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"Design And Evaluation of Novel Thiazole Derivatives Targeting Multidrug-Resistant Mycobacterium Tuberculosis"

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Abstract
Tuberculosis (TB) causes millions of deaths worldwide, and the emergence of MDR-, XDR-, and TDR-TB strains has reduced drug effectiveness. Though new drugs like pretomanid, bedaquiline, and linezolid show promise, their toxicity remains a concern. Hence, importance of innovative thiazole derivatives has gained increasing attention due to their diverse biological activities, structural versatility, and potential to act on new molecular targets within M. tuberculosis. Hence, in this paper we report a convenient and high-yielding solid-phase synthesis of novel 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives ***(3a–e)*** *used as antitubercular drugs. All the final compounds were characterised using spectral methods FTIR, ^{1}H-NMR, ^{13}C-NMR, GCMS and Elemental analysis. The compounds were screened for their in vitro antimycobacterial activity against Mycobacterium tuberculosis H37Rv strain by Microplate Alamar Blue assay (MABA) method. All the compounds exhibited very good inhibitory activity against the bacterial strain, with a MIC value of 6.25 µg/mL, comparable to the standard drug rifampicin.*

Keywords: *Organic Synthesis, 2,4-substituted thiazoles, 2-bromo-1-phenylethan-1-one, Anti-tuberculosis, Microplate Alamar Blue assay H37Rv strain.*

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I. Introduction

A serious threat to humanity is tuberculosis (TB), an infection brought by Mycobacterium tuberculosis (MTB).[1] Many types of antimicrobial medications have been created significantly for fighting microbial diseases. The World Health Organization (WHO) estimates that 1.5 million individuals died from tuberculosis (TB) in 2018. This is among the foremost ten causes of mortality worldwide and that has been connected to the emergence of HIV and AIDS, among other illnesses that are contagious.[2] Furthermore, it was anticipated that 2,51,000 TB fatalities included in HIV-positive individuals and 1.2 million HIV-negative people died of TB in 2018.[3] Despite the fact that tuberculosis is preventable and treatable, according to WHO reports, only around 2% of TB cases are reduced annually by therapy with common antitubercular medications that have been in use for decades, such as isoniazid, rifampicin, delamanid, bedaquiline, ethambutol, and pyrazinamide.[4,5] The aforementioned medications have certain harmful side effects in addition to their therapeutic effects, including hepatotoxicity, CNS toxicity, and QT prolongation.

Heterocyclic compounds are still useful templates in therapeutic Chemistry because of their wide range of biological activity and amazing structural variety.[6-8] Characterized by aromatic or partially saturated heterocyclic ring systems containing nitrogen, oxygen, or sulfur, these compounds serve as key structural scaffolds in the design of a wide range of therapeutic molecules. Among them, the thiazole ring system has drawn attention due to its many pharmacological uses, such as anticancer.[9,10] antitubercular,[11,12] antibacterial,[13,14] anti-inflammatory,[15] antioxidant,[16] antidepressant,[17] antiviral,[18] antidiabetic,[19] and antiparasitic[20] assets. Hydrazones, derived from Schiff bases, have attracted significant attention due to their diverse and potent biological properties.[21] The strategic incorporation of these moieties into thiazole–hydrazone architectures yield hybrid systems with enhanced electronic conjugation, superior cellular uptake, and advantageous pharmacodynamic profiles.[22,23] As a prominent strategy in rational drug discovery, molecular hybridization merges distinct bioactive moieties into a single molecular entity, resulting in compounds with improved efficacy, lower resistance potential, and broaden biological functions.

Distinguished from other explored hybrid and fused molecular frameworks, thiazole–hydrazone derivatives constitute a notably promising class of heterocycles, a distinction driven by their exceptional breadth of biological activity. Their molecular framework promotes high-affinity interactions with biological targets, supporting effective association with enzyme catalytic regions and receptor binding sites. The inherent flexibility of hydrazones permits extensive structural fine-tuning, thereby facilitating the design of derivatives

exhibiting augmented pharmacokinetic properties and strengthened binding interactions.[24–26.] Owing to its bis-heterocyclic nature, the thiazole–hydrazone scaffold offers considerable structural flexibility for multi-target drug development, particularly for complex disorders such as cancer that require simultaneous modulation of multiple biological pathways. Hybridization introduces several functional advantages, (a) notably the reduction of adverse sulfur-mediated effects, achieved by the hydrazone functionality (–NH–N=CH–) acting as a transition-metal scavenger that limits oxidative stress induction; (b) Coupling with the hydrazone moiety extends the π-conjugation across the framework, leading to enhanced stabilization of the thiazole ring while simultaneously conferring pH-responsive stability; (c) Furthermore, this combined framework is characterized by favorable aqueous solubility and synthetic accessibility; (d) Electron donation from the sulfur and nitrogen atoms of the thiazole ring enhances lipophilicity and membrane permeability, thereby facilitating intracellular target access, while the hydrazone unit contributes a flexible linker enriched with hydrogen bond donor and acceptor sites; together, these features define a bis-heterocyclic scaffold that integrates the complementary advantages of both motifs in drug discovery.[27-30]

More than 90 thiazole-based analogues are now undergoing healthcare studies, and certain thiazole frameworks have received approval for the treatment of various disorders. Thiazole derivatives can be comprehensively analysed as optimal frameworks for the design and synthesis of new compounds exhibiting improved biological activity.[31,32] Some of the FDA-approved thiazole-containing drugs which are used as antitubercular drugs have been mentioned in **(Figure. 1).** Phenyl-thiazole, Imidazo-thiazole, Hydrazine-thiazole, Thiazolidinone azole derivatives, Carboxamide-thiazole, Benzothiazole derivative, Amino thiazole derivatives are some of the antitubercular drugs that are used.[33] Karpoormath and his team designed and synthesized fluorophenyl-tethered thiazole compounds bearing electron withdrawing and electron-donating groups on the phenyl ring at C4 of the thiazole core resulted appreciable antimycobacterial activity against *M. tuberculosis* H37Rv strain.[34]

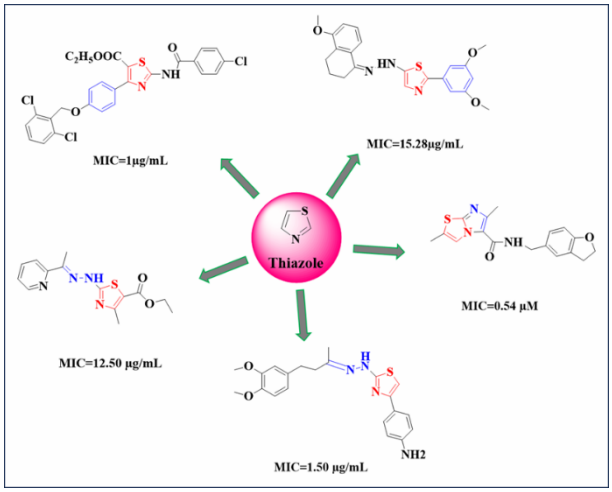


Fig. 1 Some of FDA-approved Thiazole-Containing Drugs Used as Antitubercular Agents

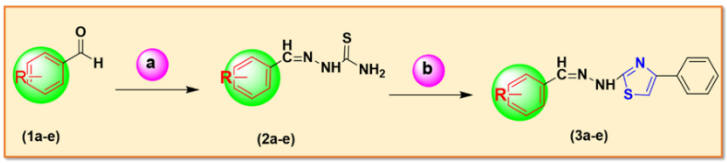
The current work focuses on the synthesis of thiazole derivatives from thiosemicarbazones is valuable due to its simple and economical synthetic pathway, high yields, and capability to generate a spectrum of structural variations. The thiazolyl hydrazone framework has emerged as a pivotal heterocyclic motif in various anti-tubercular agents, acting as a strategic molecular bridge that seamlessly integrates two pharmacophoric entities to enhance biological efficacy and target specificity.[35-38] The remarkable ability of thiazolyl hydrazone compounds to suppress Mycobacterium tuberculosis growth at low concentrations, combined with the ease of synthesising their derivatives using an efficient one-pot multicomponent approach, emphasizes their importance and reinforces their promise as potent anti-tubercular candidates.[39-42] The thiazole nucleus, being an essential heterocyclic scaffold, can be easily modified to enhance lipophilicity, bioavailability, and target specificity, leading to improved antitubercular efficacy. This versatility facilitates the fine-tuning of pharmacokinetic properties and the enhancement of biological activity. Furthermore, a lipophilic aryl moiety enhances the permeability of the Mycobacterium tuberculosis cell wall, the majority of reported anti-tubercular agents incorporate an aryl ring at one terminus of the molecule to promote efficient cellular penetration this class of heterocyclic compounds has shown a lot of promise as antitubercular drugs.[43-45] The intent of this study is to construct extremely efficient and selective anti-TB molecules with favourable drug-like properties as possible TB treatment entities. The design, synthesis, and biological evaluation of a new family of 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives **(3a–e)** are presented.

II. Materials And Methods

Melting points were measured on an electrothermal apparatus and are reported without correction. Infrared spectra (KBr pellets) were recorded using a Shimadzu FT-IR 8201 PC spectrophotometer. Proton and carbon-13 NMR spectra were acquired in DMSO-d on a Bruker DPX-500 MHz instrument and Chemical shifts are reported in parts per million (ppm) relative to tetramethyl silane (TMS) as an internal standard. Mass spectra were recorded on a Shimadzu GC–MS QP1000 EX instrument. Elemental analyses were performed using a Vario EL cube.

Chemistry

The synthesis of 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives **(3a–e)** was accomplished as shown in **Scheme 1**. Compounds **(3a–e)** were spectroscopically characterized and subjected to antitubercular screening and molecular docking analysis.

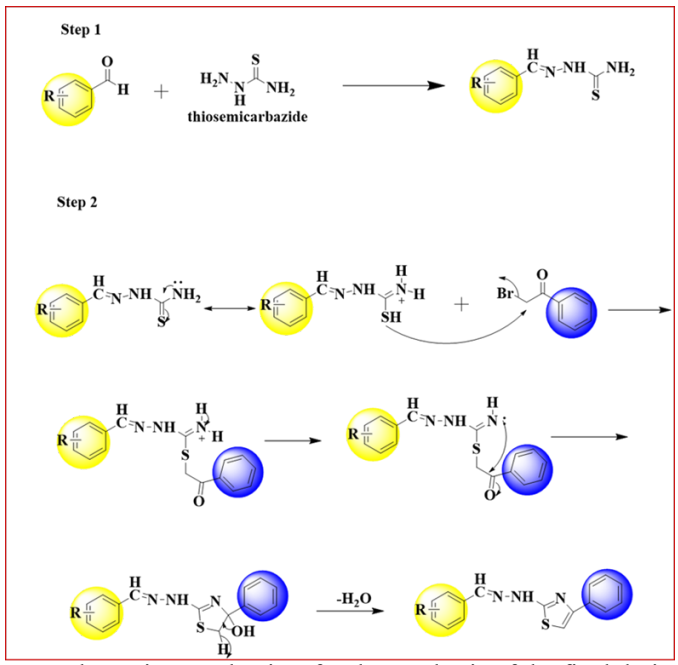


Scheme 1 Synthetic route for titled compounds **(3a-e)** [a]. [a]Reagents and Conditions: a) Thiosemicarbazone, Conc. H_2SO_4 (1-2 drops), methanol, reflux 4-6 h b) Phenacyl bromide, Crush, reflux 4-5h.

The (E)-2-(Substituted Benzylidene) hydrazine-1-carbothioamide derivatives **(2a–e)** and their corresponding 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives **(3a–e)** were synthesized according to the strategy illustrated in **(Scheme 1).** Initially, the (E)-2-(Substituted Benzylidene) hydrazine-1-carbothioamide derivatives were obtained through a condensation reaction between equimolar quantities of substituted aromatic aldehydes and thiosemicarbazide under reflux conditions. This transformation proceeds via nucleophilic attack of the terminal hydrazinic –NH group of thiosemicarbazide on the carbonyl carbon of the aldehyde, followed by dehydration, affording the corresponding imine (–C=NNH–) linkage, characteristic of thiosemicarbazones.

In the subsequent step, the preformed thiosemicarbazones were subjected to intramolecular cyclization in the presence of phenacyl bromide. The reaction mechanism involves initial alkylation of the thioamide sulfur atom by the electrophilic bromoacetophenone moiety, generating a thioether intermediate. Subsequent intramolecular nucleophilic substitution and rearrangement lead to the formation of the thiazole nucleus, thereby furnishing the final novel 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives **(3a–e)** in good yields.

This two-step synthetic pathway demonstrates the utility of thiosemicarbazones as versatile intermediates for the construction of bioactive thiazole scaffolds, enabling structural diversification through the incorporation of various aromatic substituents.



Scheme 2 Proposed reaction mechanism for the synthesis of the final derivatives **(3a-e)**

The cyclization step leading to the 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives **(3a–e)** was carried out under solvent-free conditions, representing a sustainable and environmentally benign approach to heterocyclic synthesis. In this method, the preformed (E)-2-(Substituted Benzylidene) hydrazine-1-carbothioamide derivatives were intimately mixed with 2-bromo-1-phenylethan-1-one in a mortar and pestle, and the resulting solid mixture was subjected to heating. The absence of an external solvent provides several notable advantages like solvent-free reactions generally proceed more rapidly i.e. in 4-5h than those carried out in conventional solvent systems take 24h, primarily due to the increased collision frequency and improved molecular interactions between reactants in the absence of a solvent medium. Firstly, the reaction medium being solvent-free eliminates the need for volatile organic solvents, thereby reducing both environmental impact and operational hazards. Secondly, the high concentration of reactants under neat conditions enhances the rate of cyclization and often results in improved product yields 85-95%. Additionally, solvent-free protocols minimize purification steps, making the overall process more economical and efficient. The absence of solvent increases reactant concentration and facilitates better molecular interaction, often leading to faster reaction kinetics.

Evaluation Of Antitubercular Screening

Disk diffusion assay

Following the previously reported methodology, the synthesized compounds were evaluated for their antitubercular activity.[46] The synthesized compounds were deposited onto sterile Whatman paper disks at a concentration of 50 microliters (1 mg/mL). Rifampicin is the standard drug used (1 mg/mL). Serial dilutions of the test compounds were performed directly in a 96-well microtiter plate containing 100 µL of Middlebrook 7H9 broth per well. After being parafilm-sealed and allowed to diffuse in the refrigerator for one hour, the petri plates were placed in an incubator set at 37 °C for five days. A zone measurement scale was used to measure the inhibitory zones.[47]

Resazurin microtiter plate assay

The inoculum for the MABA experiment was a 1:20 dilution of the bacterial growth from Lowenstein Jensen (LJ) medium suspended in Middlebrook 7H9 broth supplemented with 0.2% glycerol and 10% OADC (oleate-albumin dextrose- catalase).[48] All processing was carried out under the appropriate biosafety conditions. Sterilized 96-well plate outside perimeter wells were filled with 200µl of sterile deionized water to reduce medium evaporation in the test wells during incubation. Compound serial dilution was done immediately on the 96-well plate, which contained 100µl of the Middlebrook 7H9 broth. Test compounds were assessed at resulting concentrations of 0.78, 1.56, 3.125, 6.25, 12.5, and 25 µg/mL. After sealing the plates with parafilm, incubation was carried out at 37 °C for five days. Each well received 25 µL of a freshly made 1:1 mixture of Alamar Blue reagent and 10% Tween 80 after the incubation time, and the plate was then incubated for an additional 24 hours. A pink colour in the well was rated as growth, while a blue colour indicated no bacterial growth. The lowest drug concentration that stopped the colour from changing from blue to pink was known as the minimum inhibitory concentration.

III. Results And Discussion

Synthesis

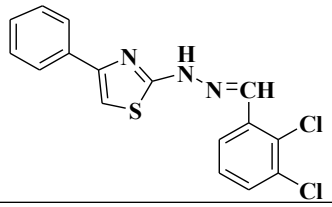
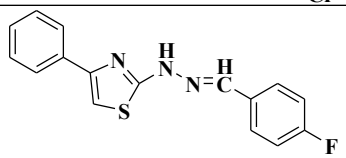
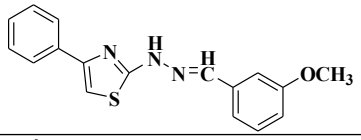
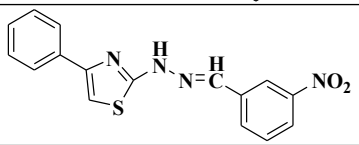
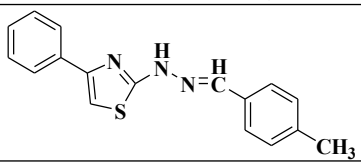
Synthesis of (E)-2-(Substituted Benzylidene) hydrazine-1-carbothioamide derivatives (2a-e).

Using a 1:1.15 molar ratio, a solution of the suitable substituted aldehyde (0.003 mol) and thiosemicarbazide (0.0026 mol) in methanol (2.5 mL) was refluxed over a water bath for 4–6 hours while a few drops of concentrated H SO were present as a catalyst. The reaction progress was monitored by thin-layer chromatography (TLC) using silica gel plates and a hexane/ethyl acetate (3:2, v/v) solvent system. Upon completion, the reaction mixture was allowed to cool to room temperature, and the resulting solid was isolated by filtration. The crude product was washed with ice-cold water (3 × 50 mL), dried, and subsequently recrystallized from ethanol to afford the pure thiosemicarbazone derivatives.

Synthesis of 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives (3a-e).

Equimolar amounts of (E)-2-(Substituted Benzylidene) hydrazine-1-carbothioamide derivatives **(2a-e)** (0.001 mol) and 2-bromo-1-phenylethan-1-one (0.001 mol) were thoroughly ground together in a mortar and pestle for 30 minutes. The resulting mixture was subsequently placed in a round-bottom flask and subjected to reflux in an oil bath for 4-5 hours under solvent free conditions, representing a solid-phase reaction. The progress of reaction was checked periodically by thin-layer chromatography (TLC) using silica gel plates and a hexane/ethyl acetate (4:1, v/v) solvent system. Upon completion of reaction, the solid product was washed with ice-cold water, filtered, dried, and recrystallized from ethanol to afford the pure compound. The optimized compounds, together with their corresponding structural derivatives, are comprehensively listed in (**Table 1).**

Table 1 Optimization of synthetic route for the target compounds **(3a-e).**

S. N	Compound	Structure	M.P	Yield (%)
1	3a		197-198	82
2	3b		138-139	88
3	3c		189-190	86
4	3d		219-220	90
5	3e		205-206	92

Spectral Analysis

(3a) (E)-2-(2-(2,3-dichlorobenzylidene) hydrazinyl)-4-phenylthiazole

Yield: 82%; Light yellow solid; m.p.: 197-198°C; IR υ max (cm-1) 3044.19, 1602.58, 1569.29, 763, 663.00; 1H-NMR (400 MHz, DMSO, δ ppm): 11.68 (1H, bs NH), 8.39 (1H, s, CH), 7.83 (2H, d, Ar-H), 7.62 (1H, d, CH), 7.43 (5H, m, CH), 7.28 (1H, s, thiazole). 13C- NMR (100MHz, DMSO, δppm):168.15, 150.95, 134.86, 134.47, 132.83, 131.09, 130.41, 129.10, 128.90, 125.97, 125.17, 104.79. GCMS m/z Calculated mass: 347.01; Found 347. CHN analysis for $C_{16}H_{11}Cl_2N_3S$ Calcd: C, 55.28; H, 3.38; Cl, 20.45; N,12.27; S, 9.31.

(3b) (E)-2-(2-(4-fluorobenzylidene) hydrazinyl)-4-phenylthiazole

Yield: 88%; Dark grey solid; m.p.: 38-139; IR υ max (cm-1) 3317.35, 3055.57, 1624.10, 1231.15, 879.63; 1H-NMR (400 MHz, DMSO, δ ppm): 11.95 (1H, bs NH), 8.15 (1H, s, CH), 7.83 (2H, d, Ar-H), 7.72 (2H, d, Ar-H), 7.40 (2H, m, CH), 7.32 (4H, m, CH). 13C- NMR (100MHz, DMSO, δppm): 171.01, 166.58, 157.36, 139.11, 135.56, 132.30, 129.86, 129.70, 129.13, 129.05, 115.84, 105.23. GCMS m/z Calculated mass: 297.07; Found 297. CHN analysis for $C_{16}H_{12}FN_3S$ Calcd: C, 64.83; H, 4.27; F, 6.41; N, 14.18; S, 10.81.

(3c) (E)-2-(2-(3-methoxybenzylidene) hydrazinyl)-4-phenylthiazole

Yield: 86%; White solid; m.p.: 189-190; IR υ max (cm-1) 3144.23, 2834.15, 1622.86, 1492.78, 1266.44; 1H-NMR (400 MHz, DMSO, δ ppm):12.05 (1H, bs NH), 8.07 (1H, s, CH), 7.85 (2H, d, Ar-H), 7.43 (2H, d, CH) 7.35 (3H, m, CH), 7.25 (2H, d, CH), 6.97 (1H, s, thiazole). 13C- NMR (100MHz, DMSO, δppm): 171.71, 160.01, 152.24, 142.61, 135.62, 131.04, 130.40, 129.76, 128.57, 121.41, 119.45, 111.66, 104.25, 55.56. GCMS m/z Calculated mass: 309.09; Found 309. CHN analysis for $C_{17}H_{12}N_3OS$ Calcd: C, 66.05, H, 4.91, N, 13.65, O, 5.25, S, 10.45.

(3d) (E)-2-(2-(3-nitrobenzylidene) hydrazinyl)-4-phenylthiazole

Yield: 90%; Yellowish Solid; m.p.:219-220; IR υ max (cm-1) 3200.31, 2860.1603.13, 1525.23, 1343.55, 691.25; 1H-NMR (400 MHz, DMSO, δ ppm):11.81 (1H, bs NH), 8.07 (1H, s, Ar-H), 7.90 (2H, d, Ar-H), 7.43 (5H, m, CH), 7.26 (2H, m, CH), 6.97 (1H, s, thiazole). 13C- NMR (100MHz, DMSO, δppm): 167.50, 150.17, 148.69, 140.35, 135.61, 132.82, 132.30, 130.84, 129.90, 129.75, 128.75, 128.56, 120.87, 105.83. GCMS m/z Calculated mass: 324.07; Found 324. CHN analysis for $C_{16}H_{12}N_4O_2S$ Calcd: C, 59.31, H, 3.83, N, 17.30, O, 9.90, S, 9.92.

(3e) (E)-2-(2-(4-methylbenzylidene) hydrazinyl)-4-phenylthiazole

Yield: 92%; Cream Color Solid; m.p.:205-206; IR υ max (cm-[1]) 3403.03, 2918.67, 1617.18, 1407.85, 913.37; [1]H-NMR (400 MHz, DMSO, δ ppm): 11.81(1H, bs, NH), 8.44 (1H, s, CH), 8.12 (2H, d, Ar-H), 7.82 (2H, d, Ar-H), 7.82 (2H, d, Ar-H), 7.55 (2H, d, CH), 7.41 (2H, m, CH), 7.31 (2H, m, CH), 7.22 (1H, s, thiazole). [13]C- NMR (100MHz, DMSO, δppm): 166.55, 157.32, 145.68, 140.21, 135.61, 134.41, 132.30, 129.88, 129.74, 129.88, 126.67, 105.23, 21.83. GCMS m/z Calculated mass: 293.10; Found 293. CHN analysis for $C_{17}H_{15}N_3S$ Calcd: C, 69.67, H, 5.25, N, 14.36, S, 10.98.

Biological activity

Antituberculosis assay

The disc diffusion method was used for the antituberculosis experiments, and **Table 2** provides a summary of the findings. The synthesized 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives **(3a–e)** were tested for their anti-tubercular potential against Mycobacterium tuberculosis *H37Rv* strain using the MABA, and their minimum inhibitory concentrations were established in comparison with the standard drug Rifampicin. The results of the in vitro anti-tubercular evaluation of the synthesized compounds and the standard drug, performed using the MABA method, are presented in **Table 2** and illustrated in (**Figure. 2).** The blue colour in the well indicated no bacterial growth, while pink colour indicated growth. The lowest drug concentration that rendered the colour from changing from blue to pink was known as the minimum inhibitory concentration.

Rifampicin used as standard drug with MIC 3.125 µg/ml. It was obvious from the observation that all the five synthesised 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives **(3a-e)** exhibited excellent anti-tubercular activity with a MIC of 6.25 µg/ ml in comparison to the standard Rifampicin with MIC values 3.125 µg/ml. Incorporation of diverse aryl substituents on the benzylidene moiety of thiazolyl hydrazones modulates the electronic and lipophilic character of the molecule, thereby influencing its ability to permeate the lipid-rich M. tuberculosis cell wall and interact with essential enzyme targets. Electron-withdrawing, lipophilic groups such as chloro and fluoro generally enhance activity, whereas electron-donating groups like methoxy or methyl contribute to improved solubility and reduced toxicity, the nitro-substituted derivative may further exhibit bioactivation within the mycobacterial environment, contributing to enhanced antimicrobial efficacy. Overall, the variation in substituents fine-tunes the electronic and lipophilic properties of the scaffold, underscoring their pivotal role in governing both cell permeability and target binding affinity of thiazolyl hydrazone-based anti-tubercular agents.

Table 2 Assessment of the anti-mycobacterial potential of the synthesized thiazole scaffolds towards *M. tuberculosis.*

Entry	Name of the Compounds	MIC (µg/ml)
3a	(E)-2-(2-(2,3-dichlorobenzylidene) hydrazinyl)-4 phenylthiazole	6.25
3b	(E)-2-(2-(4-fluorobenzylidene) hydrazinyl)-4-phenylthiazole	6.25
3c	(E)-2-(2-(3-methoxybenzylidene) hydrazinyl)-4-phenylthiazole	6.25
3d	(E)-2-(2-(3-nitrobenzylidene) hydrazinyl)-4-phenylthiazole	6.25
3e	(E)-2-(2-(4-methylbenzylidene) hydrazinyl)-4-phenylthiazole	6.25
Standard	Rifampicin	3.125

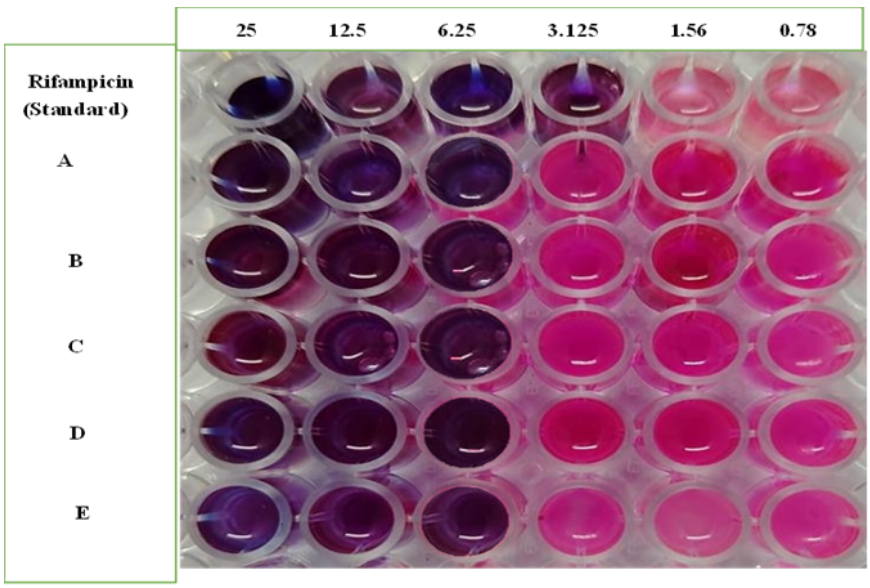


Fig. 2 In vitro antitubercular evaluation of the synthesized compounds and standard drug by the MABA method.

IV. Conclusions

Tuberculosis continues to pose a significant global health challenge, primarily driven by the rise of MDR-TB and XDR-TB strains. This escalating resistance crisis has underscored the urgent need for novel antitubercular therapeutics, directing substantial research interest toward the exploration of heterocyclic scaffolds as promising structural frameworks for drug development. The present study successfully demonstrates a facile and high-yielding solid-phase synthetic strategy for the preparation of novel 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives **(3a–e).** To verify their purity and molecular integrity, the frameworks of the produced final compounds were carefully described using a variety of analytical methods, such as FTIR, ^{1}H NMR, ^{13}C NMR, GC–MS, and elemental analysis. The newly prepared compounds were further evaluated for their in vitro antimycobacterial potential against Mycobacterium tuberculosis *H37Rv* using the Microplate Alamar Blue Assay (MABA). Remarkably, all compounds exhibited significant inhibitory activity with MIC value of 6.25 µg/mL, which is comparable to that of the standard drug rifampicin with a minimum inhibitory concentration (MIC) of 3.125 µg/mL. The promising biological activity of these 2-(2-arylidenehydrazinyl)-4-phenylthiazole derivatives highlights their potential as lead scaffolds for the development of new antitubercular agents. Moreover, the simplicity and efficiency of the solid-phase synthetic route make this approach attractive for the design and rapid synthesis of structurally diverse analogues aimed at overcoming current challenges associated with drug-resistant tuberculosis.

Acknowledgments

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Authors Contributions

Namrata N. Mundargi: Conceptualization, Data curation, Formal analysis, Investigation, Methodology, Software, Validation, Visualization, Writing – original draft, Writing – review & editing. **Susmita Rayawgol B:** Visualization, analysis, data curation. **K. Sujatha:** Supervision, project administration, formal analysis, investigation, resources. **S. Augustin:** Formal analysis, Software, Visualization.

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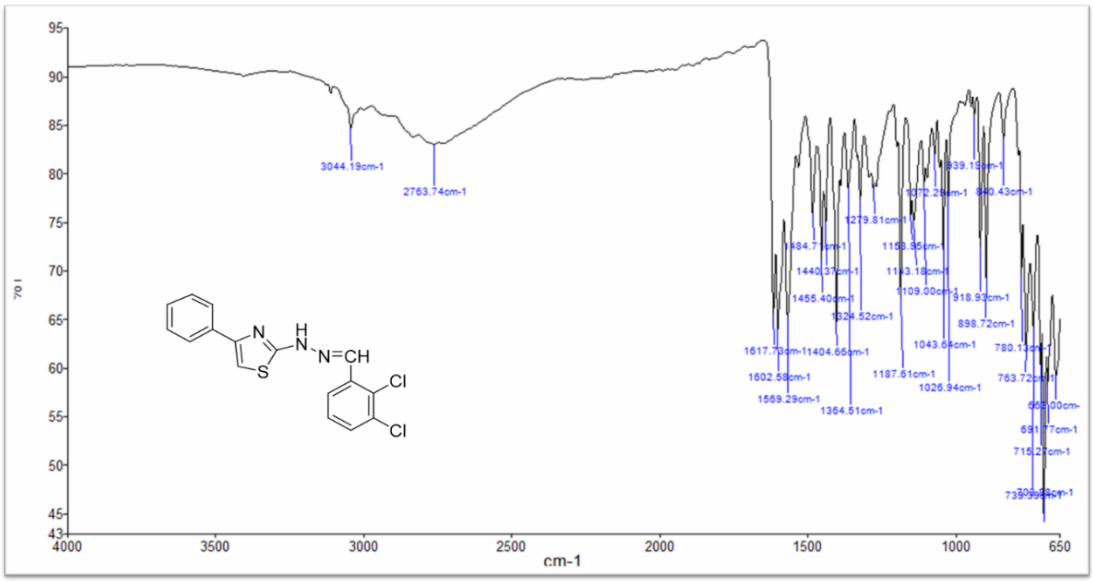
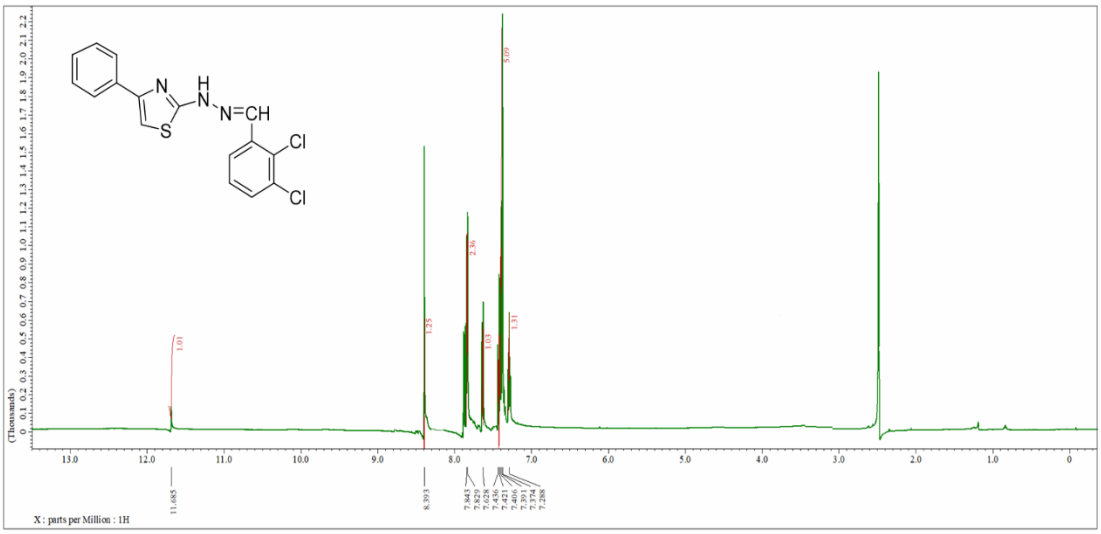
Supplimentary Information

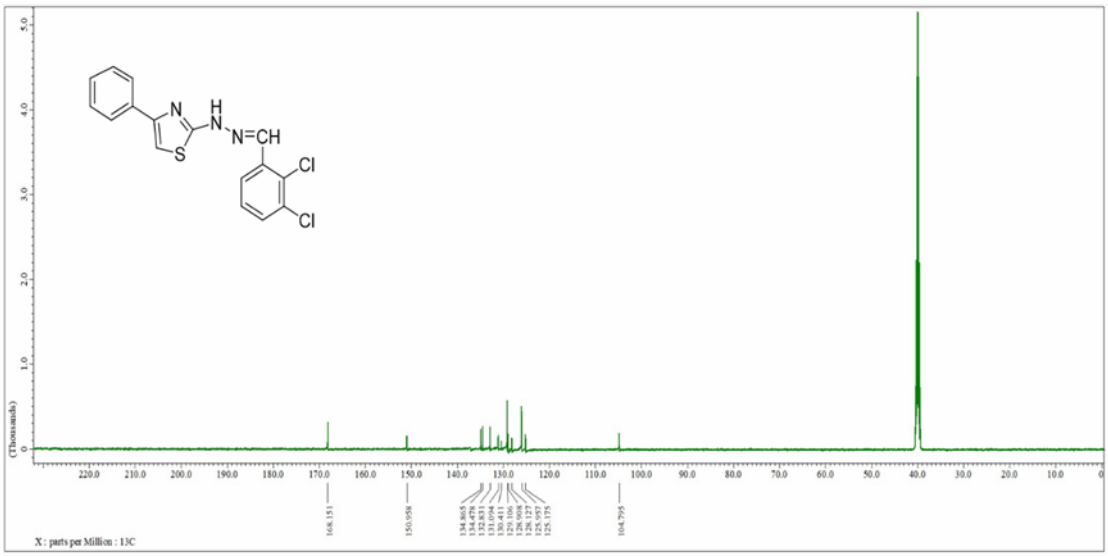
(3a) (E)-2-(2-(2,3-dichlorobenzylidene) hydrazinyl)-4-phenylthiazole



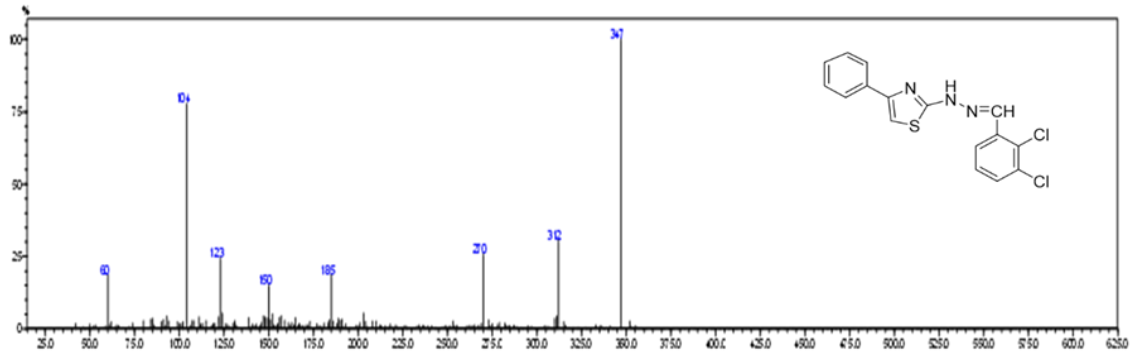
Spectra 1: FT-IR of **3a**



Spectra 2: [1]H NMR of **3a**

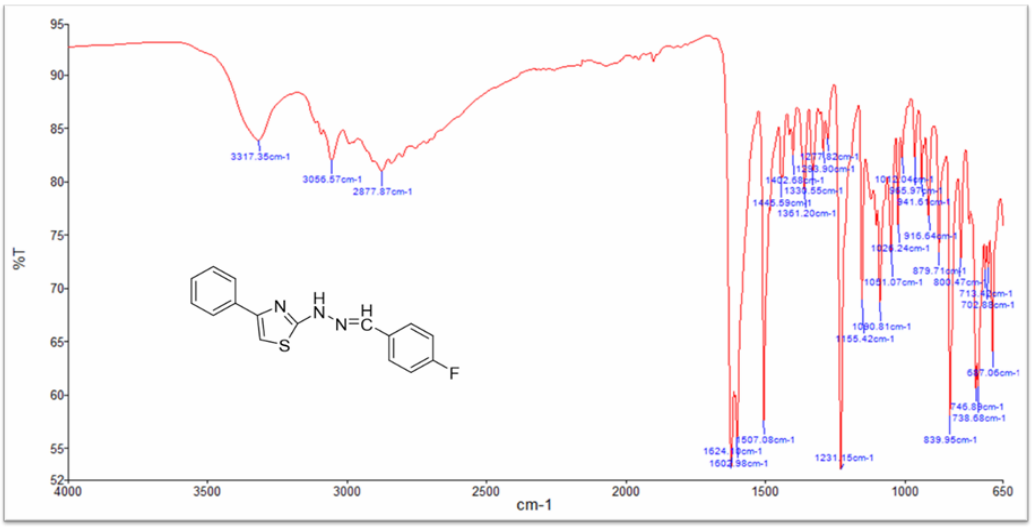


Spectra 3: ^{13}C NMR of **3a**

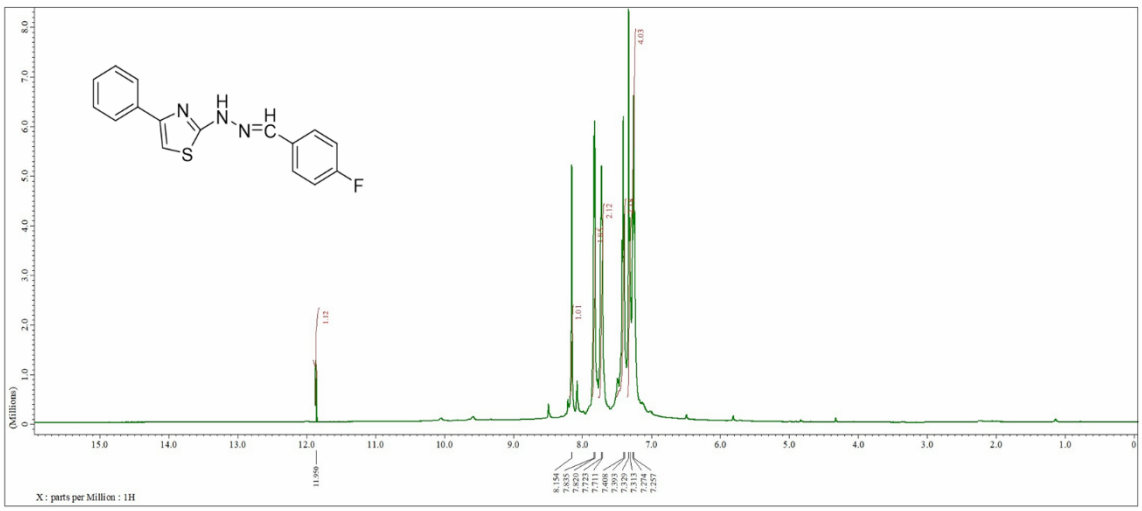


Spectra 4: GCMS of **3a**

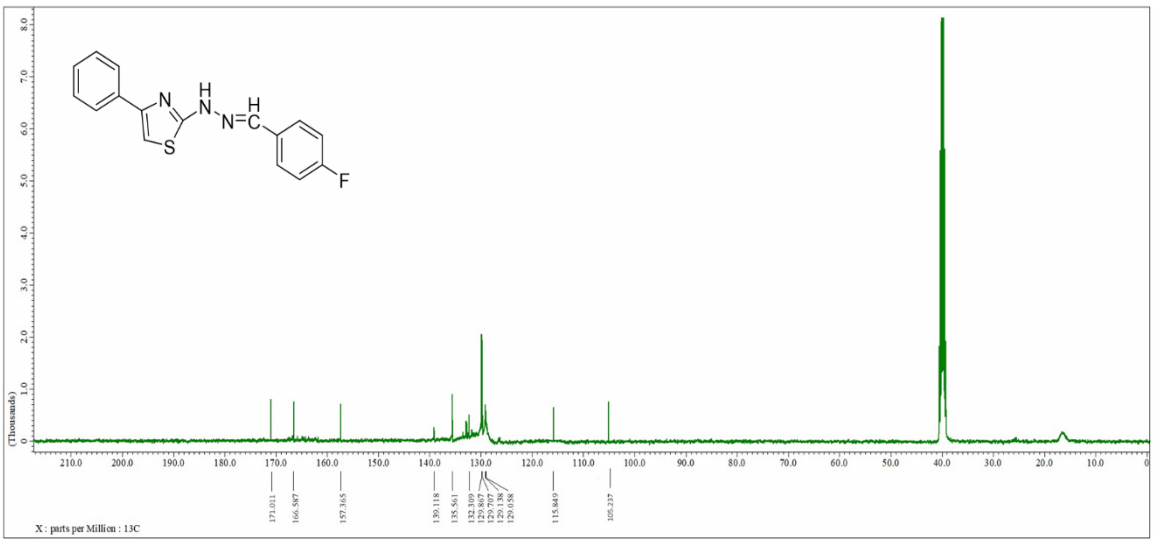
(3b) (E)-2-(2-(4-fluorobenzylidene) hydrazinyl)-4-phenylthiazole



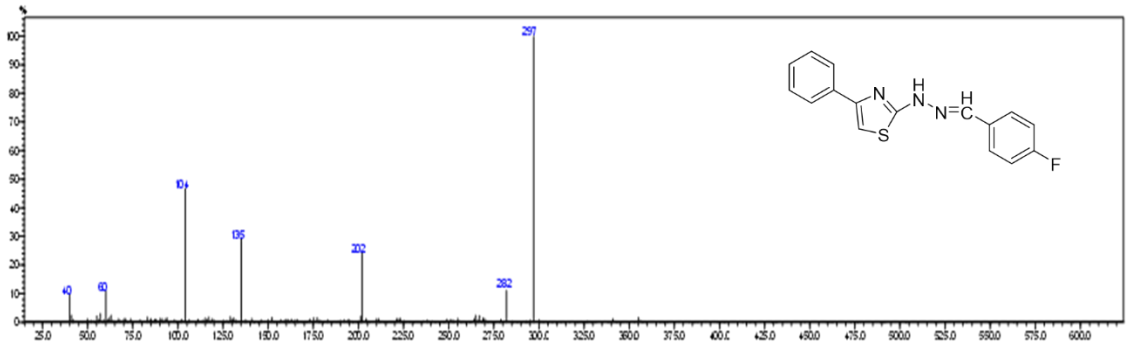
Spectra 5: FT-IR of **3b**



Spectra 6: [1]H NMR of **3b**

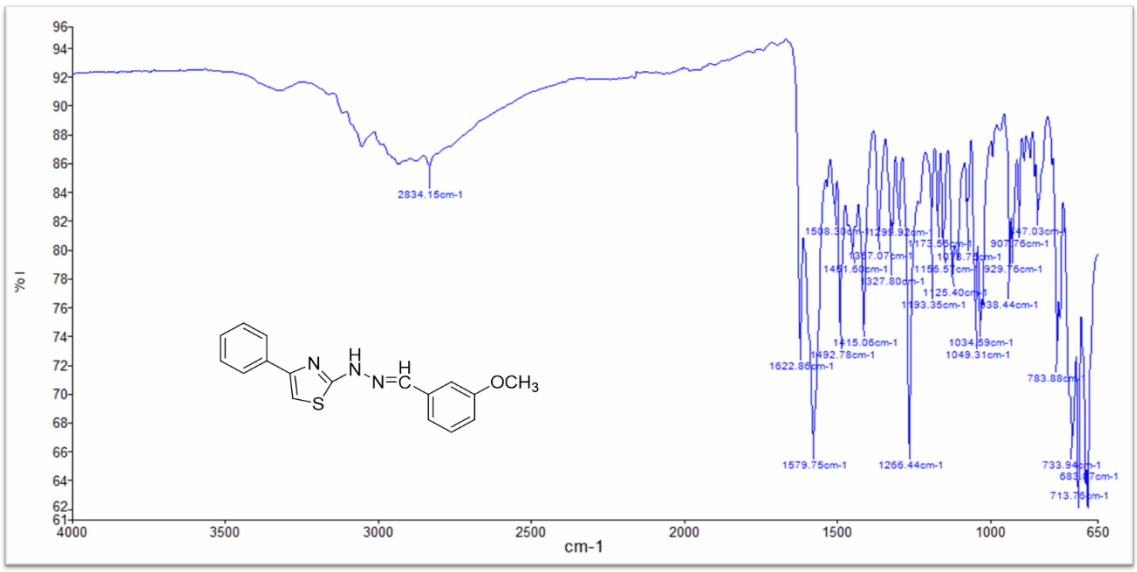


Spectra 7: [13] C NMR of **3b**

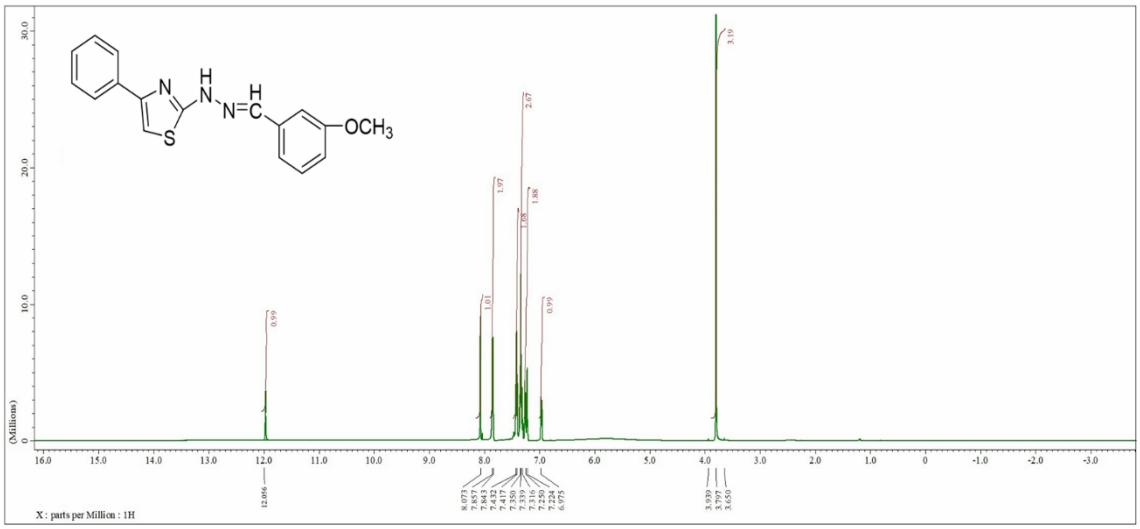


Spectra 8: GCMS of **3b**

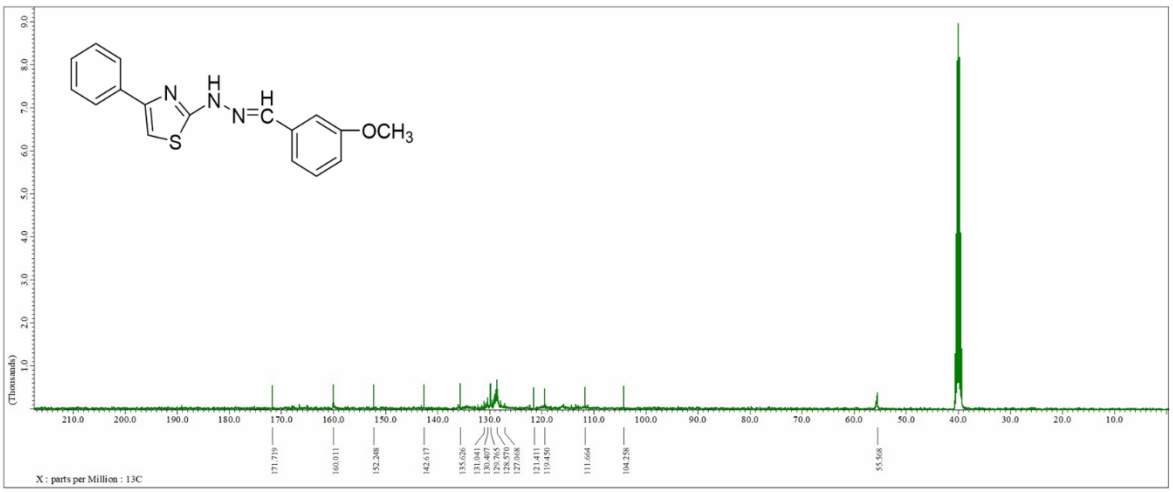
(3c) (E)-2-(2-(3-methoxybenzylidene) hydrazinyl)-4-phenylthiazole



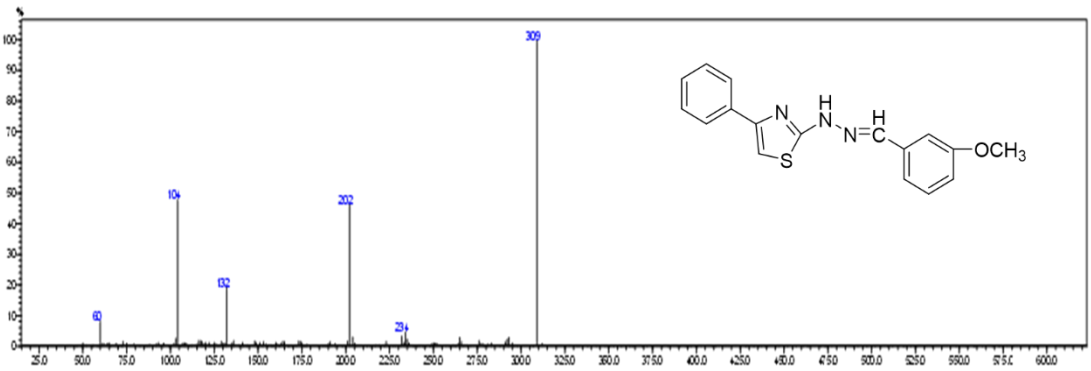
Spectra 9: FT-IR of **3c**



Spectra 10: [1]H NMR of **3c**

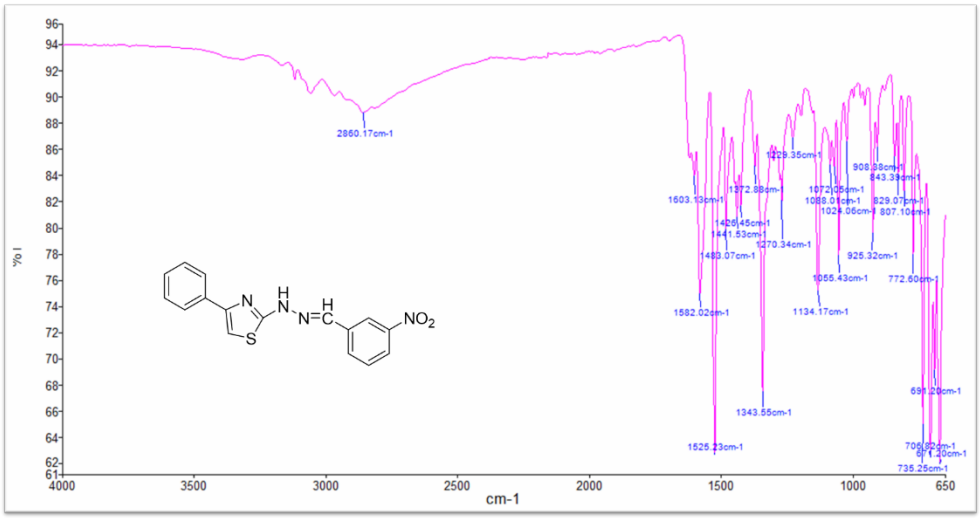


Spectra 11: [13] C NMR of **3c**

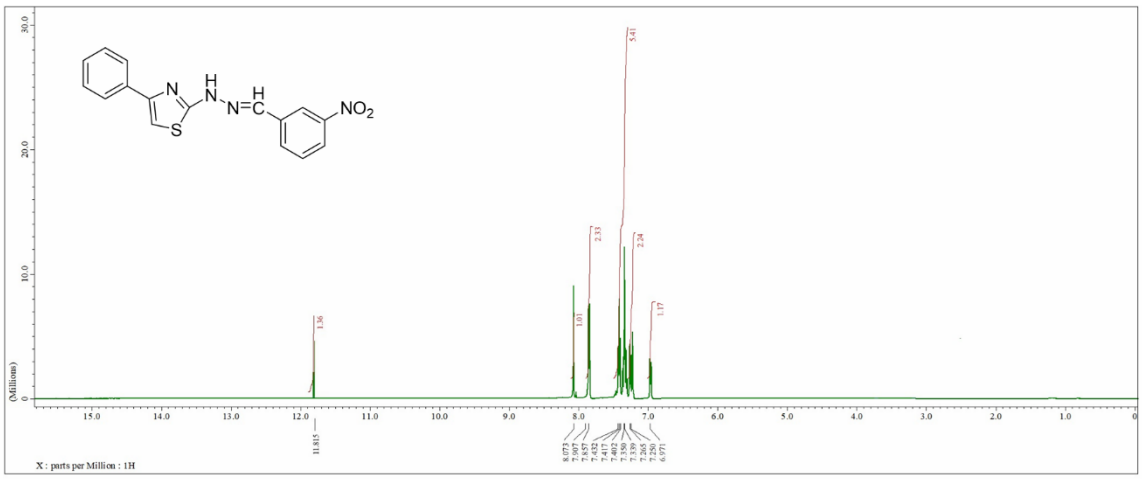


Spectra 12: GCMS of **3c**

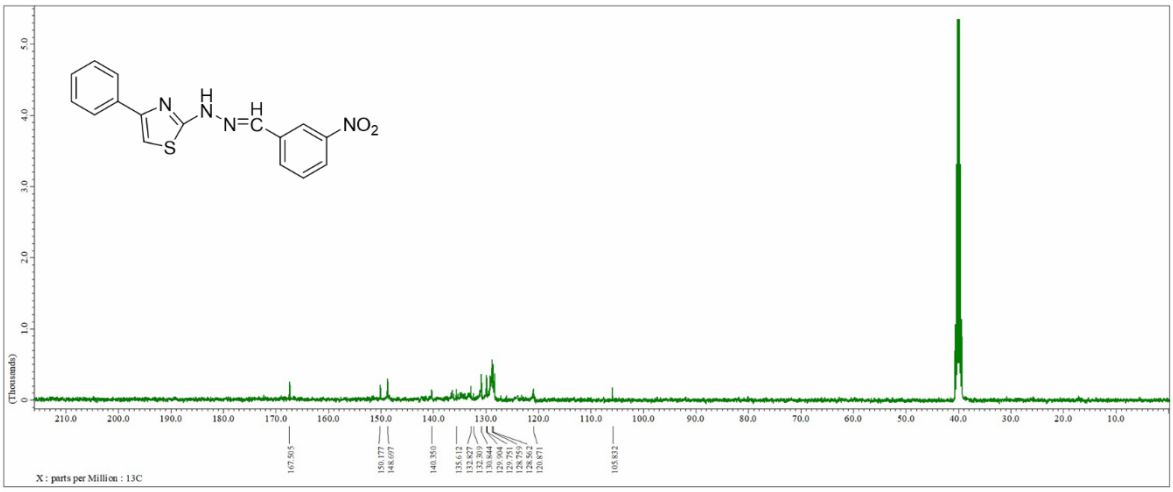
(3d) (E)-2-(2-(3-nitrobenzylidene) hydrazinyl)-4-phenylthiazole



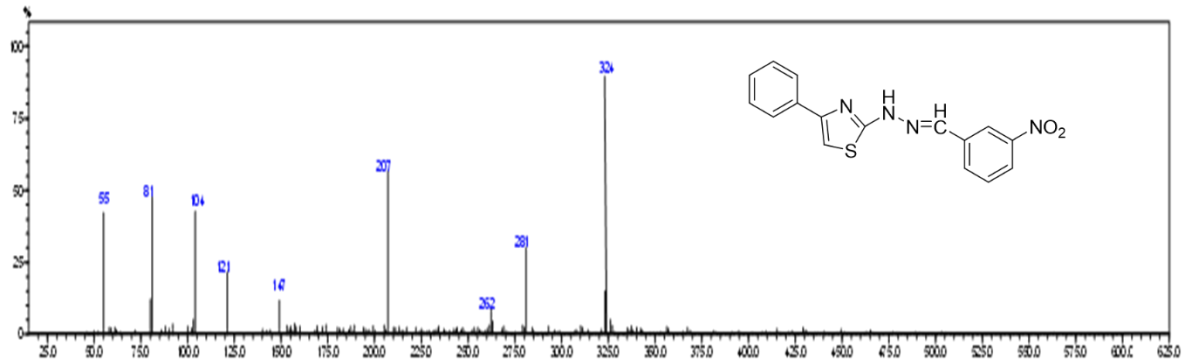
Spectra 13: FT-IR of **3d**



Spectra 14: [1]H NMR of **3d**

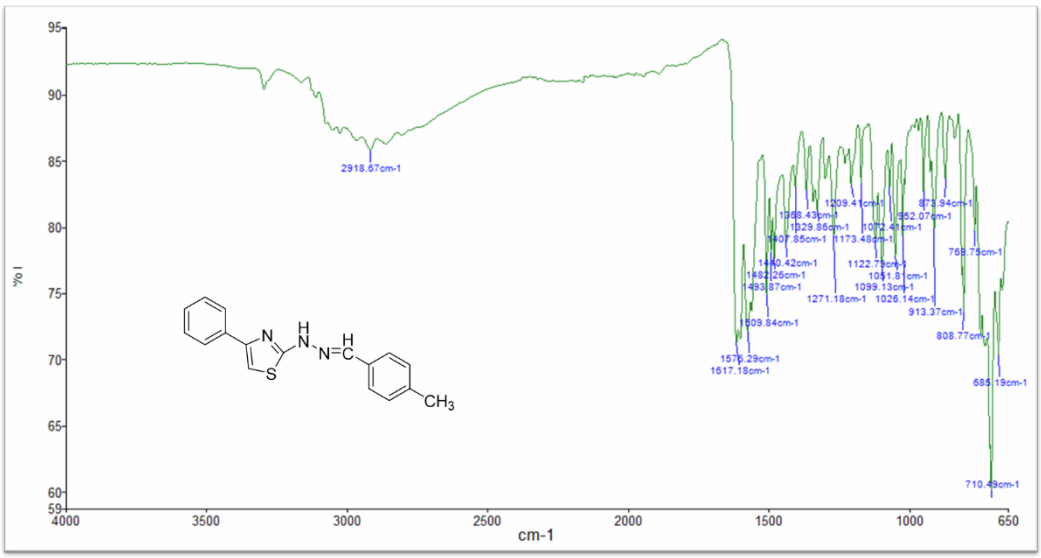


Spectra 15: ^{13}C NMR of **3d**

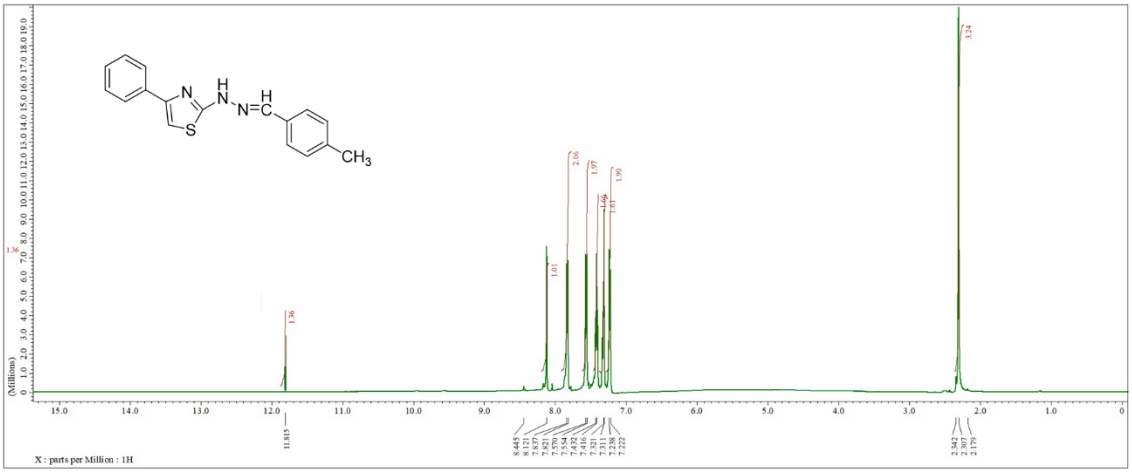


Spectra 16: GCMS of **3d**

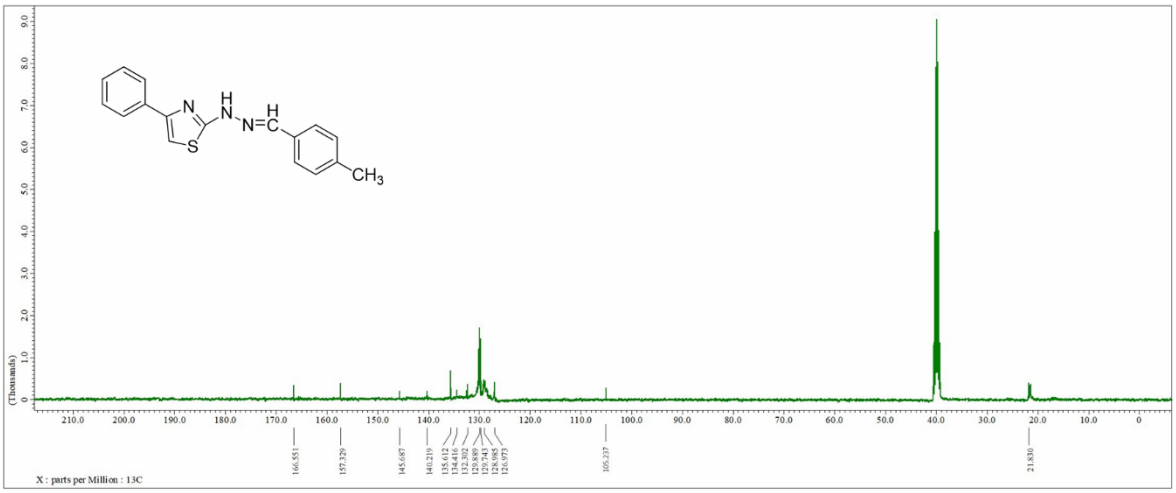
(3e) (E)-2-(2-(4-methylbenzylidene) hydrazinyl)-4-phenylthiazole



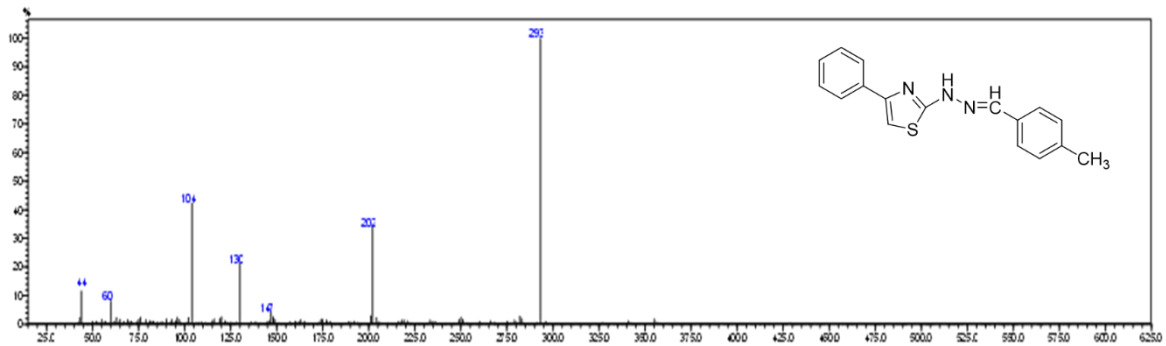
Spectra 17: FT-IR of **3e**



Spectra 18: [1]H NMR of **3e**



Spectra 19: [13] C NMR of **3e**



Spectra 20: GCMS of **3e**

Graphical Abstract