Journal of Phytonanotechnology and Pharmaceutical Sciences 2(3): 19-26, 2022

Online ISSN:2583-0376

http://jpps.ukaazpublications.com

DOI: http://dx.doi.org/10.54085/jpps.2022.2.3.4

Journal of Phytonanotechnology and Pharmaceutical Sciences

Original Article : Open Access

Synthesis, characterization, and *in vitro* evaluation of thiadiazol-2-ylimino ethenone derivatives

T. Prabha◆, C. Selvinthanuja, S. Suganya, B. Rahini, B. Nithiya, S. Vijay, K. Pandian and B. Punithkumar

Department of Pharmaceutical Chemistry, Nandha College of Pharmacy, Erode-638052, Tamilnadu, India

Article Info

Article history

Received 1 July 2022

Revised 3 August 2022

Accepted 4 August 2022

Published Online 30 September 2022

Keywords

Thiadiazole derivatives

Anti-inflammatory

Antimicrobial

In vitro study

Abstract

The infectious organism/pathogens growth and their multiplication will be either killed or inhibited by the antibiotics. It is well apparent that the healing property of the anti-inflammatory drug is because it offers antibacterial activity. By taking this hypothesis, we have synthesized a series of thiadiazole annulated benzil conjugates *via* the cyclization process and evaluated them for *in vitro* antibacterial and anti-inflammatory activity. The compounds were structurally elucidated by IR, 1HNMR, and mass spectral techniques. The synthesized compounds, *viz*., TZ1, TZ2, TZ3, and TZ4 showed significant antibacterial activity against both gram-positive (*B. subtilis* and *S. aureus*) and gram-negative pathogens (*P. fluorescens* and *P. aeruginosa*) with a maximum zone of inhibition of 13-25 mm and 06-22 mm at 200 µg/ml concentrations, respectively, when compared to standard drug ciprofloxacin (18-28 mm and 15-25 mm). Whereas, the results of an anti-inflammatory study showed the compounds at a concentration of 100-400 µg/ml produced a noteworthy inhibition on protein denaturation (73.28-84.33%) at 400 µg/ml when compared to standard 77.34%. Therefore, it could lead to the creation of new drug candidates that could be used to treat a wide range of infectious diseases, such as inflammation, cancer, *etc*.

1. Introduction

Thiadiazoles are heterocycles that belong to the azole family, which also includes imidazole and oxazole. Due to their wide range of pharmacological characteristics, conjugated 1,3-thiazole derivatives have attracted a lot of attention and have been the subject of growing levels of research in recent years. Thiadiazoles' strong aromaticity of the ring structure, which provides better *in vivo* stability, is provides them their biological activity. Since sulphur atoms provide higher liposolubility, replacing such heterocyclic frameworks with thiadiazoles typically results in analogues having better activity.

Owing to multidrug resistant pathogens, there are many antibiotics have been questionable in current medical field (Prabha *et al*., 2019). On the other hand, the antibiotics have both the immune-modulatory and anti-inflammatory properties (Andre, 2010). Inflammation depends on a various number of factors, which reflects the response of the organism to a variety of stimuli and leads to many problems. The importance of anti-inflammatory agents cannot be overstated because of their efficacy frequently as life-saving drugs in many diseases such as cancer, diabetes, arthritis, and rheumatic fever, *etc*.

The several diaryl heterocyclic compounds substituted on the central heterocyclic ring have been explored as potential scaffolds for the anti-inflammatory activity (Singh *et al*., 2019). Among the nitrogen-containing five-member heterocycles, considerable attention has been focused on thiadiazole conjugates owing to their fascinating biological activities such as antimicrobial drug sulfathiazole, antiretroviral drug ritonavir, antineoplastic drug tiazofurin, antifungal drug abafungin, *etc*., 1,3-thiadiazole derivatives, have shown extensive biological activities, anti-inflammatory, anti-microbial, antitubercular, anticonvulsant, antioxidant, anticancer and plant growth regulator activities (Rouf *et al*., 2015).

In this context, and because of our long-standing interest in the chemistry of the privileged benzyl annulated thiadiazole scaffold (Prabha *et al*., 2019), the study encouraged us to further explore the thiadiazole motif as an active pharmacophore to exploit its anti-inflammatory and antibacterial property. However, there are numerous examples of nitrogen containing heterocyclic scaffold being used as an anti-inflammatory agent. To support this further, an *in vitro* anti-inflammatory and antibacterial activities were also performed owing to Inflammation is an unspecific response of the immune system to the pathogen.

2. Materials and Methods

All the chemicals (Merck, Hi-Media and Sigma-Aldrich, SD Fine Chem., Mumbai) in this synthesis were of AR and LR grade and were obtained and used without further purification.

2.1 Experimental section

The melting points in open capillary technique were calculated using the Thomas Hoover equipment, and the results are presented as unchanged. Using the KBr pellet approach, IR spectra in the range of 4000 cm^{-1} to 400 cm^{-1} on a Shimadzu 8300, Kyoto, Japan, were obtained to characterize the produced components. The DMSO solvent and trimethylsilane, which served as an internal standard, were utilised to record the hydrogen spectral data using a Bruker AVIII 500 FT NMR spectrometer. Parts per million (ppm) scale measurements of the chemical shifts (d) were performed. The direct

Corresponding author: Dr. T. Prabha

Professor, Department of Pharmaceutical Chemistry, Nandha College of Pharmacy, Erode-638052, Tamilnadu, India

E-mail: drtpappa@yahoo.com

Tel.: +91-9965557346

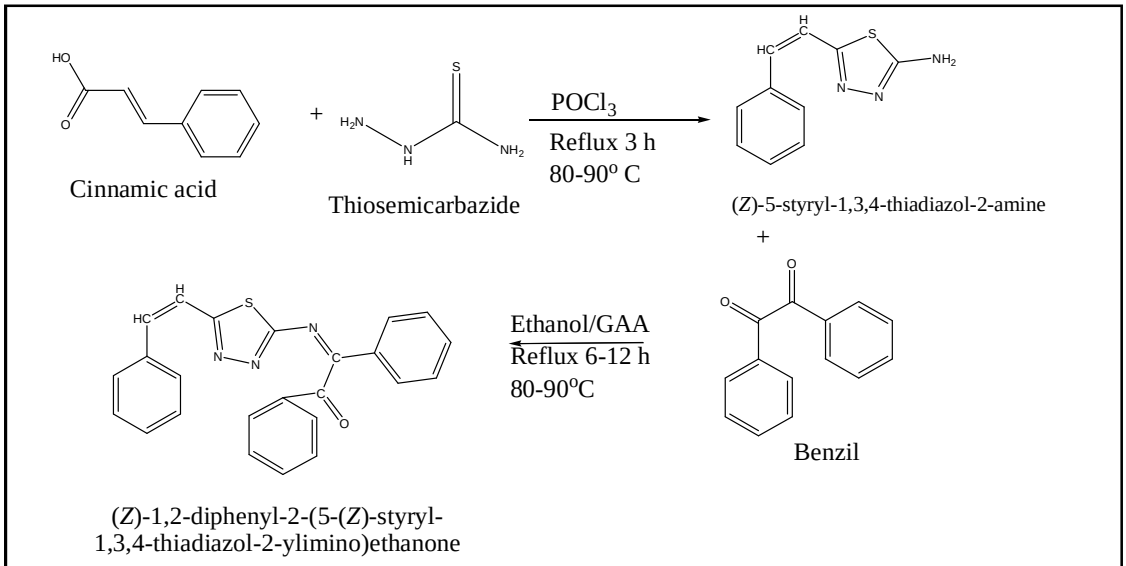
sample injection was used to record the mass spectra by using a Jeol GC match II HR mass spectrometer (EI ionization, 70 eV).

2.1.1 Synthesis of thiadiazole scaffolds

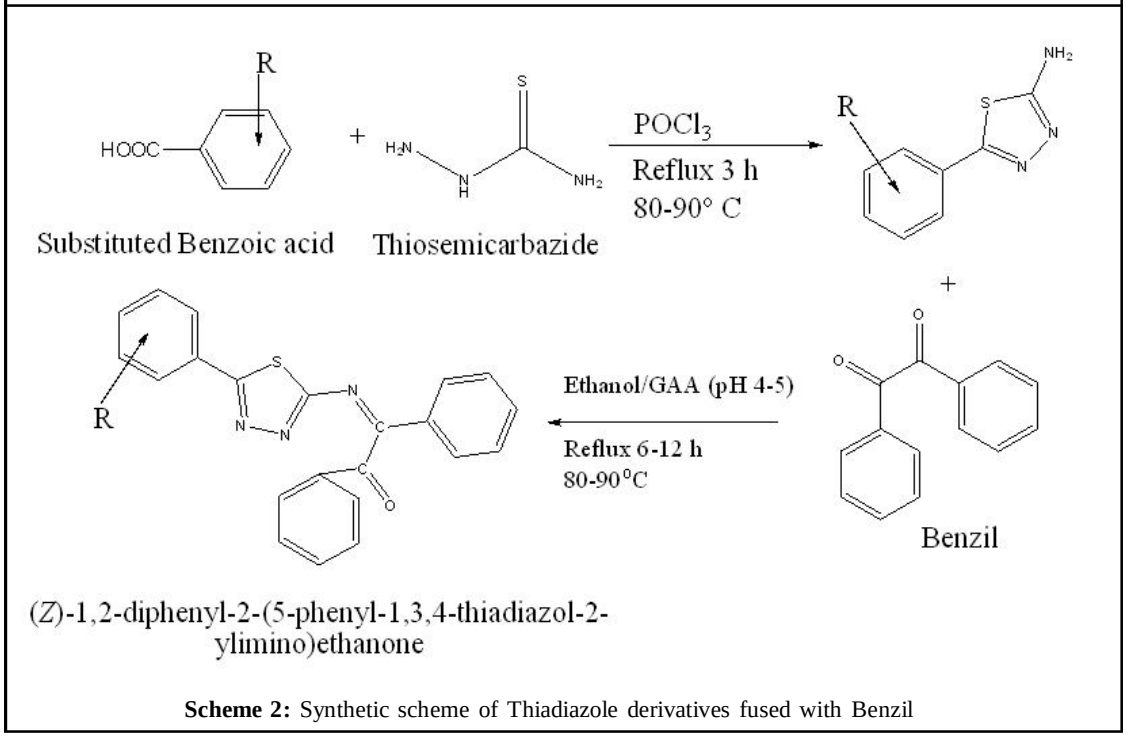
In our research, the thiadiazole derivatives were prepared by the reaction of an equimolar amount of substituted aromatic acid (10 mm) with thiosemicarbazide (10 mm) was dissolved in 10 ml of $POCl_3$ and refluxed at 80°C for 3-4 h to afford the intermediate product (Scheme 1 and 2) (Ivan *et al*., 2014).

2.1.2 Synthesis of thiadiazole derivatives hybrid with benzil

And to the above obtained intermediate thiadiazole compounds, an equimolar concentration of benzil and 10 ml of ethanol was added followed by the addition of catalytic amount of glacial acetic acid to maintain the pH 4-5.Then, this mixture was the refluxed at 80°C for 6-12 h to get a desired thiadiazole derivatives hybrid with benzil. After adding the reaction mixture to cold ice, the precipitates were collected and filtered before being dried. The material was purified by recrystallizing with pure ethanol (Scheme 1 and 2) (Prabha *et al*., 2019; Kiruthiga *et al*., 2018).



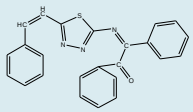
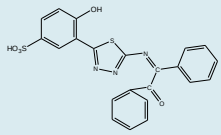
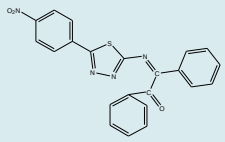
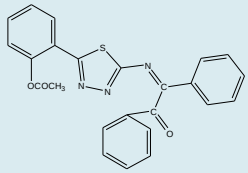
Scheme 1: Synthetic scheme of Thiadiazole derivatives fused with Benzil



Scheme 2: Synthetic scheme of Thiadiazole derivatives fused with Benzil

Substitution pattern for R= TZ-1: cinnamic acid;TZ-2: sulpho salicylic acid; TZ-3: P-nitro benzoic acid; TZ-4: acetylsalicylic acid

Table 1: Structures of synthesized thiadiazole derivatives fused with benzil

S.No.	Compound code	Structure	IUPAC name
1	TZ-1		(Z)-1,2-diphenyl-2-(5-(Z)-styryl-1,3,4-thiadiazol-2-ylimino)ethanone
2	TZ-2		(Z)-4-hydroxy-3-(5-(2-oxo-1,2-diphenylethylideneamino)-1,3,4-thiadiazol 2-yl)benzenesulfonic acid
3	TZ-3		(Z)-2-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-ylimino)-1,2-diphenylethanone
4	TZ-4		(Z)-2-(5-(2-oxo-1,2-diphenylethylideneamino)-1,3,4-thiadiazol-2-yl) phenyl acetate

2.2 Biological evaluation

2.2.1 Antibacterial activity

Liquid Mueller Hinton agar media was prepared and 18 h culture of gram-positive microorganisms such as *Bacillus subtilis* (MTCC 1305), *Staphylococcus aureus* (MTCC 3160) and gram-negative microorganisms such as *Pseudomonas fluorescens* (1749) and *Pseudomonas aeruginosa* (MTCC 1688) obtained from Chandigarh and Coimbatore, were used for this study. The synthesized compounds at different concentrations (100, 200, 400 µg/ml) were dissolved, respectively, in ethanol and tested for their antibacterial activity. A control experiment also performed to avoid any solvent effect on microbial action (Prabha *et al*., 2019; Chandrashekara *et al*., 2017).

2.2.2 Minimum inhibitory concentration

The technique of serial two-fold dilution was used to estimate the MIC of synthesised products (Prabha *et al*., 2019). The equal volume of media infected with the bacterial suspension was produced in a set of test tubes. All tubes received drug administrations at decreasing drug concentrations (200, 100, and 50 g/ml), with the exception of one tube that acted as a control sample for the observable growth of the microbe. The culture was kept at 37°C for 24 h while being maintained at room temperature. The tubes were visually checked to evaluate the microorganism's development based on the turbulence that occurred. The amount of the synthesised substance needed to stop the growth was shown as a tube filled with transparent medium.

2.2.3 Assessment of *in vitro* anti-inflammatory activity

2.2.3.1 Inhibition of albumin denaturation

The inhibition of albumin denaturation was assessed through previously reported Juvekar *et al*. (2009) method. In concise, the reaction mixture consists 1ml of synthesized compounds and as well a standard drug aspirin at various concentrations (100, 200, 400 µg/ml). The remaining procedure was followed as per the above said method. The protein denaturation was calculated in term of its percentage inhibition by using the following formula:

Percentage inhibition = (Abs control – Abs sample) × 100/Abs control.

3. Results

3.1 Spectral interpretation of synthesized compounds

The yield of the synthesized derivatives was obtained as acceptable range (14-27%). The synthesised compounds' percentage yield and melting point were noted and uncorrected representations were produced on them (Tables 2 and 3). The key reactions involved were the intermediate formation of thiadiazole and subsequent addition of benzil on the $-NH_2$bond that forms the final products of thiadiazole derivatives. Depending on their chemical shifts and multiplicities, the signals of the corresponding protons of the final compounds were confirmed in the ^{1}H-NMR. Owing to the ring closure, the compounds' infrared spectroscopy exhibit the following appearances: (N-H stretch), 1659 (C=N stretch), 1325 (C-N stretch), 2922 (N-H stretch), and 1676 (C=N stretch). The 1,3,4-thiadiazole core was coupled with characteristic signals for protons that occurred around 7.14 and 7.40 ppm, as well as signals from the distinctive amino group (4.06 ppm) and ethylene protons (6.56 ppm) were also observed for thiadiazole derivatives.

Table 2: Characterization for the thiadiazole derivatives fused with benzil

S.No.	Code	Color of the compound	Molecular formula	Molecular weight (mole)	melting point M(°C)	λ max (nm)	% Yield (w/w)
1	TZ-1	Pale yellow	$C_{24}H_{17}N_3OS$	395	98 - 103.2	340, 259	27.12 %
2	TZ-2	Creamy white	$C_{22}H_{15}N_3O_5S_2$	465	162.7 - 167	341, 261	18.57%
3	TZ-3	Pale yellow	$C_{21}H_{14}N_4O_3S$	414	220.8 – 221.2	341, 259	14.61%
4	TZ-4	Creamy white	$C_{24}H_{17}N_3O_3S$	427	152.2 – 158.6	341, 260	22.99%

Table 3: Solubility profile of the synthesized thiadiazole derivatives

S.No.	Code	Solvents							
		Water	DMSO	Ethanol	Methanol	Acetone	Ethyl acetate	Chloroform	Petroleum ether
1	TZ-1	+	+++	+++	+++	+++	+++	+++	+++
2	TZ-2	+	+++	+++	+++	+++	+++	+++	+++
3	TZ-3	+	+++	+++	+++	+++	+++	+++	+++
4	TZ-4	+	+++	+++	+++	+++	+	+++	+++

Keywords: +++ - Freely soluble; + - Insoluble.

3.2 Spectral characterization

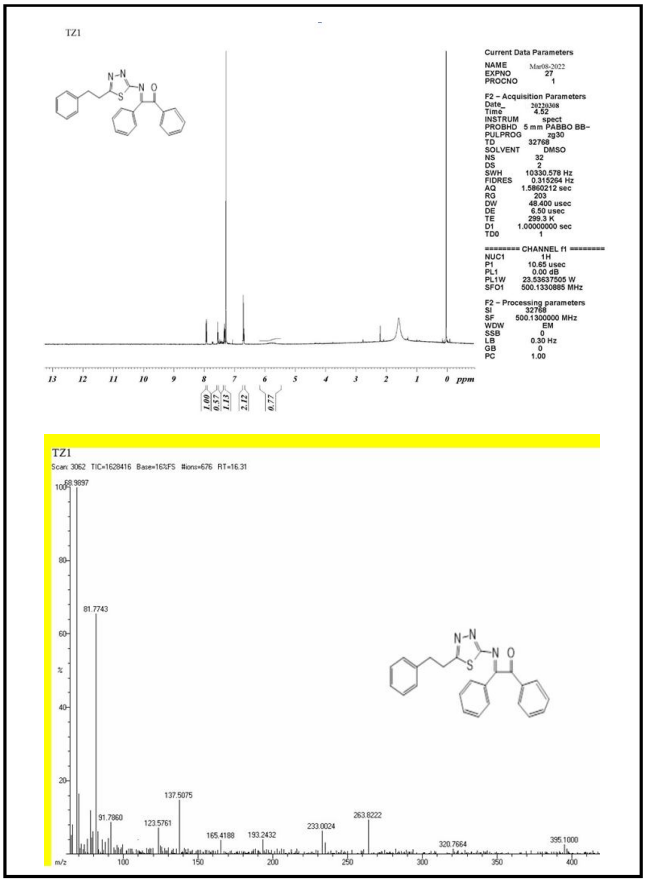
Compound TZ-1: (Z)-1,2-diphenyl-2-(5-(Z)-styryl-1,3,4-thiadiazol-2-ylimino) ethanone. IR (KBR) cm-$^{-1}$ 3063 (C-H stretch), 3316 (N-H stretch), 1659 (C=N stretch), 1578 (C=C stretch), 1450 (C-H bending), 1315 (O-H bending), 1211 (C-O stretch), 1174 (C-O stretch), 1097 (C-O stretch), 1023 (C-O stretch), 725 (C=C bending). NMR (δ ppm) 7.2-7.9 (aromatic CH), 6.6-6.7 (CH=CH). Mass m/z M^+ =395 ($C_{24}H_{19}N_3OS$), 320 ($C_{18}H_{15}N_3OS$), 232 ($C_{11}H_9N_3OS$), 192 ($C_8H_6N_2OS$), 136 ($C_8H_{11}NO$), 122 ($C_8H_{10}O$), 91 (C_7H_7). There could be the 15 aromatic protons found in the TZ1 compound.

Compound TZ-2: (Z)-4-hydroxy-3-(5-(2-oxo-1,2-diphenylethy lideneamino)-1,3,4-thiadiazol-2-yl) benzenesulfonic acid. IR (KBR) cm-$^{-1}$ 3316 (N-H stretch), 3063 (C-H stretch), 1659 (C=C stretch), 1579 (C=C stretch), 1488 (C-H bending), 1450 (C-H bending), 1325 (C-N stretch), 1211 (C-0 stretch), 1174 (C-O stretch), 998 (C=C bending), 876 (C-H bending), 725 (C=C bending). NMR (α ppm) 7.5-7.7 (aromatic CH), 6.1 (aromatic OH), 2.3-2.5 (SO_3H, C=O). Mass m/z M^+ = 465 ($C_{22}H_{15}N_3O_5S_2$), 384 ($C_{22}H_{15}N_3O_2S$), 294 ($C_{16}H_{11}N_3OS$), 255 ($C_{15}H_{13}NOS$),221($C_{15}H_{12}NO$),148 ($C_9H_{10}NO$),138 ($C_8H_{11}NO$), 123 ($C_8H_{10}O$),91(C_6H_6O). There could be the 17 aromatic protons found in the TZ2 compound.

Compound TZ-3: (Z)-2-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-ylimino)-1,2-diphenylethanone. IR(KBR) cm-$^{-1}$ 3316 (N-H stretch), 3063 (C-H stretch), 1670 (C=C stretch), 1450 (O-H bending), 1211 (C-O stretch), 1174 (C-O stretch), 875 (C –H bending), 718 (C=C bending). NMR (α ppm) 2.1-2.5 (C-N), 6-6.7 (CH=CH), 7.2 -7.6 (aromatic CH). Mass m/z M^+ =414 ($C_{22}H_{14}N_4O_3S$), 369 ($C_{22}H_{15}N_3OS$), 293 ($C_{16}H_{11}N_3OS$), 219 ($C_{10}H_9N_3OS$), 181 ($C_9H_{11}NOS$), 138 ($C_8H_{11}NO$), 123 ($C_8H_{10}O$). There could be the 14 aromatic protons found in the TZ3 compound.

Compound TZ-4: (Z)-2-(5-(2-oxo-1,2-diphenylethylideneamino)-1,3,4-thiadiazol-2-yl) phenyl acetate. IR (KBR) cm-$^{-1}$ 3316 (N-H stretch), 3063 (O-H stretch), 2922 (N-H stretch), 1676 (C=N stretch), 1578 (C=C stretch), 1450 (C-H bending), 1325 (C-N stretch), 1211 (C-O stretch), 1174 (C-O stretch). NMR (α ppm) 7.6-8 (aromatic CH), 2.5 ($OCOCH_3$), 2.1-3 (C-N). Mass m/z M^+ =427 ($C_{24}H_{17}N_3O_3S$), 384 ($C_{22}H_{15}N_3O_2S$), 294 ($C_{16}H_{11}N_3OS$), 257 ($C_{15}H_{15}NOS$), 224 ($C_{15}H_{14}NO$), 148 ($C_9H_{10}NO$), 138 ($C_8H_{11}NO$), 123 ($C_8H_{10}O$), 92 (C_6H_6O). There could be the 14 aromatic protons found in the TZ4 compound.

The NMR and MASS chromatogram of synthesized compounds TZ1-TZ4 are presented in Figure 1.



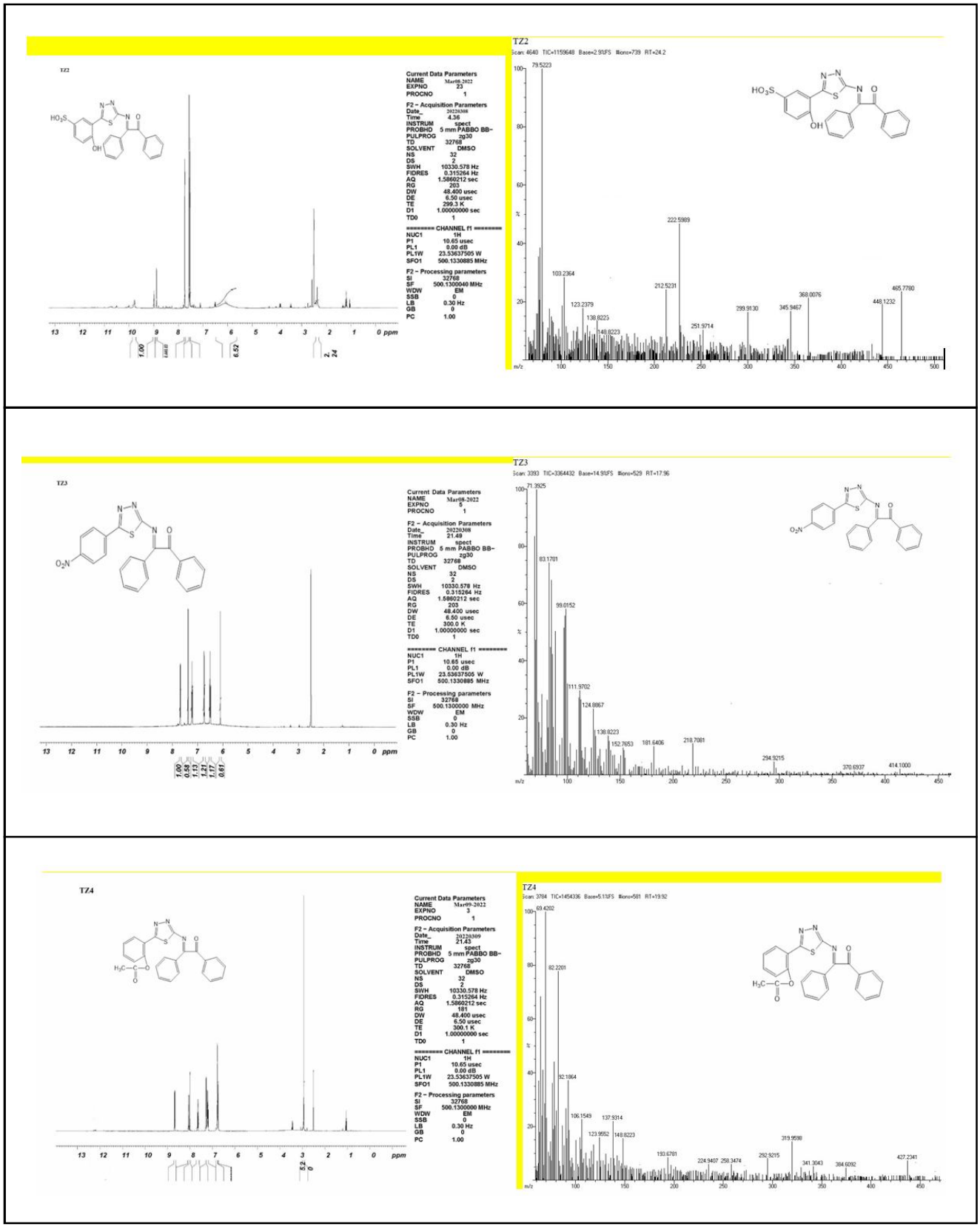


Figure 1: NMR and MASS chromatogram of synthesized compounds TZ1-TZ4.

3.3 Result on antibacterial study

Among the all four synthesized compounds, the compounds TZ1, TZ2, TZ3, and TZ4 showed good MIC value at 50 µg/ml and showed the noteworthy antibacterial activity against both gram-positive and gram-negative pathogen with maximum zone of inhibition, *i.e.*, about within the range of 13-25 mm and 06-22 mm at 200 µg/ml concentrations, respectively, when compared to standard drug ciprofloxacin, whose value lies between in the range of 18-28 mm and 15-25 mm for 200 µg/ml concentrations (Figure 2 and Table 4).

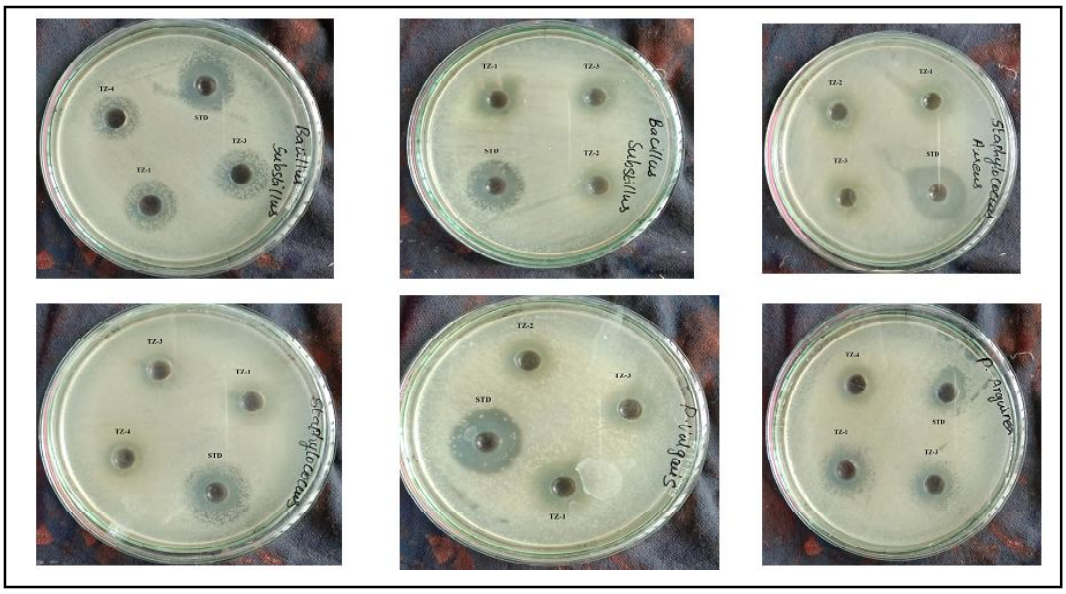


Figure 2: Glimpses of antibacterial activity against gram-negative and gram-positive pathogens.

Table 4: Antibacterial activity (zone of inhibition in mm) of synthesized compounds

Compound code	Gram-positive bacteria *B.subtilis* *S. aureus* (µg/ml)				Gram-negative bacteria *P. fluorescens* *P. aeruginosa* (µg/ml)			
	100	200	100	200	100	200	100	200
TZ1	14	25	11	24	13	22	11	19
TZ2	12	22	11	20	10	19	10	20
TZ3	13	25	09	19	10	16	09	18
TZ4	12	13	-	-	-	06	05	08
Ciprofloxacin	16	28	18	28	16	24	15	25

3.4 Results on *in vitro* anti-inflammatory study

All the synthesized 1,3,4-thiadiazole derivative compounds were evaluated for *in vitro* anti-inflammatory study. The compounds of TZ-1, TZ-2, TZ-3, TZ-4 of concentration 100 µg/ml, 200 µg/ml, 400 µg/ml were seen for inhibition, and the values compared against the standard drug aceclofenac and the results were shown in Table 5 (Prabha *et al.*, 2018).

Table 5: Effect of synthesized compounds on percentage inhibition of protein denaturation

S.No.	Compound code	Concentration(µg/ml)	Absorbance (nm)	%protein inhibition
1.	TZ-1	100200400	0.00330.00530.0163	95.693.1279.03
2.	TZ-2	100200400	0.0230.0250.016	69.6567.4979.48
3.	TZ-3	100200400	0.0270.0250.033	65.3879.0584.33
4.	TZ-4	100200400	0.0260.0240.021	66.2369.2273.28
5.	Standard (Aceclofenac)	100200400	0.00560.0440.017	90.1680.3377.34

4. Discussion

The new series of thiadiazole annulated benzil conjugates were synthesized *via* cyclization and evaluated for their *in vitro* antibacterial and anti-inflammatory activity. The key reactions involved were the intermediate formation of thiadiazole and subsequent addition of benzil on the $–NH_2$bond that forms the final products of thiadiazole derivatives. According on their chemical shifts, the signals of the corresponding protons of the final compounds were confirmed in the ^{1}H-NMR.

Thiadiazolidine ring is present in penicillin which exerts the antibacterial action *via* inhibiting peptidoglycan cell wall synthesis of bacteria. Similarly, it is thought that the thiadiazole ring could have the antibacterial action by inhibiting the cell wall synthesis. It is generally known that 1,3,4-thiadiazoles have antibacterial and antifungal activities that are comparable to that of well-known sulphonamide therapies. Some cephalosporins and cephamycins have a 1,3,4-thiadiazole ring as a structural component, and these compounds have strong *in vitro* action both against gram-positive and gram-negative organisms (Ivanildo *et al*., 2014). As a result, a variety of biological activities are displayed by 1,3,4-thiadiazoles, may be as a result of the toxophoric –N, C, S groups (Serban *et al*., 2018).

The rate of absorption into the bacterial cell and its ability to inhibit of DNA gyrase are the two elements that affect the Minimum Inhibition concentration (MIC) of thiadiazole. The thorough study of antibacterial activity revealed that each of these drugs' inhibitory levels displayed a wide variety of zones of inhibition towards the strains of bacteria. By using the twofold serial dilution technique, the substances were tested for their ability to combat gram-positive (*B. subtilis* and *S. aureus*) and gram-negative (*P. fluorescens* and *P. aeruginosa*) bacterial strains. Along with the screened compounds, *viz*., TZ-2, TZ-3, and TZ-4 (-SO_3H, -NO_2 and -$OCOCH_3$ substituent) bearing deactivating group, *i.e.*, electron withdrawing groups and the compounds TZ-1 (CH=CH) bearing strongly activating group, *i.e.*, electron-donating group in its phenyl ring system exhibited the prominent antibacterial activity (Bahare *et al*., 2014; Awale *et al*., 2013) showed good MIC value of 50 µg/ml against both gram-positive and negative pathogen, while compared to that of standard drug ciprofloxacin (Abdel-Rahman *et al*., 2007).

Whereas, the compounds TZ-2 and TZ-4 showed the modest activity against bacterial infection and the MIC value was 100 µg/ml, and with no activity with this concentration level. This is might be the presence of electron-donating atoms in its phenyl ring system. However, the compound TZ-1 and TZ-3 possess the CH=CH, NO_2 groups, whose antibacterial activity has been used in the elimination of pathogens (Bezerra *et al*., 2017).

Inflammation is one of the body's most important mechanisms for protecting itself against danger. The anti-inflammatory activity also done owing to inflammation is an unspecific response of the immune system to pathogens, such as assault by bacteria. Infection with pathogenic microbes often results in a significant inflammatory response. Based on this declaration, a microbial infection will cause fluid accumulation in the injured/infected site and leads to inflammation and swelling. By considering the above discussion, an *in vitro* anti-inflammatory activity was also done. By the application of external stress such as acid, alkali, and heat, *etc*., the protein loses its tertiary and secondary structure along with their biological function and thereby cause inflammation condition (Deattu *et al*., 2012).

An additional capacity to prevent protein denaturation was carried out as part of the research into the mechanism of the synthesised compound's anti-inflammation effect. By applying an external source of stress or substance, such as a strong acid or base, a strong inorganic salt, an organic solvent, or heat, proteins can become denaturized, losing both their secondary and tertiary structures. When denatured, the majority of biological proteins cease to function biologically. Protein denaturation is a well-known contributor to inflammation. The potential of synthetic substances to suppress protein denaturation was investigated as part of the research into the mechanism of the anti-inflammation effect. It was successful in preventing albumin denaturation caused on by heat. Aceclofenac, a common anti-inflammatory medication, is matched with the control.

5. Conclusion

The new series of thiadiazole fused with benzil derivatives were synthesized, characterized, and evaluated for their antibacterial and anti-inflammatory activity. The chief reactions concerned with the thiadiazole intermediate formation by the addition of respective diverse aromatic acid with thiosemicarbazide, followed by the addition benzil on the NH_2 center yielded the desired product. Besides, the synthesized compounds showed the noteworthy action on antibacterial and anti-inflammatory activities owing to the presence of heterocyclic ring system, more polar analogs, deactivating and activating groups like, –Cl and –NO_2 moiety in its phenyl system. Thus, it might lead to produce the novel drug candidates for treating the many infectious diseases like inflammation, cancer, arthritis, *etc.*

Conflict of interest

The authors declare no conflicts of interest relevant to this article.

References

Abdel Rahman, A. A. H., Abdel Megied, A. E. S., Hawata, M. A. M., Kasem, E. R. and Shabaan, M. T. (2007). Synthesis and antimicrobial evaluation of Some chalcones and their derived pyrazoles, pyrazolines, isoxazolines, and 5,6-Dihydropyrimidine-2- (1H)-thiones. Monatshefte FürChemie - Chemical Monthly, **138**(9):889-897.

Andre, G. B. (2010). Immuno-modulation and anti-inflammatory benefits of antibiotics: The example of tilmicosin. Canadian Journal of Veterinary Research, **74**(1):1-10.

Awale, A. G., Gholse, S. B. and Utale, P. (2013). Synthesis and antimicrobial evaluation of some novel Schiff bases derived from benzothiazole derivative. International Journal of Scientific and Engineering Research, **4**(6):1972-1979.

Bahare, R. S. and Ganguly, S. (2014). Effect of electronegative groups on the antimicrobial activity. **3**(1):112-119. 5-disubstituted Thiazolidine-2,4-diones. Anti-infective agents.

Bezerra, C. F.; Camilo, C. J.; Nascimento, D.; Silva, M. K.; Freitas, T. S. D.; Ribeiro-Filho, J. and Coutinho, H. D. M. (2017). Vanillin selectively modulates the action of antibiotics against resistant bacteria. Microbial Pathogenesis, **113**:265-268.

Chandrashekara, R.; Jisha, M. S.; Merugumolu, V. K. and Kumar, H. (2017). Synthesis, antibacterial and antifungal evlaution of novel pyrazoline derivatives. Research Journal of Pharmacy and Technology, **10**(5):1481-1484.

Deattu, N.; Narayanan, N. and Suseela, L. (2012). Evaluation of anti-inflammatory and antioxidant activities of polyherbal extract by *in vitro* methods. Research Journal of Pharmaceutical, Biological and Chemical Sciences, **3**(4):727-732.

Ivan Hameed R.T.; Ali Hussein R. A.; Raya Raad T. A.; Mohammed, M. H. and Khlood, H.D.A. (2014). Synthesis, characterization and biological activities of some azo derivatives of aminothiadiazole derived from nicotinic and isonicotinic acids, Arabian Journal of Chemistry, **7**(5):687-694, ISSN 1878-5352.

Ivanildo, M. S.; João da, S. F.; Priscila, B. and Gomes da, S. S. (2014). Synthesis and antimicrobial activities of 5-arylidene-thiazolidine-2,4-dione derivatives. Bio Med Research International, ArticleID 316082.

Juvekar, A.; Sakat, S.; Wankhede, S.; Juvekar, M. and Gambhire, M. (2009). Evaluation of antioxidant and anti-inflammatory activity of methanol extract of *Oxalis corniculata*. Planta Medica, **75**(09):146-155

Kiruthiga, N.; Prabha, T.; Selvinthanuja, C.; Srinivasan, K. and Sivakumar, T. (2018). Multidocking studies on 2-phenyl-4h-chromen-4-one hybrid and evaluation of antidiabetic activity, Journal of Pharmaceutical Sciences and Research, **10**(12):3018-324.

Prabha, T.; Aishwaryah, P.; Manickavalli, E.; Chandru, R.; Arulbharathi, G.; Anu, A. and Sivakumar, T. (2019). A chalcone annulated pyrazoline conjugates as a potent antimycobacterial agents: Synthesis and *in silico* molecular modeling studies. Research J. Pharm. and Tech., **12**(8):3857-3865.

Rouf, A. and Tanyeli, C. (2014). Bioactive thiazole and benzothiazole derivatives. Eur. J. Med. Chem., 2015 Jun 5;97:911-27. doi: 10.1016/j.ejmech.2014.10.058. Epub 2014 Oct 22. PMID: 25455640.

Serban, G.; Stanasel, O.; Serban, E. and Bota, S. (2018). 2-Amino-1,3,4-thiadiazole as a potential scaffold for promising antimicrobial agents. Drug Des. Devel. Ther., s12:1545-1566. doi: 10.2147/DDDT.S155958. PMID: 29910602; PMCID: PMC5987787.

Singh, G.; Kaur, R.; Chandel, P.; Singla, N. and Kumar, A. (2019). Rationally synthesized coumarin based pyrazolines ameliorates carrageenan induced inflammation through COX-2/Pro- inflamma-tory cytokine inhibition. Med. Chem. Comm., **10**(3):1-19.

Prabha, T.; Jubie, S.; Selvamani, P.; Latha, S. and Sivakumar, T. (2019). Dual evaluation of some novel chalcone annulated pyrazolines as anti-inflammatory and antimicrobial agents *via in silico* target study on cyclooxygenase-2, Int. J. Res. Pharm. Sci., **10**(4):3159-3169.

Thangavelu, P. and Thangavel, S. (2018). Design, synthesis, and docking of sulfadiazine schiff base scaffold for their potential claim as inhaenoyl-(Acyl-carrier-protein) reductase inhibitors. Asian Journal of Pharmaceutical and Clinical Research, **11**(10):233-237.

Citation **T. Prabha, C. Selvinthanuja, S. Suganya, B. Rahini, B. Nithiya, S. Vijay, K. Pandian and B. Punithkumar (2022). Synthesis, characterization, and *in vitro* evaluation of thiadiazol-2-ylimino ethenone derivatives. J. Phytonanotech. Pharmaceut. Sci., 2(3):19-26. http://dx.doi.org/10.54085/jpps.2022.2.3.4**