INTERNATIONAL JOURNAL OF PHARMACEUTICAL SCIENCES
[ISSN: 0975-4725; CODEN(USA): IJPS00]
Journal Homepage: https://www.ijpsjournal.com

Review Article

Pharmacological Profile of Thiadiazole

Chaitali Gaikar*, Sunayana Ghodgaonkar, Chetana Mayekar, Purva Gambhirrao, Pragati Gharatkar, Sanchita Ghode, Aditi Ghadge

Shivajirao S. Jondhale College of Pharmacy, Thane, India

ARTICLE INFO

Published: 7 Apr 2026
Keywords:
Thiadiazole; Heterocyclic compounds; Antimicrobial; Antifungal; Insecticidal; Antiviral; Anticancer; Antidiabetic; Biological activity; Drug design
DOI:
10.5281/zenodo.19461875

ABSTRACT

Thiadiazoles are aromatic, electron-deficient five-membered heterocycles containing sulfur and nitrogen atoms, widely recognized as versatile scaffolds in medicinal and agricultural chemistry. Their conjugated and lipophilic ring system acts as an effective bioisostere for thiazole, oxadiazole, oxazole, pyrimidine, and benzene, contributing to enhanced stability and improved biological activity. A broad range of thiadiazole derivatives has demonstrated significant antimicrobial, antifungal, insecticidal, antiviral, anticancer, and antidiabetic activities. Among these, 1,3,4-thiadiazoles are particularly prominent due to their favorable physicochemical properties and diverse structural adaptability. Numerous studies report potent antimicrobial and antifungal effects, including submicromolar antimycobacterial activity and strong inhibition of clinically important pathogens. Thiadiazole-based frameworks also exhibit promising insecticidal and antiviral potential, with several derivatives outperforming standard reference agents. In oncology research, thiadiazole hybrids have shown notable cytotoxicity across multiple human cancer cell lines, with some compounds reaching nanomolar efficacy. Furthermore, thiadiazole derivatives display remarkable antidiabetic activity through α-amylase and α-glucosidase inhibition, with several compounds demonstrating superior potency to acarbose. Overall, thiadiazole heterocycles continue to serve as valuable lead structures for the development of multifunctional therapeutic and agrochemical agents.

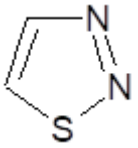
INTRODUCTION

Thiadiazole is an aromatic five-membered ring compound that contains one sulfur atom and two nitrogen atoms. It possesses a hydrogen-bonding domain and a two-electron donor system, which enable it to act as an anhydrase.[1]

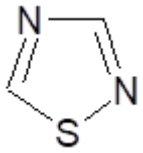
Thiadiazoles are considered to be determined from thiophene by supplanting two-CH= (methine) bunches by pyridine-type nitrogens (-N=) and

***Corresponding Author:** Chaitali Gaikar
Address: *Shivajirao S. Jondhale College of Pharmacy, Thane, India.*
Email : chaitaligaikar4911@gmail
Relevant conflicts of interest/financial disclosures: The authors declare that the research was conducted in the absence of any commercial or financial relationships that could be construed as a potential conflict of interest.

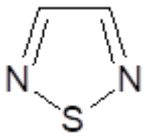
incorporate four isomeric individuals depending on the relative positions of the nitrogen iotas.Thiadizole compounds follow 4 different isomeric forms, such as 1,2,3-thiadizole, 1,2,4-thiadizole, 1,2,5-thiadizole, and 1,3,4-thiadizole.[2]



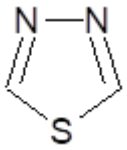
1,2,3-Thiadiazole



1,2,4-Thiadiazole



1,2,5-Thiadiazole



1,3,4-Thiadiazole

1,3,4-Thiadiazoles are widely employed as bioisosteric substitutes for heterocyclic rings such as pyrimidine, pyridine, azine, oxadiazole, oxazole, thiazole, and benzene in drug development. This ring system is conjugated, weakly basic, planar, and electron-deficient in nature.[3]

Thiadiazole derivatives exhibit a broad spectrum of biological activities, including antibacterial, antifungal, insecticidal, antiviral,[4] Anticancer,[5] antidiabetic,[6] antioxidant,[7] Anticonvulsant effects.[8]

The biological activity of thiadiazoles arises from the strong aromatic nature of their ring structure, which provides greater stability within living systems. Thiadiazoles serve as bioisosteric replacements for the thiazole ring and are also considered bioisosteres of oxadiazole, oxazole, and benzene. Replacing these heterocyclic systems with a thiadiazole ring generally results in analogues with enhanced biological activity, as the presence of sulfur increases lipophilicity.[9]

Antibacterial activity:

Mousa. L. Al-Smadi., synthesized 1,2,3-thiadizole compounds using the hole diffusion method and evaluated for their antimicrobial activity against human pathogenic microorganisms, including gram-positive S. aureus and gram-negative E. coli, local resistant P. aeruginosa and reference pseudomonas aeruginosa and the fungus Candida albicans. The compound 4-(4-(2-(4-Chloro-3-Methylphenoxy)Ethoxy)Phenyl)-1,2,3-,Thiadiazole (3c) showed the highest activity against *C. albicans* and was also effective against certain Gram-positive and Gram-negative bacteria, indicating its potential as a novel antibacterial agent.[10]

Angelova T. V. et al., reported 4-methyl-1,2,3-thiodiazole compound exhibits antimycobacterial activity against microbacterium tuberculosis. Compound N'-[(E)-(4-hydroxy-3-methoxyphenyl)methylidene]-4-methyl-1,2,3-thiadiazole-5-carbohydrazid (3d) exhibited potent antimycobacterial activity at a submicromolar concentration, showing the lowest MIC value of 0.0730 µM against Mycobacterium tuberculosis H37Rv. Additionally, it demonstrated very low cytotoxicity toward normal human embryonic kidney (HEK-293T) and mouse fibroblast (CCL-1) cell lines.[11]

Mahendrasingh et al., investigated antibacterial and antifungal activities of all newly synthesized 1,3,4-thiadiazole derivatives were investigated. For antibacterial evaluation, the test organisms included *Staphylococcus aureus* ATCC 9144, *Bacillus cereus* ATCC 11778, *Escherichia coli* ATCC 25922, and *Pseudomonas aeruginosa* ATCC 2853. Antifungal activity was assessed using *Aspergillus niger* ATCC 9029 and *Aspergillus fumigatus* ATCC 46645.[12]

Umar P. B. et.al.,synthesized 1,3,4-thiadiazole compounds were tested for antibacterial activity using the disc diffusion method against pathogenic

bacteria, including Gram-positive strains *Staphylococcus aureus* (SA) and *Bacillus cereus* (BC), and Gram-negative strains *Escherichia coli* (EC) and *Pseudomonas aeruginosa* (PA). Compounds5-Phenyl-N-(4-(trifluoromethyl)benzyl)-1,3,4-thiadiazol-2amine (4e) and N-(4-Fluorophenyl)-5-phenyl-1,3,4-thiadiazol-2-amine (4f) exhibited good biological activity.[13]

Joshi D. S. et al., evaluated the antitubercular activity of all the newly synthesized 1,3,4-thiadiazole compounds against the *Mycobacterium tuberculosis* H37Rv strain using the Microplate Alamar Blue Assay (MABA) method, with pyrazinamide and isoniazid as standard reference drugs. The in vitro results indicate that compounds N-(5-(4-Chlorophenyl)-1,3,4 -oxadiazol-2-yl)-4-(1H-pyrrol1-yl)benzamide (4c), N-(5-(4-Bromophenyl)-1,3,4-oxadiazol-2-yl)-4-(1H-pyrrol1-yl)benzamide (4d), N-(5-(4-Chlorophenyl)-1,3,4-thiadiazol-2-yl)-4-(1H-pyrrol1-yl)benzamide (5c), and N-(5-(4-Bromophenyl)-1,3,4-thiadiazol-2-yl)-4-(1H-pyrrol1-yl)benzamide (5d) showed the highest activity in the series, with an MIC value of 3.12 µg/mL.[14]

Rezki N. *et al.*, reported that all newly obtained compounds were tested in vitro for their ability to inhibit the growth of various pathogenic microorganisms, including three Gram-positive bacteria, three Gram-negative bacteria, and three fungal strains. Antimicrobial activity was determined by measuring the minimum inhibitory concentration (MIC) using the broth dilution method. The MIC represents the lowest concentration of a compound that prevents visible microbial growth. Among the tested molecules, diethyl 4,4′-[(1,3,4-thiadiazol-2,5-diyl)bis(sulfanediyl)]dibutanoate (2) and its hydrazide analogue 4,4′-[(1,3,4-Thiadiazol-2,5-diyl)bis(sulfanediyl)]dibutanehydrazide (3) showed notable antibacterial activity against both Gram-positive and Gram-negative organisms with MIC values of 16–31.25 µg/mL, and moderate antifungal effects with MIC values of 31.25–62.5 µg/mL.[15]

Antifungal Activity:

Zheng Q. *et al.*, synthesized 5-methyl-1,2,3-thiadiazole derivatives and evaluated their antifungal activity. Fungal growth inhibition was tested using the potato dextrose agar method against various fungi, including *A. solani*, *B. cinerea*, *C. arachidicola*, *C. beticola*, *C. lagenarium*, *F. oxysporum*, *G. zeae*, *P. triticina*, *P. infestans*, *P. piricola*, *P. sasakii*, and *R. solani*. All compounds showed antifungal activity at 50 µg/mL. Series I compounds were particularly effective, showing over 70% inhibition against *B. cinerea* and over 60% against *P. sasakii*. Notably, compound I1 inhibited *B. cinerea* by 85%, III8 inhibited *P. sasakii* by 87%, and III1 inhibited *P. piricola* and *P. sasakii* by 69% and 65%, respectively.[16]

Karaburun Ç. A. et al., evaluated the antifungal activity of synthesized 1,3,4-thiadiazole compounds *in vitro* against various *Candida* species, using fluconazole as the reference drug The compounds were tested against *C. albicans* (ATCC 90028 and ATCC 10231), *C. crusei* (ATCC 6258), *C. parapsilosis* (ATCC 22019), *C. tropicalis* (ATCC 13803), *C. glabrata* (ATCC 2001), *C. famata*, and *C. lusitaniae*. Among the series, compounds 2-((5-((4-Chlorophenyl)amino)-1,3,4-thiadiazol-2-yl)thio)-1-(2,4-difluorophenyl)ethan-1-one(3k) and 2-((5-((4-Chlorophenyl)amino)-1,3,4-thiadiazol-2-yl)thio)-1-(2,4-dichlorophenyl)ethan-1-one (3l) exhibited outstanding antifungal activity against all tested strains, with compound 3l showing the highest potency against *C. albicans* ATCC 10231.

The enhanced antifungal effects of compounds 3k and 3l are attributed to the presence of fluoro and chloro substituents at the second position of the phenyl ring. Moreover, all synthesized compounds demonstrated favorable predicted pharmacokinetic profiles.[17]

Caixia W. et al., synthesized thiourea derivatives containing the 1,3,4-thiadiazole moiety (compounds 4a–4r) were evaluated for their antifungal activity against phytopathogenic fungi. Four representative fungi from the Chinese agroecosystem—*Curvularia lunata*, Cotton Fusarium wilt, *P. P. var. nicotianae*, and *Fusarium* spp.—were selected for screening. The commercial fungicide triadimefon was used as the reference standard. The results indicate that most of the compounds (N-Ethyl-N'-[5-(ethylthio)-1,3,4-thiadiazol-2-yl]-thiourea 4a– N-(4-Trifluoromethylphenyl)-N′-[5-(allylthio)-1,3,4-thiadiazol-2-yl]-thiourea 4r) display notable antifungal activity.[18]

Zhou Y. et al., conducted Preliminary in vitro antifungal studies of compounds Y1–Y22 were conducted against ten pathogenic fungal strains. A total of 22 flavonol derivatives containing a 1,3,4-thiadiazole moiety were designed and synthesized, and their structures were confirmed using NMR and HRMS analyses. The antifungal evaluation revealed that compound 4-((3-(thiazol-2-ylthio)propyl)oxy)-3-(3-fluorophenyl)-2H-chromen-2-one (Y18) exhibited strong activity against *B. cinerea*, with an EC_{50} value of 2.4 μg/mL, which was significantly better than that of azoxystrobin (21.7 μg/mL).[19]

Zoumpoulakis P. et al., reported that the synthesized compounds displayed strong antifungal activity, with MIC values of 0.06–0.50 μmol/mL and MFC values of 0.07–0.75 μmol/mL. They were generally more potent than ketoconazole and bifonazole, except compound N-{5-[2-(N-Dimethylsulfamoyl)-4,5-dimethoxy-benzyl]-1,3,4-thiadiazol-2-yl}-N-isopropylamine(4d), which was slightly less active against a few fungal strains. Compound N-{5-[2-(N-Dimethylsulfamoyl)-4,5-dimethoxy-benzyl]-1,3,4-thiadiazol-2-yl}-N-butylamine (4e). showed the highest activity. Fulvia fulvum was the most sensitive fungus, while Aspergillus versicolor was the most resistant. Overall, the thiadiazole derivatives demonstrated significantly superior antifungal activity, reaching 8–10 times higher potency in certain cases.[20]

Insectisidal Activity:

Wang H. et al.,synthesized two series of target compounds—one containing a benzoyl ring and the other incorporating a 5-methyl-1,2,3-thiadiazole ring adjacent to a tert-butyl group. At 200 μg/mL, both series showed similar insecticidal activity against *P. xylostella*, though compounds 4-methyl-1,2,3-thiadiazole-5-carbonyl chloride (VII) exhibited stronger effects.[21]

Suzuki J. et al., evaluated the insecticidal activities of seven 1,2,4-oxadiazoles and twenty-five 1,2,4-thiadiazoles were tested against *N. lugens*, *N. cincticeps*, and *A. craccivora*. Both 1,2,4-thiadiazole derivatives [Methyl-5-(3-pyridyl)-1,2,4-thiadiazole (7m-2)and 3-Methyl-5-(1-methyl-1,2,5,6-tetrahydropyridin-3-yl)-1,2,4-thiadiazole(9m-2)]showed very low inhibition of EPI binding to membranes, with nAChR binding activities below 10%. This indicates that these compounds display nearly identical insecticidal effects on both imidacloprid-resistant and susceptible strains of *N. lugens*.[22]

Dong Lia Yue et al., designed and synthesized novel 1,2,4-triazole-containing 1,2,3-thiadiazole derivatives and evaluated their insecticidal activity against *Aphis laburni* using the leaf-dip method. In addition, the antiviral activity against TMV was

examined under both curative and induction models following established literature methods.[23]

Madkour H. F. et al.,synthesized several thiadiazole derivatives using readily available starting materials. The insecticidal potential of the newly obtained compounds was evaluated against 4th instar larvae of *Spodoptera littoralis*, and most of them displayed good activity. Compound 7-Amino-2-(2-chlorophenyl)-5-(4-chlorophenyl)-5H-[1,3,4]thiadiazolo [3,2-a]pyrimidine-6-carbonitrile (8) showed the highest potency, exhibiting the lowest LC_{50} value of 114.99 ppm.[24]

Antiviral activity:

Dong Li Wei et al., synthesized acrylamide derivatives containing a 1,2,3-thiadiazole moiety were evaluated in vitro for their cytotoxic and anti-HBV activities in 2.2.15 cells, with lamivudine used as the reference antiviral drug. Among all the tested compounds, N-(1-bromo-1-(4-chlorophenyl)-3-oxo-3-(piperidin-1-yl)prop-1-en-2-yl)-4-methyl-1,2,3-thiadiazole-5-carboxamide (9c) exhibited the strongest anti-HBV activity, showing an IC_{50} value of 3.59 μg/mL, which was approximately three times higher than that of the standard drug lamivudine.[25]

Fujiwara M. et al., identified TDA derivatives as novel HIV-1 specific non-nucleoside reverse transcriptase inhibitors (NNRTIs), though their high lipophilicity and strong plasma protein binding limited effectiveness. To address this, a new series was synthesized, and one compound, N-methyl-N-propyl O-[3,5-dichloro-2-amino-4-(1,3,4-thiadiazol-2-yl)phenyl] carbamate (RD4-2217), showed strong inhibition of multiple HIV-1 strains with reduced lipophilicity and protein binding. Its antiviral evaluation is ongoing in the presence of increasing human serum concentrations.[26]

Hu Yuzhi et al., synthesized twenty-one coumarin derivatives containing 1,3,4-oxadiazole or 1,3,4-thiadiazole moieties and evaluated their antiviral activities.among them, compound N-(5-((2-hydroxy-3-((2-oxo-2H-chromen-4-yl)oxy)propyl)thio)-1,3,4-thiadiazol-2-yl)-4-methylbenzamide(Y5) exhibited the higher antiviral activity at a concentration of 500 μg/mL.(EC50 =218.6 μg/mL).[27]

Brai A. et al.,designed and synthesized novel 1,3,4-thiadiazole derivatives as inhibitors of DDX3X to evaluate their antiviral activity. The antiviral potential was assessed using a phenotypic assay known as the BiCycle Assay, which measures the half-maximal inhibitory concentration (IC_{50}) against the HIV-1 wild-type reference strain NL4-3 in TZM-bl cells. The compound2-(2-(4-hydroxyphenyl)-1,3,4-thiadiazol-5-yl)isoindoline-1,3-dione (24) demonstrated the strongest anti-HIV-1 effect, showing an IC_{50} of 2.8 μM.[28]

Yu Lu et al., evaluated the antiviral effects of the synthesized compounds against cucumber mosaic virus (CMV) using the half-leaf method. Several of the compounds demonstrated notable in vivo activity, with compounds (2E)-3-(2,4-dimethoxyphenyl)-1-(4-hydroxyphenyl)-2-((phenylthio)imino)-3-(thiophen-2-yl)prop-1-en-1-one(4e) and (2E)-3- (3,4-dimethoxyphenyl)-1-(thiophen-2-yl)prop-2-en-1-one) (4f) showing particularly strong curative effects of 55.9% and 50.2%, respectively—both higher than ribavirin (36.8%). In contrast, the compounds displayed protective and inactivation activities comparable to those of ribavirin.[29]

Anticancer activity:

Chidella K. et al., synthesized 1,2,4-thiadiazole-linked imidazo[1,2-b]pyridazine (10a–j) derivatives were tested for their anticancer

potential against four human cancer cell lines — breast (MCF-7), lung (A549), prostate (DU-145), and breast (MDA-MB-231) — using the MTT assay. An initial structure–activity relationship (SAR) analysis revealed that compound 2-(3-(3,4,5-Trimethoxyphenyl)-1,2,4-thiadiazol-5-yl)-3-(thiophen-2-yl)imidazo[1,2 b]pyridazine(10b), bearing a 3,4,5-trimethoxy group on the phenyl ring attached to the thiadiazole core, exhibited the most potent activity, with IC_{50} values of 0.09 ± 0.0076 µM (MCF-7), 0.012 ± 0.002 µM (A549), 0.017 ± 0.0041 µM (DU-145), and 0.034 ± 0.0053 µM (MDA-MB-231).[30]

Trafalis T. D. et al. reported the evaluation of novel triazolo[3,4-b][1,3,4]thiadiazole derivatives for anticancer potential, where compounds KA39, 2-((6-(2,5-dinitrophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-3-yl)methyl)-N,N-diethyl4,5 dimethoxybenzenesulfonamide (6e), and 2-((6-(2,5-dinitrophenyl)-[1,2,4]triazolo[3,4-b][1,3,4]thiadiazol-3-yl)methyl)-N,N-diisopropyl4,5-dimethoxybenzenesulfonamide(7d) 7d showed the strongest activity against several human cancer cell lines, with KA39 being the most effective. The presence of a 2,5-dinitrophenyl group at the C-6 position was found to be crucial for enhanced activity. Furthermore, in vivo studies revealed low acute toxicity and marked tumor growth inhibition (~62–68%) in an HT-29 xenograft model, underscoring KA39, KA25, and KA26 as promising anticancer leads.[31]

Sudhakar S. G. D. et al., synthesized 1,2,4-thiadiazole derivatives containing a 1,2,4-oxadiazole moiety were evaluated for their anticancer potential against four human cancer cell lines—MCF-7 (breast), A549 (lung), Colo-205 (colon), and A2780 (ovarian)—using the MTT assay. Etoposide served as the reference drug. Most of the compounds exhibited moderate to strong anticancer activity, with IC_{50} values ranging from 0.10 ± 0.02 to 22.1 ± 5.76 µM, compared to the positive control (IC_{50} = 0.13 ± 0.017 to 3.08 ± 0.135 µM).[32]

Mhaidat M. N. et al. evaluated the acute cytotoxicity of 1,2,3-thiadiazole and 1,2,3-selenadiazole compounds against several cancer cell lines,breast (HMT3522, MCF7), colorectal (SW480, HCT116), and melanoma (MV3, C32)—using the MTT assay. Compound 1-(1,2,3-selenadiazole-4-yl)carbaldehyde (4b) showed activity against all tested tumor cell lines, with IC_{50} values ranging from 52.17 to 114.79 µg/mL. In comparison, 1,3,5-tris(1,2,3-thiadiazole-4-yl)benzene (4c) exhibited stronger cytotoxic effects across all cancer cell lines.[33]

Shaikh A. S. et al., reported the synthesis of a new series of 1,3,4-substituted thiadiazole derivatives (8b–g) obtained from 4-substituted thiazol-2-chloroacetamides (4b–g) and characterized using FT-IR, ^{1}H NMR, ^{13}C NMR, and mass spectrometry. The synthesized compounds (8a–g) were evaluated for their in vitro anticancer activity against hepatocellular carcinoma (HepG-2), lung carcinoma (A549), breast carcinoma (MCF-7), and pseudo-normal embryonic liver (L02) cell lines using the MTT assay. Among them, compounds 2-Chloro-N-[4-(4-methoxyphenyl)-1,3-thiazol-2-yl]acetamide (4j) and 2-[(5-amino-1,3,4-thiadiazol-2-yl)thio]-N-[4-(4-methoxyphenyl)-1,3-thiazol-2-yl]acetamide (8d) showed the highest anticancer potency, with GI_{50} values of 1.82, 2.61, 2.38 µM and 2.98, 2.85, 2.53 µM against MCF-7, A549, and HepG-2 cells, respectively, comparable to doxorubicin.[34]

Janowska S.et al., discovered and synthesized new thiosemicarbazide and 1,3,4-thiadiazole derivatives, which were evaluated for their in vitro anticancer activity against two breast cancer cell lines using the MTT assay and DNA biosynthesis

analysis. The results showed that all compounds displayed dose-dependent cytotoxicity toward MCF-7 and MDA-MB-231 cells, with compound 2-(2-Trifluorometylophenylamino)-5-(3-methoxyphenyl)-1,3,4-thiadiazole (ST10) showing the highest activity against MCF-7 (IC_{50} = 49.6 µM).[35]

Dawood M. K. et al. confirmed the structures of the newly synthesized 1,3,4-thiadiazole derivatives using elemental and spectral analyses. Selected compounds were evaluated for anticancer activity against the HCT-116 colon carcinoma cell line, and their structure–activity relationship (SAR) was examined. Compounds 5-(4-Chlorophenyl)-N-(3,5-diphenyl-1,3,4-thiadiazol-2(3H) ylidene)-1,3,4-oxadiazol-2-amine (6), 1-(5-((5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl)imino)-4-phenyl 4,5-dihydro-1,3,4-thiadiazol-2-yl)ethanone (13a) and 5-((5-(4-Chlorophenyl)-1,3,4-oxadiazol-2-yl)imino)-N,4 diphenyl-4,5-dihydro-1,3,4-thiadiazole-2-carboxamide (19a) showed weak inhibitory effects on HCT-116 cells, with IC_{50} values of 9 µg/mL.[36]

Antidiabetic activity:

Hussain R. et al., reported the synthesis of a series of hybrid 1,3,4-thiadiazole–fused–1,2,4-thiadiazole derivatives incorporating a 1,4-benzodioxine ring, which were subsequently evaluated for their in vitro α-amylase and α-glucosidase inhibitory activities. All the synthesized analogs exhibited notable inhibitory potency toward both enzymes, with IC_{50} values ranging from 0.70 ± 0.01 to 30.80 ± 0.80 µM for α-amylase and 0.80 ± 0.01 to 29.70 ± 0.40 µM for α-glucosidase, demonstrating activity comparable to or exceeding that of the standard drug acarbose.[37]

Khan S. et al., reported that diabetes mellitus (DM), caused by the harmful activity of α-amylase and α-glucosidase enzymes, is commonly treated with enzyme inhibitors that often have side effects. To find safer alternatives, 17 benzimidazole-based thiadiazole derivatives were synthesized and tested. These compounds showed significant inhibitory activity against both enzymes, with IC_{50} values ranging from 1.10 to 24.20 µM for α-amylase and 2.10 to 26.10 µM for α-glucosidase, depending on the substituents on the aromatic ring.[38]

Shulgau Z. et al., evaluated sulfur-containing derivatives, particularly thiadiazole heterocycles,compounds 5′–9′a–c were screened for their potential antidiabetic activity based on their ability to inhibit α-glucosidase enzyme activity.. The results revealed that these compounds exhibited significantly higher inhibitory effects compared to the reference drug acarbose (49.5%). Notably, compound 2-(5-((6-Methyl-2-oxo-4-phenyl-1,2-dihydropyridin-3-yl)carbamoyl)-1,3,4-thiadiazol-2 yl)benzoic acid (9′b) demonstrated an IC_{50} value of 3.66 mM, which is approximately 3.7 times lower than that of acarbose (IC_{50} = 13.88 mM), indicating superior α-glucosidase inhibitory potency.[39]

Datar A. P. et al., reported both in vitro and in vivo evaluations of the synthesized of thiadiazole compounds. In the in vitro study using porcine α-amylase, N-(5-(4-nitrophenyl)-1,3,4-thiadiazol-2-yl) acetamide(TD1) showed the highest activity, while acarbose was used as the standard α-glucosidase inhibitor. Acarbose reduces glucose absorption by slowing carbohydrate digestion and may help prevent or delay diabetic symptoms. The pancreatic α-amylase inhibition results showed that only 2-(5-phenyl-1,3,4-thiadiazol-2-ylamino)-N-ptolylacetamide(TD7) exhibited activity comparable to acarbose. In the in vivo study on alloxan-induced diabetic rats, TD1, N-(4-nitrobenzilidene)-5-phenyl-1,3,4- thiadiazol-2-

amine(TD2), and TD7 significantly lowered blood glucose levels at a dose of 35 mg/kg (p.o.). Considering both in vitro and in vivo findings, TD7 emerged as the most promising compound.[40]

CONCLUSION

Thiadiazole derivatives represent a versatile and pharmacologically important class of heterocyclic compounds. Their strong aromaticity, bioisosteric behavior, and sulfur-induced lipophilicity contribute to enhanced biological activity across diverse therapeutic and agricultural applications. The consistent demonstration of potent antibacterial, antifungal, antiviral, insecticidal, anticancer, and antidiabetic activities underscores the thiadiazole scaffold as a valuable lead structure for drug discovery. Further optimization, structure–activity relationship studies, and in vivo evaluations are expected to facilitate the development of safe and effective thiadiazole-based agents for future medicinal and agrochemical use.

REFERENCES

1. Sayiner S. Hakan et al., Synthesis and characterization of new 1,3,4 thiadiazole derivatives: study of their antibacterial activity and CT-DNA binding Royal Society of Chemistry Adv., 2022, (12) 29628, DOI: 10.1039/d2ra02435g
2. Gupta R. R., Kumar M., Gupta V., Heterocyclic Chemistry Five Mebered heterocyclic Springe International Edition, Volume II, 547
3. Upare A. A. Upare et al., Biological activity of oxadiazole and thiadiazole derivatives Applied Microbiology and Biotechnology, 2022, 106, 3490, doi: https://doi.org/10.1007/s00253-022-11969-0
4. Wu Zhibing,et al., Design, Synthesis, Antibacterial Activity, and Mechanisms of Novel 1,3,4-Thiadiazole Derivatives Containing an Amide Moiety. Journal of Agricultural and Food Chemistry, 2021, 69 (31), 8660, DOI: 10.1021/acs.jafc.1c01626
5. Zhong Xinmin et al.,Synthesis and biological activity of myricetin derivatives containing 1,3,4-thiadiazole scaffold Chemistry Central Journal, 2017, 11, Article no.106 , 2, DOI: 10.1186/s13065-017-0336-7
6. Anthwal Tulika et al., Diverse Biological Activities of 1,3,4-Thiadiazole Scaffold Chemistry 2022, 4, 1654, doi: https://doi.org/10.3390/ chemistry4040107
7. Yakan Hasan et al.,Synthesis, Characterization, and Antioxidant Activities of New 1,3,4- Thiadiazoles Based on Benzoic Acid, El-Cezerî Journal of Science and Engineering, 2021 Vol: 8, No: 1, 157,Doi: https://doi.org/10.31202/ecjse.794370
8. Singh k. Arvind et al., design, synthesis and anticonvulsant activity of some 1, 3, 4-thiadiazol derivatives, Int. J. Chem. Sci., 2012, 10(3), 1490, Doi: https://hosturl.link/n9UOhD
9. Sahu S. et al., Synthesis and Evaluation of Antimicrobial Activity of 1, 3, 4-Thiadiazole Analogues for Potential Scaffold Journal of Pharmacopuncture 2021;24(1):32-40pISSN: 2093-6966 • eISSN: 2234-6856, doi: https://doi.org/10.3831/KPI.2021.24.1.32
10. Al-Smadi L. Mousa et al., Synthesis, Characterization, and Antimicrobial Activity of New 1,2,3-Thiadiazole and 1,2,3-Selenadiazole Derivatives. Hindawi Journal of Chemistry, 2022, Volume 2022, article ID 5228067, 3-8, doi: https://doi.org/10.1155/2022/5228067
11. Angelova T. Violina et al., Development of New Antimycobacterial Sulfonyl Hydrazones and 4-Methyl-1,2,3-thiadiazole-Based Hydrazone Derivatives. Antibiotics, 2022,

11(5), 14-18, doi: https://doi.org/10.3390/antibiotics11050562

12. Mahendrasinh M. Raj, Patel V. Hemul, Raj M. Lata and Patel K. Naynika Synthesis and biological evaluation of some new 1,3,4-thiodiazole derivatives for their antimicrobial activities, International Journal of Pharmaceutical, Chemical, and Biological Science.IJPCBS 2013, 3(3), 815, Doi: www.ijpcbs.com
13. Kumar Phani Balusu et.al,Synthesis and Biological Evaluation of Novel 1,3,4 Thia di azole Heterocyclic Derivatives as Novel Anti-Microbial Agents. Int. J. Pharm. Sci. Rev. Res., 2016, 37(1), Article No. 36, 201-204-, doi: https://www.researchgate.ne t/ publication/306211276.
14. Joshi D.Shrinivas, Tiwari Sahilkumar and Kulka H. Venkatarao et al., Synthesis and Antitubercular Activity of Novel 1,3,4-Oxadiazole and 1,3,4-Thiadiazole Derivatives., Indian Journal of Heterocyclic Chemistry 2017,Vol. 27, Number 04, 419-420, Doi: https://connectjournals.com/file_full_text/2786604H_417-422.pdf
15. Rezki Nadjet et al., Synthesis of Novel 2,5-Disubstituted-1,3,4-thiadiazoles Clubbed 1,2,4-Triazole, 1,3,4-Thiadiazole, 1,3,4-Oxadiazole and/or Schiff Base as Potential Antimicrobial and Antiproliferative Agents, Molecules, 2015, 20, 16054 doi:10.3390/molecules200916048
16. Zheng Qingxiang et al., 5-Methyl-1,2,3-thiadiazoles Synthesized via Ugi Reaction and Their Fungicidal and Antiviral Activities J. Agric. Food Chem. 2010, 58, 7846–7855 DOI:10.1021/jf100619
17. Karaburun Çagrı Ahmet et al., Synthesis and Evaluation of New 1,3,4-Thiadiazole Derivatives as Potent Antifungal Agent s Molecules 2018, 23, 5-15 doi:10.3390/molecules23,123129
18. Caixia Wang et al., Design, Synthesis and Antifungal Activity of Novel Thioureas Containing 1,3,4-Thiadiazole and Thioether Skeleton. Chem. Res. Chin. Univ. 2016, 32, 615-620 ,doi: 10.1007/s40242-016-6023-8
19. Zhou Yuanxiang et al., Novel Flavonol Derivatives Containing 1,3,4-Thiadiazole as Potential Antifungal Agents: Design, Synthesis, and Biological Evaluation ACS Omega 2024, 9, 17297−17306, doi: http://pubs.acs.org/journal/acsodf
20. Zoumpoulakis P. et al., Synthesis of novel sulfonamide-1,2,4-triazoles, 1,3,4-thiadiazoles and 1,3,4-oxadiazoles, as potential antibacterial and antifungal agents. Biological evaluation and conformational analysis studies, Bioorganic & Medicinal Chemistry (2012), 20, 1572–1577,doi: https://doi.org/10.1016/j.bmc.2011.12.031
21. Wang Huan et al., Synthesis and Insecticidal Activity of N-tert-Butyl-N, N0-diacylhydrazines Containing 1,2,3-Thiadiazoles J. Agric. Food Chem. 2011, 59, pg no. 633 DOI:10.1021/jf104004
22. Suzuki Jun et al., Synthesis and insecticidal activity of 1,2,4-oxadiazole and 1,2,4-thiadiazole derivatives J. Pestic. Sci., 2011 ,36(3), 397-401, DOI: 10.1584/jpestics.G11-28
23. Dong Lia Yue et al- Synthesis and biological evaluation of novel 1,2,4-triazole containing 1,2,3-thiadiazole derivatives Chinese Chemical Letters, 2013, 24(12), 1135, doi: https://doi.org/10.1016/j.cclet.2013.06.024
24. F. H. Madkour et al., Novel heterocycles baased on 1,3,4-Thiadizole scaffold as insecticides J. Environ. Sci. Institute of Environmental Studies and Research – Ain Shams University, 2017, Vol.40, No.2, 41, doi:10.21608/jes.2017.20047.

25. Dong Li Wei et al., Synthesis and antiviral activity of new acrylamide derivatives containing 1,2,3-thiadiazole as inhibitors of hepatitis B virus replication. European Journal of Medicinal Chemistry, 2010, 45, 1920-1923, Doi: https://doi.org/10.1016/j.ejmech.2010.01.032
26. Fujiwara Masatoshi et al., Thiadiazole Derivatives: Highly Potent and Selective Inhibitors of Human Immunodeficiency Virus Type 1 (HIV-1) Replications In Vitro Microbiol. Immunol., 1997, 41(4), 301-303, Doi: https://hosturl.info/QSEFyq
27. Hu Yuzhi et al., Coumarin derivatives containing the 1,3,4 oxadiazole/thiadiazole moiety discovered as potential anti tobacco mosaic virus agents Molecular Diversity, 2024, 3-4, Doi: https://doi.org/10.1007/s11030-024-11098-y
28. Brai Annalaura et al., Synthesis and Antiviral Activity of Novel 1,3,4-Thiadiazole Inhibitors of DDX3X Molecules. 2019, 24(21), 13-15 doi: 10.3390/molecules24213988
29. Yu Lu et al., Synthesis and Antiviral Activity of Novel 1,4-Pentadien-3-one Derivatives Containing a 1,3,4-Thiadiazole Moiety, Molecules 2017, 22, 3-4 doi:10.3390/molecules22040658
30. Chidella Karunakar et al., Design and Synthesis of Novel 1,2,4-Thiadiazole linked imidazo[1,2 b]pyridazine as Anticancer Agents Chemical Data Collections, 2020, 30, 9-10, doi: https://doi.org/10.1016/j.cdc.2020.100554
31. TrafalisT. Dimitrios et al., Anticancer Activity of Triazolo-Thiadiazole Derivatives and Inhibition of AKT1 and AKT2 Activation Pharmaceutics 2021, 13(4), 11 , Doi: https://doi.org/10.3390/pharmaceutics13040493
32. Sudhakar S. G. D. et al- Design, Synthesis and Anticancer Activity of 1,2,4-Thiadiazole Derivatives Bearing 1,2,4-Oxadiazole , Russian Journal of General Chemistry, 2019, Vol. 89, No. 8, 1696, DOI: 10.1134/S1070363219080243
33. Mhaidat M. Nizaret al., synthesis, antimicrobial and in vitro antitumor activities of a series of 1,2,3-thiadiazole and 1,2,3-selenadiazole derivatives Drug Design, Development and Therapy, 2015, 9, 3647–3650 DOI: https://doi.org/10.2147/DDDT.S86054
34. Shaikh A. Samin et al., Synthesis, biological evaluation, and molecular docking of novel 1,3,4-substituted-thiadiazole derivatives as potential anticancer agent, BMC Chemistry 2024, 18, 119, Doi: https://doi.org/10.1186/s13065-024-01196-1
35. Janowska Sara et al., New 1,3,4-Thiadiazole Derivatives with Anticancer Activity, Molecules 2022, 27, 1814. 5-21, doi: https://doi.org/ 10.3390/molecules27061814
36. Dawood M. Kamal et al- Synthesis and Anti-cancer Activity of 1,3,4-Thiadiazole and 1,3-Thiazole Derivatives Having 1,3,4-Oxadiazole Moiety, Journal of Heterocyclic Chemistry 2014, vol 00, DOI: https://doi.org/10.1002/jhet.2250
37. Hussain Rafaqat et al- Molecular iodine-promoted oxidative cyclization for the synthesis of 1,3,4-thiadiazole-fused- [1,2,4]-thiadiazole incorporating 1,4-benzodioxine moiety as potent inhibitors of α-amylase and α-glucosidase: In vitro and in silico study, Sec. Medicinal and Pharmaceutical Chemistry, 2022, 10, 05, doi: https://doi.org/10.3389/fchem.2022.1023316
38. Khan Shoaib et al- Synthesis, in vitro biological assessment, and molecular docking study of benzimidazole-based thiadiazole derivatives as dual inhibitors of α-amylase and α-glucosidase, Sec. Medicinal and

Pharmaceutical Chemistry, 2023, 11, 07, doi: https://doi.org/10.3389/fchem.2023.1125915

39. Shulgau Zarina et al- Synthesis, Computational Study, and In Vitro α-Glucosidase Inhibitory Action of 1,3,4-Thiadiazole Derivatives of 3-Aminopyridin-2(1H)-ones, Pharmaceuticals, 2024, 17, 377, 5-13, doi: https://doi.org/10.3390/ph17030377
40. Datar A. Prasanna et al- Design and Synthesis of Thiadiazole Derivatives as Antidiabetic Agents, Med chem, 2012, 4(4), 397-399, DOI: 10.4172/2161-0444.100017

HOW TO CITE: Chaitali Gaikar, Sunayana Ghodgaonkar, Chetana Mayekar, Purva Gambhirrao, Pragati Gharatkar, Sanchita Ghode, Aditi Ghadge, Pharmacological Profile of Thiadiazole, Int. J. of Pharm. Sci., 2026, Vol 4, Issue 4, 1132-1142. https://doi.org/10.5281/zenodo.19461875