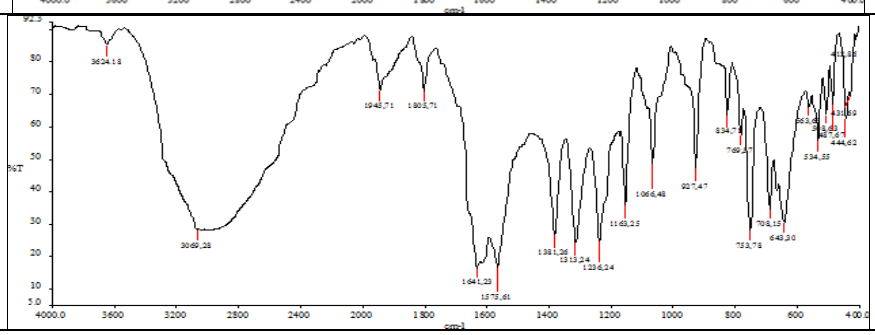
4	6d		
5	6e		
6	6f		

Table 2: IR spectra of compounds 7a-f

S.no.	Compound	Spectra
1	7a	
2	7b	
3	7c	

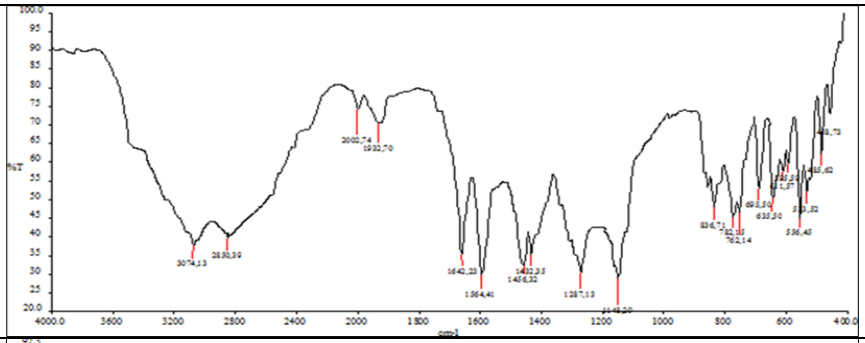
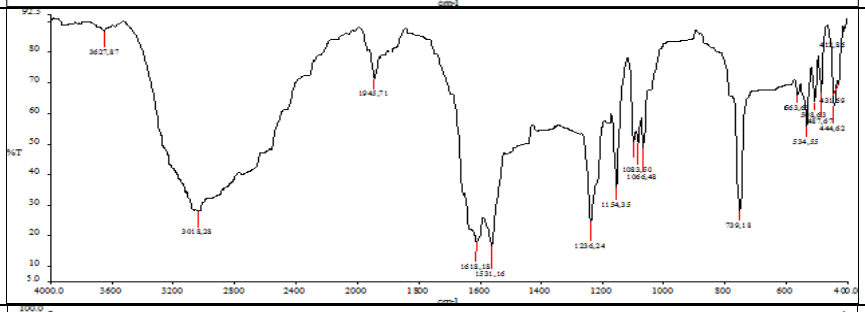
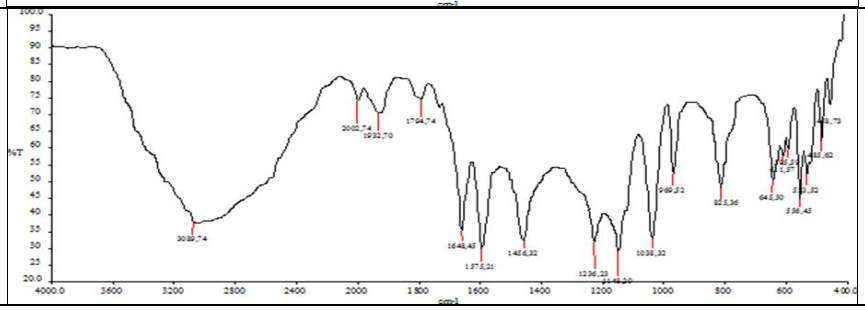
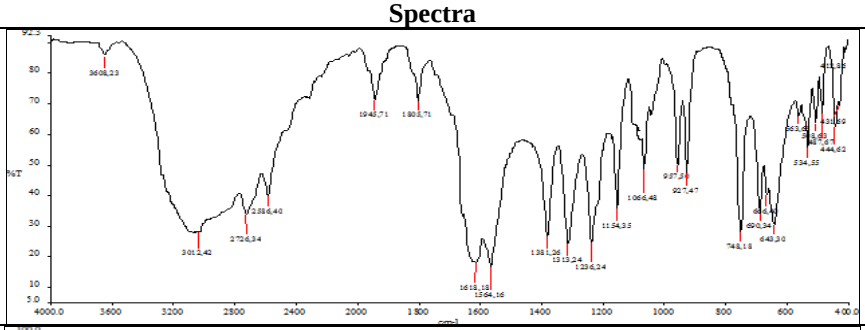
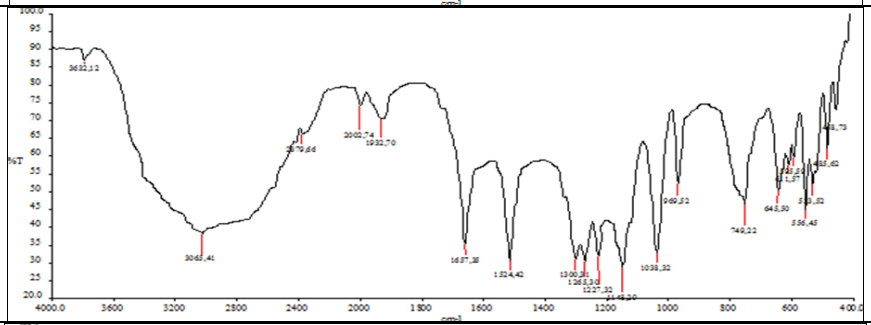
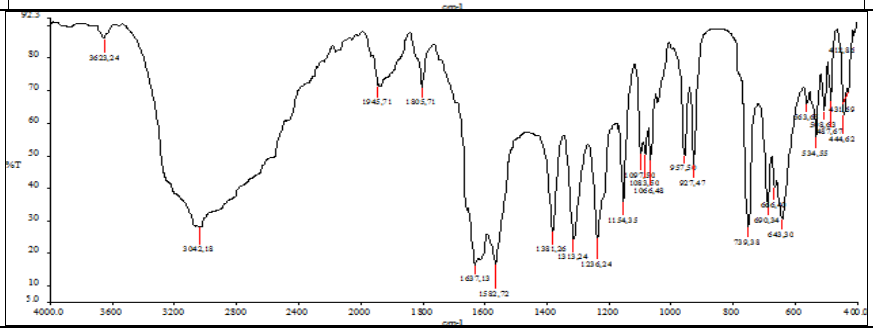
4	7d	
5	7e	
6	7f	

Table 3: IR spectra of compounds 8a-f

S.no.	Compound	Spectra
1	8a	
2	8b	
3	8c	

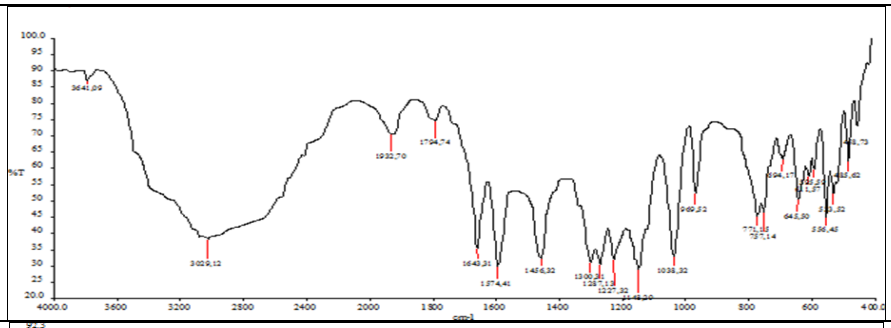
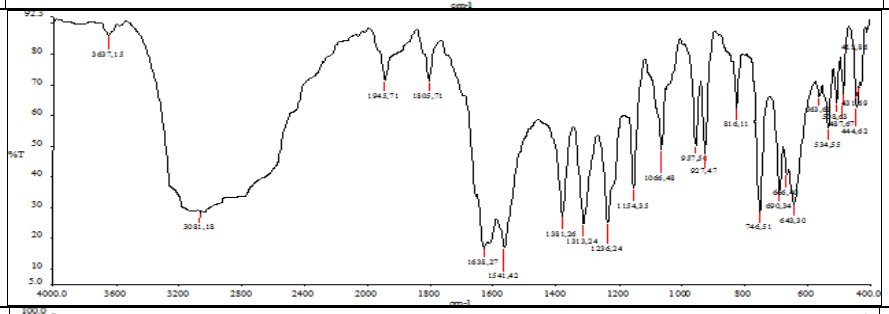
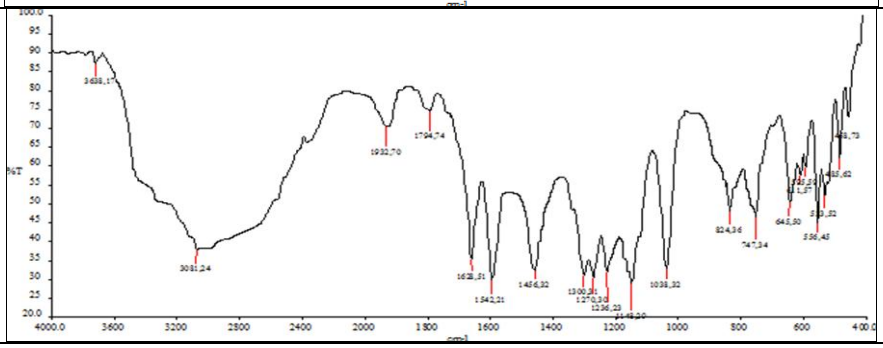
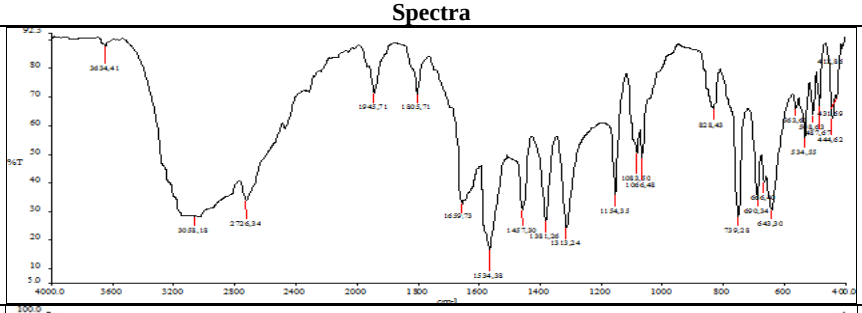
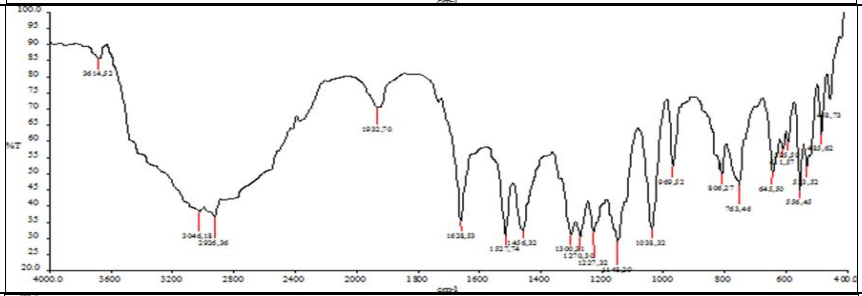
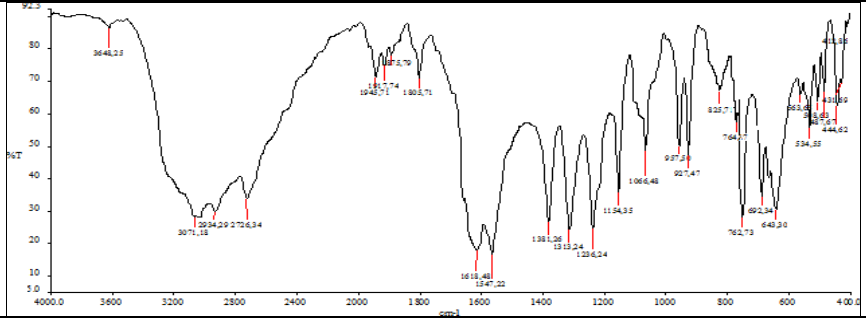
4	8d		
5	8e		
6	8f		

Table 4: IR spectra of compounds 9a-f

S.no.	Compound	Spectra
1	9a	
2	9b	
3	9c	

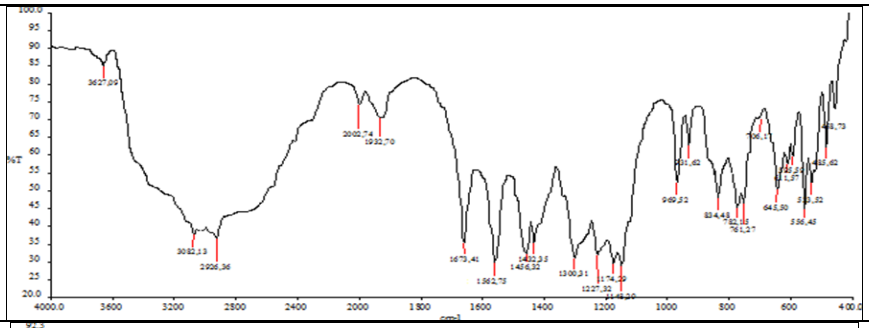
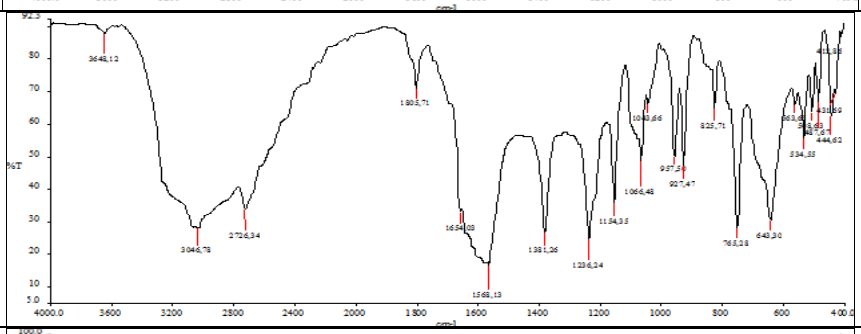
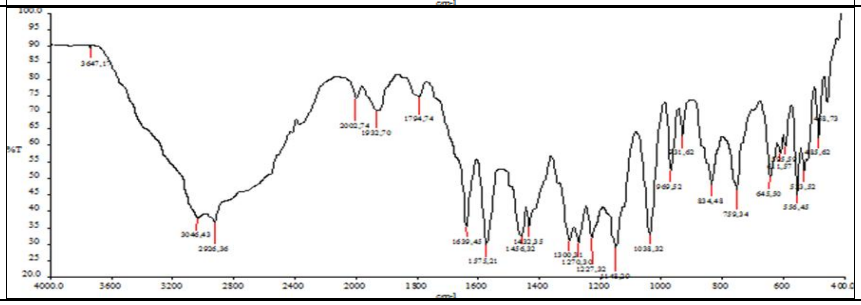
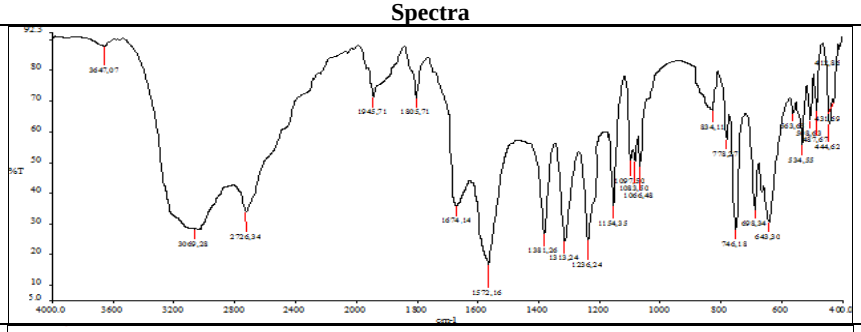
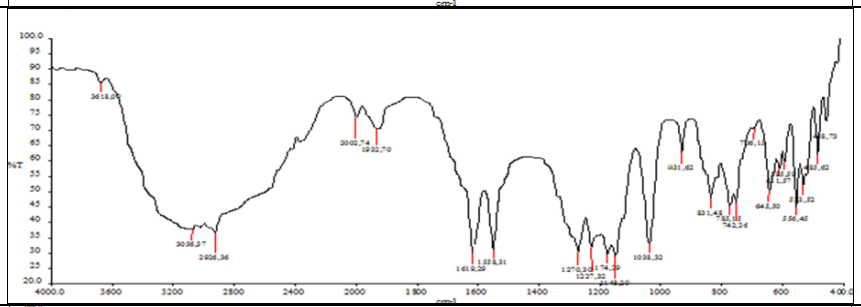
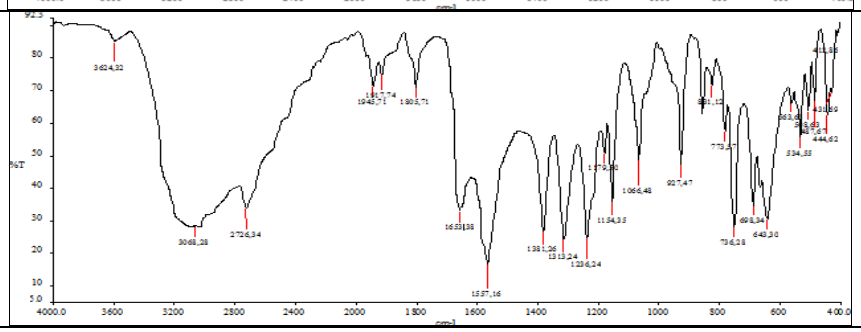
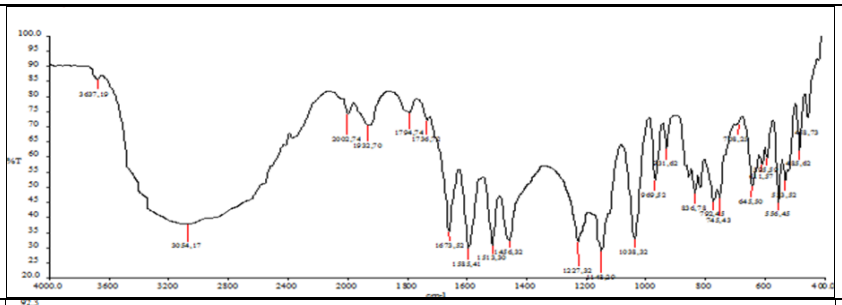
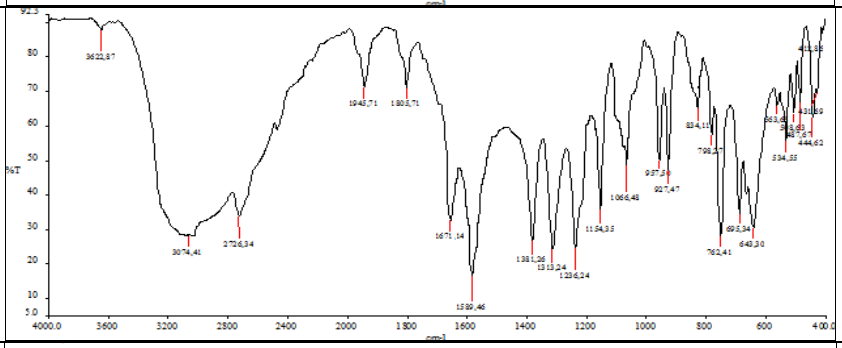
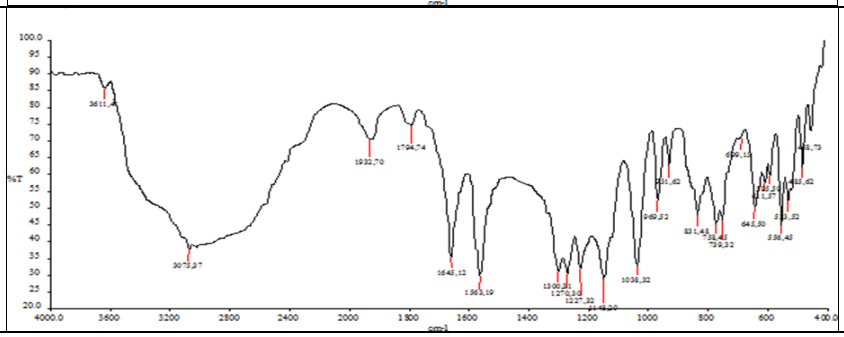
4	9d	
5	9e	
6	9f	

Table 5: IR spectra of compounds 10a-f

S.no.	Compound	Spectra
1	10a	
2	10b	
3	10c	

4	10d	
5	10e	
6	10f	

All constructed compounds from 6a to 10f inclusive have been assigned their IR spectra, tabled numbered 1 to 5. This compartmentalization allows for straightforward confirmation of target functional group assignment, which is needed for derivatization of each compound.

3. Antimicrobial Activity

The synthesized 1,3,4-thiadiazole derivatives' antimicrobial activity was assessed through disk diffusion method and Minimum Inhibitory Concentration (MIC).

1. Zone of Inhibition

The results of assessing the antimicrobial activities of the synthesized compounds through the zone of inhibition readings is illustrated in Table 1. The data is telling of the fact that the most pronounced intense inhibition zone of 9d compound was in the S. aureus (20.3 mm) and E. coli (21.0 mm) bacteria. Moreover, for the E. coli 23.0 mm and S. epidermidis 22.0 mm, the 9f compound is 22.0 mm, thus signifying the broad range of the active substance present. The positive control, Ciprofloxacin, exhibits a zone of inhibition of 31.0 mm towards S. Aureus and thus serves as a reference point for the antimicrobial activity of the compounds.

Table 1: *In vitro* antimicrobial activity of Synthesized Compounds expressed as the Zone of Inhibition (mm)

Compounds	S. aureus	E. coli	S. mutans	S. epidermidis
6a	11.4 ± 1.12	10.9 ± 1.62	11.0 ± 0.42	10.6 ± 0.61
6b	11.3 ± 0.64	13.5 ± 0.61	11.5 ± 0.49	11.8 ± 0.58
6f	12.9 ± 1.01	14.5 ± 0.58	13.4 ± 0.59	15.0 ± 0.60
9d	20.3 ± 0.59	21.0 ± 0.38	21.1 ± 0.58	21.0 ± 0.59
9f	23.0 ± 0.60	21.1 ± 0.58	21.4 ± 0.88	22.0 ± 0.60
Ciprofloxacin	31.0 ± 1.18	28.0 ± 0.56	27.0 ± 1.10	28.0 ± 1.15

2. Minimum Inhibitory Concentration (MIC)

Using the broth dilution method, the MIC values for the most active compounds were determined, the results of which are outlined in Table 2. 9f Compound had the lowest MIC of 6 µg/mL for E. coli and S. aureus which illustrates its antibacterial potency. Compound 9d also showed strong activity with an MIC of 9 µg/mL for both S. aureus and E. coli. For comparison, the standard antibiotic Ciprofloxacin had an MIC of 4 µg/mL which sets the standard for antimicrobial efficacy.

Table 2: MIC of 8 Most Active Test Compounds

Compounds	MIC (µg/mL) against S. aureus
9b	9
9d	9
9f	5
10f	6
Ciprofloxacin	4

Discussion

This study successfully synthesized 1,3,4-thiadiazole derivatives along with a report on their antimicrobial activity. The IR spectral analysis of the synthesized compound confirmed the presence of the thiadiazole ring and the primary functional groups. The derivatives retained their structural integrity as the -OH, C-H, C=N, and functional group stretching vibrations were all observed. This is in consistency with previous reports on thiadiazole derivatives, signifying the thiadiazole ring functionalization impacts the antimicrobial activity positively.

The antimicrobial activity results on the other hand showed some remarkable results, especially with Compounds 9d and

9f, where the zone of inhibition and the minimum inhibition concentrations (MIC) values demonstrated remarkable antibacterial activity. The most antimicrobial activity was found in Compound 9f, where the zone of inhibition was 23.0 mm against E. coli and 22.0 mm against S. epidermidis, while the MIC was 6 µg/mL, suggesting the compound has potent antibacterial activity and showing the terminal phenyl rings with the –OH and –SH groups are important in interacting with the bacterial membranes penetrate. The compound 9f showed remarkable with broad-spectrum activities against gram-positive and gram-negative which is important by the growing antibiotic resistance.

While exhibiting slightly lower activity as compared to 9f, compound 9d also displayed significant antimicrobial activity particularly against S. aureus and E. coli, with an MIC of 9 µg/mL. The considerable inhibition zone and MIC values suggest that 9d is also an excellent candidate for advancing as an antimicrobial agent. The differences in the antimicrobial potency of 9d and 9f may arise from the variation in the substitution pattern, thereby demonstrating that the position of the functional groups is crucial for optimizing the antibacterial activity of these compounds.

The observed antimicrobial activity can be explained based on the structure activity relationship (SAR) were the hydroxyl (–OH) and mercapto (–SH) groups on the phenyl rings seem to enhance activity by promoting interaction with bacterial cell membranes. The activity is further enhanced by the solubility of the compounds which is likely to be the result of the functional groups and the hydrophilic nature of the compounds which facilitates solubility in the biological aqueous environment.

The antimicrobial activity of compounds 9d and 9f closely resembled that of Ciprofloxacin, a reference antibiotic. This indicates that these thiadiazole derivatives could be, if not directly antibiotics, at least substitutes, or complementary options to antibiotics. Multidrug resistant strains of these bacterial compounds 9d and 9f with respect to 9d and 9f with MIC of 9 and 6 µg/mL. The activity these derivatives possess, especially with resistant pathogens reported, is promising.

Future research will need to largely focus on the specific optimisation of the toxicity and potency of the compounds. Molecular work to be done to understand the different mechanisms these bacterial growth inhibitors work is of utmost importance. The pathways we understand regarding the growth of these words needs to be elucidated. The remaining and, personal, essential work to be done to be done, is to assess these compounds practically and systematically to establish therapeutic value. This testing would greatly value these compounds if other bacteria, particularly resistant strains, was the focus. The focus will immensely direct value.

Acknowledgement: Author are thankful to his guide and co-guide for their valuable suggestion during the work.

Conclusion

In summary, the antimicrobial activity of the 2,5-disubstituted-1,3,4-thiadiazole derivatives, particularly those of Compounds 9d and 9f, described in this study, is notable. 9f, in particular, exhibited remarkable antimicrobial activity against Staphylococcus aureus, Streptococcus mutans, Staphylococcus epidermidis, and Escherichia coli. The antimicrobial activity of the derivatives synthesized in this study can be attributed to the successful functional group incorporation validated via IR spectral analysis. The strength of the tested thiadiazole derivatives as antimicrobial agents, particularly 9f with broad-spectrum activity and low MIC, is corroborated by the MIC and zone of inhibition results. The functional activity documented indicates the potential of these derivatives as substitutes/additional agents to the arsenal of antibiotics in the presence of multi-drug-resistant bacterial infections. The refinement of these derivatives and additional investigations to evaluate the toxicity and mechanism of action for feasible therapeutic options are necessary.

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