Educational Administration: Theory and Practice
2024, 30(5), 1989-1999
ISSN: 2148-2403
https://kuey.net/

Research Article

Exploring The Antibacterial Efficacy Of Thiadiazole Derivatives: A Systematic Review

Abhijeet Singh Sandhu[1], Manish Pathak[1]*

[1]Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Swami Vivekanand Subharti University, Meerut (U.P) INDIA-250005

***Corresponding author:** Dr. Manish Pathak
Associate Professor, Faculty of Pharmacy, Swami Vivekanand Subharti University, Meerut, (U.P) INDIA-250005,
e-mail: manishpharm01@gmail.com, Contact no: +91-9125532749

Citation: Manish Pathak, et al (2024), Exploring The Antibacterial Efficacy Of Thiadiazole Derivatives: A Systematic Review, *Educational Administration: Theory and Practice*, *30*(5), 1989-1999, Doi: 10.53555/kuey.v30i5.3210

ARTICLE INFO

ABSTRACT

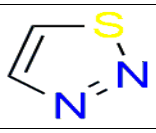
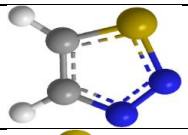
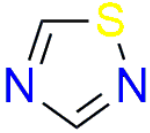
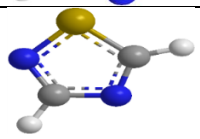
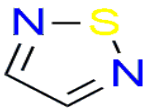
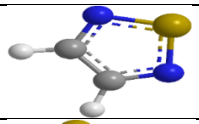
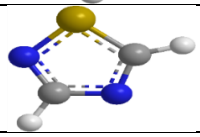
Thiadiazole and its derivatives represent a crucial heterocyclic nucleus with substantial significance in medicinal chemistry, particularly due to their potent antimicrobial properties against diverse microbes including bacteria and fungi. This review underscores the therapeutic potential of novel thiadiazole derivatives as bactericidal agents, aimed at addressing the escalating issue of microbial resistance. These derivatives exhibit notable antimicrobial activity, holding promise for the efficacious treatment of various microbial diseases.

Keywords: Thiadiazole, Antimicrobial activity, Antibacterial activity

INTRODUCTION

Thiadiazole is biologically active 5-membered ring system which contain hydrogen binding domain, sulfur atom and two –electron donor nitrogen system. Thiadiazoles exists in nature in four isomeric forms as follow: 1,2,3- thiadiazole; 1,2,4- thiadiazole; 1,2,5- thiadiazole; 1,3,4- thiadiazole **(Table 1)** . The mesoionic character of the five –membered heterocyclic rings by isolation of distinct areas of positive and negative biophores allows the thiadiazole rings to easily cross cellular membranes and strongly interact with biological targets.[1]

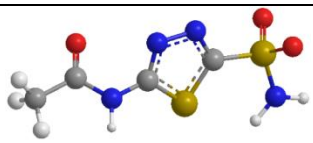
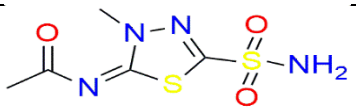
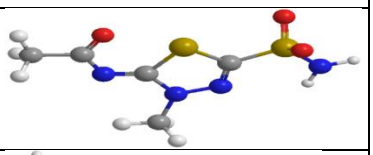
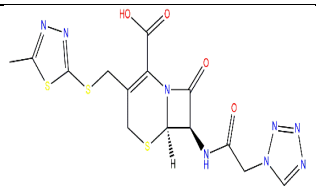
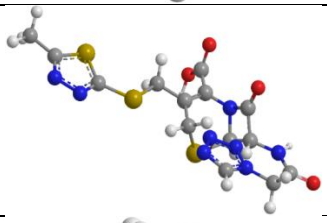
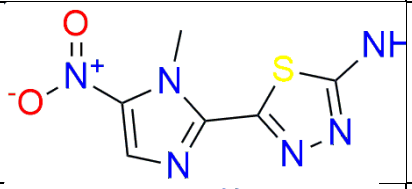
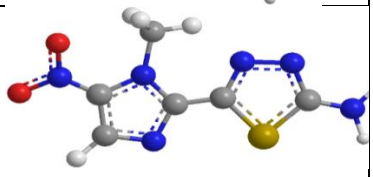
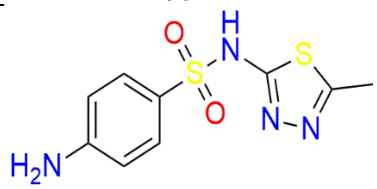
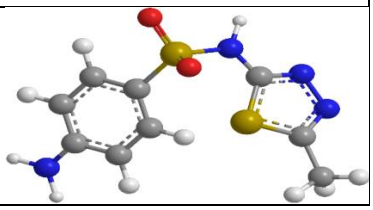
Table 1: Thiadiazole deriatives chemical structure with their 3D Conformer

Name	Chemical Structure	3D Conformer
1,2,3- thiadiazole		
1,2,4- thiadiazole		
1,2,5- thiadiazole		
1,3,4- thiadiazole		

Thiadiazoles are highly effective in the fight against bacterial infections; the existence of a broad spectrum of antimicrobial action is a priori necessary for the resistance of antibiotics. The search for and study of thiadiazoles against various pathogens has shown their necessary properties for the necessary action for their effectiveness as useful agents in bacterial diseases. Furthermore, the existence of a sulfur atom in the

thiadiazole derivative results in high liposolubility, which increases pharmacokinetic properties and biological activity of compounds with thiadiazole ring. The synthetic compounds containing thiadiazole rings exhibit a broad spectrum of biological activities, such as antibacterial[2], anticancer[3], antiparasitic[4], and antiviral[5] actions. Moreover, there are many drugs containing thiadiazole ring in the market, such as carbonic anhydrase inhibitors, acetazolamide, and methazolamide as diuretic drugs, cefazolin as the first generation cephalosporin, sulfamethizole as an antimicrobial sulfonamide, and the antiparasitic drug, megazol (**Table. 2**).

Table 2: Drugs containing thiadiazole ring

Name	Chemical structure	3D Conformer
Acetazolamide		
Methazolamide		
Cefazoline		
Megazol		
Sulphamethizole		

THIODIAZOLE AS BACTERIOCIDALS

The antibacterial characteristics of thiodiazole derivatives have made them a promising class of bactericidal drugs. The potential of these chemicals to counteract antibiotic resistance and function as substitute treatments for different types of bacterial illnesses has been thoroughly investigated. The capacity of thiodiazole derivatives to impede the growth of several bacterial pathogens is indicative of their antibacterial properties. Novel dithiocarbamate-containing 4H-chromen-4-one derivatives, such as thiodiazole copper, have demonstrated noteworthy inhibitory effects against plant pathogens, including Xanthomonas oryzae pv. oryzae and Xanthomonas axonopodis pv. citri. Notably, certain compounds have demonstrated these inhibitory effects more effectively than commercial agents.[6]

In a similar vein, 1, 3, 4-oxadiazole thioethers labelled with imidazole have proven to be more potent antibacterials against various plant diseases; in fact, several of these derivatives have minimal EC50 values that are higher than those of conventional commercial medications.[7]Through the synthesis of novel 1,3,4-thiadiazoles based on thiophene-2-carboxylic acid, molecules with potent antibacterial activity against both fungus Candida albicans and a range of Gram-positive and Gram-negative bacteria have been found.[8] According to these results, 1, 3, and 4-thiadiazole derivatives may be used as bioactive substances in pharmacological and therapeutic contexts.Furthermore, a novel class of degradable polymers with excellent antibacterial capabilities against Pseudomonas aeruginosa has been created: thioimidazolium poly (ionic liquid). This polymer can decay in specific settings, which lessens its influence on the environment.[9]Comparing the antibacterial properties of derivatives of thiazole, imidazolidine, and tetrahydropyrimidine, it was found that several thiazole derivatives significantly inhibited the growth of Bacillus cereus and Salmonella typhimurium.[10]

This demonstrates the bactericidal potential of thiazole derivatives. Furthermore, 1,2,4-triazolo[4,3-a] pyridine moiety-containing quinazoline thioether derivatives have been synthesised and assessed potential

antimicrobial agents in agriculture; certain compounds have encouraging in vitro antibacterial properties against phytopathogenic bacteria.[11]

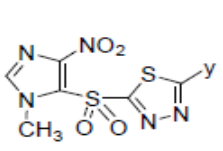
MOA OF THIODIAZOLE DERIVATIVES AS BACTERIOCIDALS

Beta-lactams and polymyxins, thiodiazole derivatives cause bacterial mortality by interfering with the formation of bacterial cell walls and membrane structure.[12] Thiodiazole compounds with particular functions, like 1, 3, and 4-oxadiazole thioether derivatives, show antibacterial activity by perhaps disrupting the purine metabolism of bacteria.[13] Tailored 1, 3, 4-oxadiazole thioether/sulfoxide/sulfone derivatives with pyridinium exhibit improved antibactearial activity, indicating that structural alterations may increase effectiveness.[14] Certain thiazole derivatives have an efficient bactericidal impact against infections that are resistant to many drugs by acting as dual DNA gyrase and dihydrofolate reductase (DHFR) inhibitors.[15] Triazolo-thiadiazole moieties found in novel thiouracil derivatives block SecA ATPase, a critical enzyme for bacterial growth and division.[16] Derivatives of thiazole-quinolinium have bactericidal action by inducing FtsZ polymerization, which stops bacterial cell division.[17] Conditional mutant transcriptional profiling suggests that thiazole derivatives may also function by blocking bacterial acetyl coenzyme-A carboxylase.[18]

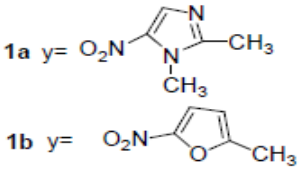
Antimicrobial & Antibacterial Activity of Thiodiazole Derivatives

Thiadiazole derivatives have antimicrobial properties that include antibacterial and antifungal properties.[19] These properties are outlined below: The ability of a novel class of 2-(1-methyl-4-nitro-1H-imidazol-5-ylsulfonyl)-1,3,4-thiadiazoles **(1a-c)** to inhibit bacterial growth. The traditional agar dilution method was used to evaluate three drugs in vitro against a panel of microorganisms, including gram-positive and gram-negative bacteria. Promising antibacterial activity were demonstrated by Compound **(1b)** against gram-positive bacteria, such as Staphylococcus aureus, Staphylococcus epidermidis, and Bacillus subtilis, on a 1, 3, 4-thiadiazole scaffold containing 5-(5-nitrofuran-2-yl)-residue. [20]
Synthesis of 2,5-di-[5-amino-1,3,4-thiadiazole-2-thiomethyl] was carried out by Solomon et al.Utilising the standard drug ampicillin trihydrate (50 µg/mL), -1,3,4-thiadiazoles **(2)** were found to exhibit in vitro antibacterial activities against both Gram-positive (S. aureus, S. cerevisiae, and C. diphtheriae) and Gram-negative (E. coli and P. aeruginosa) bacteria at MICs of 100 µg/mL and 200 µg/mL. When compared to the common medication ampicillin, the tested compounds showed good action against Gram-positive bacteria but less activity against Gram-negative bacteria.[21] Some new biologically active 1,2,4-triazolo[3,4-b][1,3,4] thiadiazole and its Schiff bases **(3a-e)** and tested their antibacterial activity against B. subtillis, S. aureus, P. aeruginosa, and E. coli in vitro. When compared to normal medications, compounds **3a, 3b**, and **3c** demonstrated **1521** substantial inhibition against all strains, normal medications included ampicillin, gentamycin, tetracycline, and chloramphenicol.[22] Using standard drug ampicillin trihydrate at MIC of 50 µg/mL, Dabholkar et al. synthesised 1,3-bis-imino-[5- (substituted) phenylamino-1,3,4-thiadiazol-2-yl-] – 5,5 dimethylcyclohexanes **(4a–d)** and investigated there in vitro antibacterial activities towards Gram-positive (S. aureus, C. diphtheria, and S. cerevisiae) and Gram-negative (E. coli and P. aeruginosa) bacteria at MIC of 100 µg/mL and 200 µg/mL. The synthesised compounds were found to be more effective against S. aureus, C. diphtheria, and S. cerevisiae.[23]
A novel series of Bis-[thiadiazol-2-yl-tetrahydro-2H-pyrazolo[3,4-d] [1,3] thiazole] methanes was synthesised by Cherkupally et al. The antibacterial properties of the compounds were evaluated in relation to two types of bacteria: Proteus vulgaris, Salmonella typhimurium, and Escherichia coli, and Gram-negative bacteria, Bacillus subtilis, Staphylococcus aureus, and Micrococcus luteus. They came to the conclusion that the antibacterial activity of the methylpyrazole moiety **(5h),** N- (3fluorophenyl) **(5e),** and (4-methoxyphenyl) **(5c)** had demonstrated notable results, nearly matching that of the common medication Ampicillin. These compounds **(5a-h)** were also tested for their antifungal activity against Aspergillus fumigates, Trichophyton rubrum, Trichophyton mentagrophytes, and Candida albicans. Compound **(5c)** demonstrated strong activity against T. mentagrophytes and T. Rubrum, compound **(5e)** demonstrated activity against C. albicans, and compound **(5h)** demonstrated strong activity against both C. albicans and T. mentagrophytes, these substances have about the same action as regular amphotericin B. It's noteworthy that compounds **5e** and **5h** shown strong antifungal activity against Candida albicans. The majority of these novel compounds shown noteworthy efficacy against the test fungus and were promising candidates for additional research and development.[24]
1, 4-bis(6-(substituted phenyl)-] is a brand-new series [1,2,4].-triazolo [3,4-b]Phenyl substitutes **(6a-d)** and 4-bis(-1,3,4-thiadiazoles)Palekar et al. synthesised 4-thiazolidinones, which demonstrated antibacterial activity against a range of bacterial and fungal species. Potential antibacterial action was demonstrated by some of these substances.[25]
Production and antimicrobial properties of 1-[1,3,4-thiadiazol-2-yl] Tehranchian et al. studied -3-methylthio-6,7-dihydrobenzo[c]thiophen-4(5H) ones **(7a-c).** High activity was shown by each of these substances against S. epidermidis, Bacillus subtilis, and Staphylococcus aureus.[26] A group of fifteen novel cyclopropanecarboxamides **(8a-f)** were synthesised by Liu et al. and their antifungal efficacy was evaluated in vivo. Conclusion: Compounds **(8d)** and **(8e)** showed more antifungal activity (79.38%) than the other compounds.[27] Novel 5-[isopropylthiazole] 2-substituted Kumar et al. synthesised bundled 1, 2, 4-triazole **(9a-d**) and 1, 3, 4 oxadiazoles, then assessed their antifungal efficacy. They came to the general conclusion that

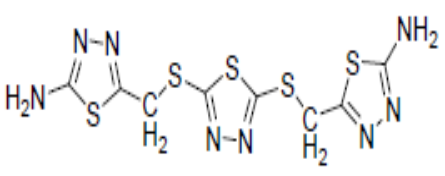
compound **(9b)** had outstanding antifungal activity.[28] Chen et al. created novel 1, 3, 4-thiadiazole compounds that are pyrazolyl-substituted and fungicidally active. Compounds **(10)** and **(11a-d)** may be concluded to have fungicidal activity against Rhizoctonia solani.[29] The 2-(1-adamantylamino) - 1, 3, 4-thiadiazole derivatives **(12)** were synthesised by Kadi et al. and evaluated for their in vitro antibacterial and antifungal properties against a range of Grampositive and Gramnegative bacteria as well as the yeast-like pathogen Candida albicans. A number of compounds demonstrated strong antifungal activity against Candida albicans and good or moderate activities, especially against the tested Gram-positive bacterium Bacillus subtilis.[30] 2-(3-chloro-1-benzothien-2-yl)-1,3,4-thiadiazole derivatives were synthesised by Sharba et al. **(13)** and their antibacterial and antifungal activity was assessed. Several compounds demonstrated notable antibacterial efficacy in comparison to the corresponding conventional medications.[31] In order to assess the in vitro antifungal and antibacterial efficacy of their newly synthesised Sulfonamide-1,2,4 thiadiazole derivatives **(14a-b)** against all micromycetes, Camoutsis et al. compared them to the commercially available standard medication bifonazole. The best activity was obtained by an analogue with a methylpiperazine reactive group, according to SAR research.[32] Matysiak et al. synthesised a variety of [2-(2,4-Dihydroxyphenyl)-1,3,4-thiadiazole analogues **(15)** and assessed them in vitro antifungal efficacy against Candida nonalbicans spp. rather than C. alhicans. Certain substances show greater activity than the antifungal medications that have been evaluated in comparison. The antifungal activities of 2-amino-1,3,4-thiadiazole derivatives were greater than those of other analogues. The Villar technique yields derivatives with significant antifungal activity that have a narrow range of lipophilicity values.[33] Liu et al. synthesised and evaluated the antifungal efficacy of new sulfoxide derivatives with a 1,3,4-thiadiazole moiety replaced with trimethoxyphenyl (**16**). This compound **(16)** has strong antifungal properties against Sclerotinia sclerotiorum, according to the bioassay data, with EC50 values ranging from 19.91 to 63.97 μg/mL. Following a 12-hour treatment with compound **(16)** at a concentration of 100 μg/mL, there was a noticeable decline in the mycelial reducing sugar, D-GlcNAc, soluble protein, pyruvate content, and chitinase activity. [34] In order to test a range of 1,2,3-thiadiazole and 1,2,3-selenadiazole derivatives for their antiamoebic properties against the HM1: IMSS strain of Entamoeba histolytica, Hayat et al. synthesised the compounds. The researchers came to the conclusion that compounds with 2-(quinolin-8-yloxy) acetohydrazones **(17)** had greater activity than their cyclized derivatives (1,2,3-thiadiazole and 1,2,3-selenadiazole derivatives). According to SAR tests, the molecule with the most potent antiamoebic activity was one that included a quinoline ring and a hydrazone connection with a free N-H group. All of these compounds were found to be harmless within the concentration range of 1.56–50 μM, according to cytotoxic experiments conducted on the human breast cancer MCF-7 cell line.[35] Jazayeri et al. demonstrated the effective synthesis and antibacterial activity of several gatifloxacin analogues with a nitroaryl-1,3,4-thiadiazole moiety **(18a-d)** connected to the piperazine ring at C-7 position. Good antibacterial activity was demonstrated by four compounds against a panel of gram-positive and gram-negative bacteria. With regard to gram-positive bacteria, such as Staphylococcus epidermidis (MIC = 0.0078 μg/mL), Bacillus subtilis (MIC = 0.0039 μg/mL), Enterococcus faecalis (MIC = 0.125 μg/mL), and Micrococcus luteus (MIC = 0.125 μg/mL), the SAR analysis of the compound with the title demonstrated that nitrofuran analogue demonstrated more powerful inhibitory activity. With relation to gatifloxacin, the reference medication, and other synthetic substances. Using the MTT assay, the target compounds' cytotoxic activity against normal mouse fibroblast (NIH/3T3) cells was also evaluated. According to the findings, these substances have antibacterial action at non-cytotoxic concentrations.[36] The antibacterial efficacy of 1, 3, 4-thiadiazole phenyl oxazolidinones **(19)** against gram-positive and gram-negative organisms was synthesised and reported by Thomasco et al. The efficacy of these compounds is further increased by converting the C5 acetamide group to a thioacetamide, according to SAR research.[37] Novel imidazo[2,1-b] benzisoxazolyl methylene bridgedLamani et al. synthesised [1,3,4] thiadiazoles **(20a-c),** which were later discovered to have antibacterial and antifungal properties. Every molecule with nitroso, bromo, or thiocynato showed antifungal and antibacterial properties.[38] In order to combat a variety of Gram-positive and Gram-negative bacteria, Khalaj et al. synthesised several linezolid analogues with nitroaryl-1, 3, 4-thiadiazole moiety **(21a-c).** These analogues were then tested for their cytotoxic potential against NIH/3T3 normal mouse fibroblast cells through the use of the MTT assay. In comparison to other synthesised compounds and the reference medication linezolid, it can be concluded that the nitrofuran analogue **(21b)** exhibited more potent inhibitory activity. Additionally, compound **(21c)** was found to exhibit potent antibacterial activity against Gram-positive bacteria at non-cytotoxic concentrations.[39]



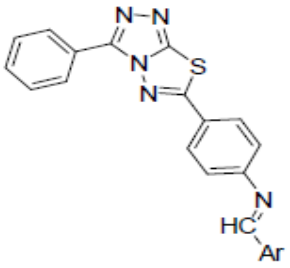
(1)



1a y= O_2N 1b y= O_2N 1c y= CH_3CONH-



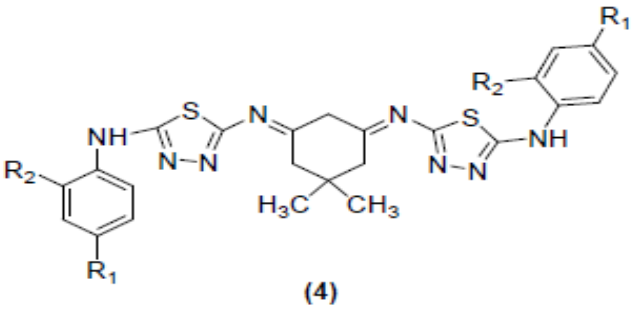
(2)



(3)

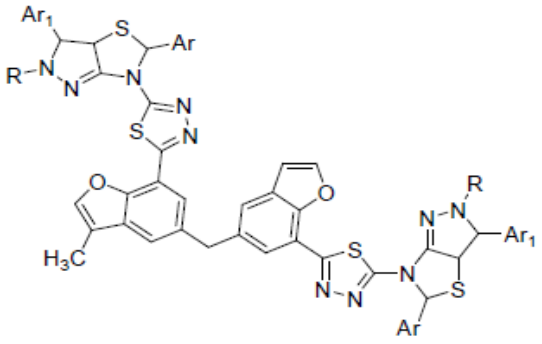
Ar

3a= 4-CH_3-C_6H_4-CHO
3b= 4-OH_3-OCH_3-C_6H_3-CHO
3C= 3-OC_2H_5-OC_2H_5-C_6H_3-CHO
3d= C_6H_5-CHO
3e= 2-OH-C_6H_4-CHO



(4)

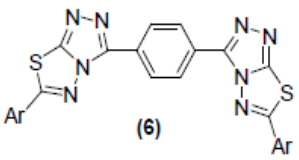
	R_1	R_2
4a	H	H
4b	CH_3	H
4C	Cl	H
4d	OCH_3	H



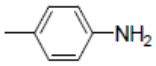
(5)

Ar = Ar_1= 4–OCH_3-C_6H_4-

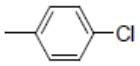
5a: R= H
5b: R= C_6H_5
5c: R= 4-OCH_3-C_6H_4
5d: R= 4-Cl-C_6H_4
5e: R= 3-F-C_6H_4
5f: R= C_6H_4-CH_2
5g: R= Isopropyl
5h: R= Methyl



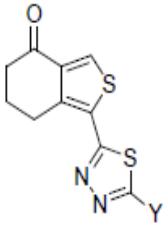
(6)

6a: Ar = 

6b: Ar = 

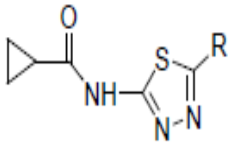
6c: Ar = 

6d: Ar = 



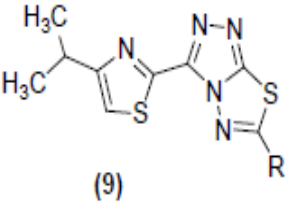
(7)

7a: Y = NH_2
7b: Y = SH
7c: Y = SCH_3



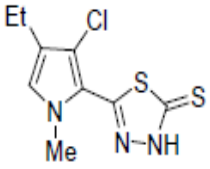
(8)

8a: R= H
8b: R= CH_3
8C: R=C_2H_5
8d: R= o-CH_3-C_6H_4
8e: R= m-CH_3-C_6H_4
8f: R= o-Cl-C_6H_4

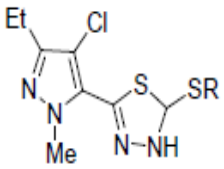


(9)

9a: R= C_6H_5
9b: R= 4-NO_2-C_6H_4
9c: R= 4-OCH_3-C_6H_4
9d: R= 4-Cl-C_6H_4

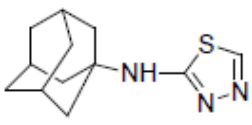


(10)

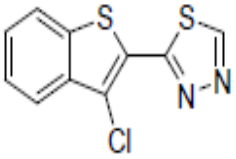


(11)

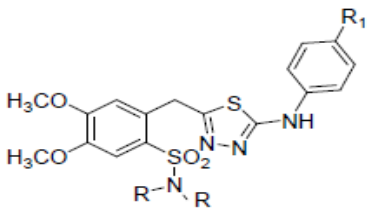
11a : R= Methyl
11b : R= propyl
11c : R= Allyl
11d : R= Amyl



(12)

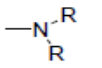


(13)

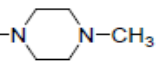


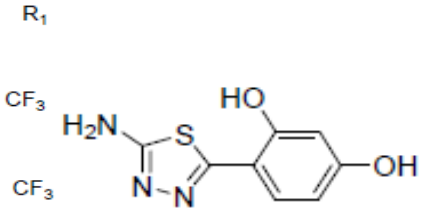
(14)

14(a): =

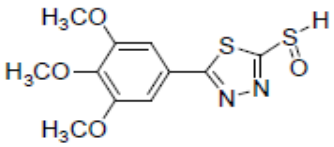


14(b): =

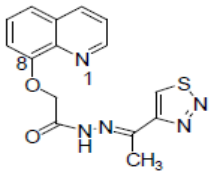




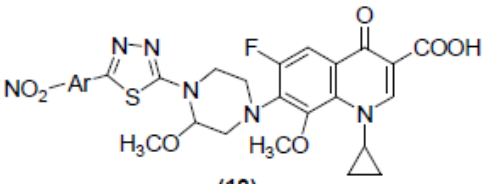
(15)



(16)

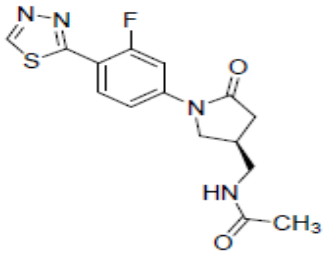


(17)

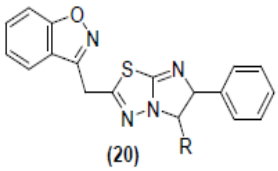


(18)

18a = 5-nitrofuran-2-yl
18b = 5-nitrothiophen-2-yl
18c = 1-methyl-5-nitroimidazol-2-yl
18d = nitrophenyl

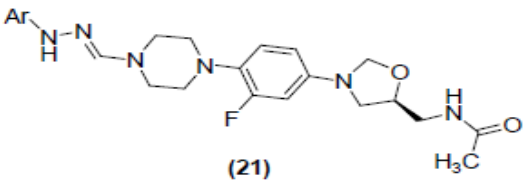


(19)

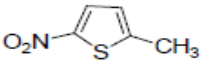


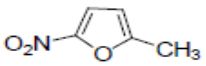
(20)

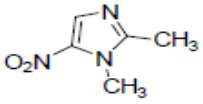
20a: R = Br
20b: R = NO
20c: R = SCN

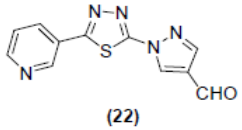


(21)

21(a): Ar = 

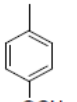
21(b): Ar = 

21(c): Ar = 

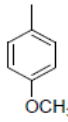


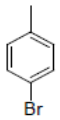
(22)

22a: R= 

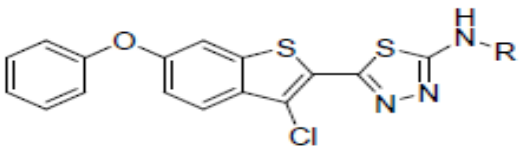
22b: R= 

22c: R= 

22d: R= 

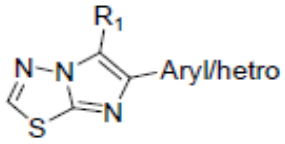
22e: R= 

22f: R= 

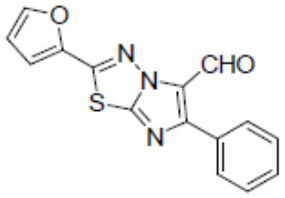


(23)

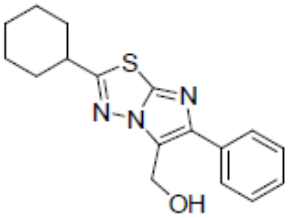
23a: R= C_6H_5
23b: R= 3-Cl-C_6H_5
23c: R= 4-OCH_3-C_6H_4
23d: R= 2-NO_2-C_6H_4
23e: R= 2-OCH_3-C_6H_4
23f: R= 2-CH_3-C_6H_4

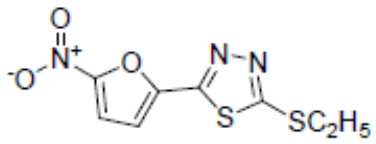


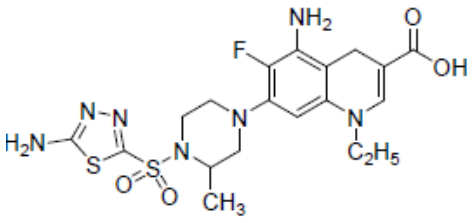
Aryl =phenyl,4-Cl-phenyl,4-NO_2-phenyl
Hetro = furyl,coumarinyl
R_1 = Br,SCN



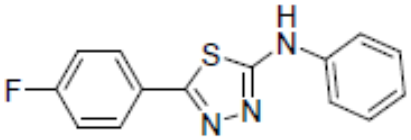
(24) **(25)**

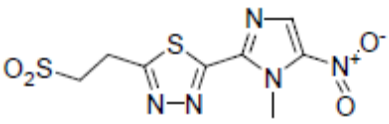


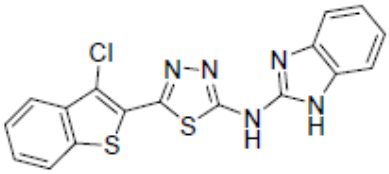




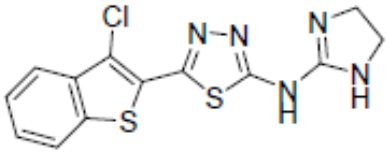
(26) **(27)** **(28)**

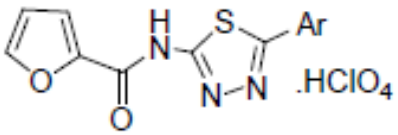






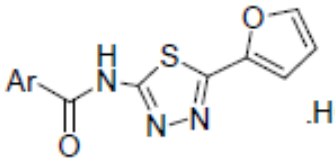
(29) **(30)** **(31)**





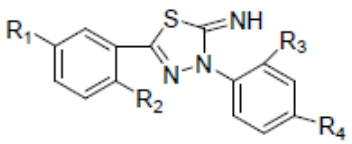
33a: Ar = C_6H_5
33b: Ar = p-$C_6H_4CH_3$
33c: Ar = p-$C_6H_4NHCOCH_3$
33d: Ar = p-$C_6H_4OCH_3$

(32) **(33)**



34a: Ar = C_6H_5
34b: Ar = p-$C_6H_4CH_3$
34c: Ar = p-$C_6H_4NHCOCH_3$
34d: Ar = p-$C_6H_4OCH_3$

(34)



(35)

	R_1	R_2	R_3	R_4
35a	H	H	H	H
35b	H	H	NO_2	NO_2
35c	Cl	H	H	H
35d	Cl	H	NO_2	NO_2
35e	H	Cl	H	H
35f	H	Cl	NO_2	NO_2
35g	H	NH_2	H	H
35h	H	NH_2	NO_2	NO_2

Some unique 3-Aryl-1 [(5-(pyridin-3-yl)-1,3,4-thiadiazol-2-yl] was synthesised by Prathap et al. By using the Vilsmeier-Haack procedure, 1Hpyrazole-4-carbaldehydes **(22a-f)** were synthesised and there in vitro antitubercular activity was evaluated. When compounds **22a, 22c, 22d,** and **22e** with electron withdrawing groups were compared to the standard medicine pyrazinamide, which has a MIC value of 100 µg/mL and is a first-line antitubercular medication, they demonstrated good activity at MIC values of MIC 50-100 µg/mL.[40] Vasoya and colleagues synthesised 2-(3′-chloro-5′-phenoxybenzo[b]thiophen-2′-yl)-5-arylamino-1,3,4-thiadiazole derivatives **(23af)** and assessed their efficacy as an antitubercular agent against Mycobacterium tuberculosis at a minimum inhibitory concentration (MIC) of 6.25 µg/ml. The results demonstrated 98% inhibition when compared to the standard drug Rifampin at a concentration of 0.25 µg/ml. P-methoxyphenyl **(23c)**, 2-methylphenyl **(23f),** and 2-methoxyphenyl **(23e)** compounds were the most effective among the subsituents at R.[41] A series of 2-sulfonamido/trifluoromethyl-6-(4'-substituted aryl/heteroaryl)imidazo[2,1-

b]-1,3,4-thiadiazoles was synthesised by Gadad et al**. (24)**. The chosen substances' first in vitro anti-TB efficacy against Mycobacterium tuberculosis was assessed. The findings indicate that one molecule demonstrated strong anti-tubercular activity with a MIC of 20 µg/mL, while five compounds shown moderate to good anti-tubercular activity with % inhibition of 29, 43, 58, 31 and 41, respectively, at a MIC of >6.25 µg/mL.[42] In order to test a series of 2,6-disubstituted and 2,5,6-trisubstituted imidazo[2,1-b][1,3,4]thiadiazole derivatives for antitubercular activity against Mycobacterium tuberculosis, Kolavi et al. synthesised the compounds. At a MI of >6.25 µg/mL, the results indicated that four analogues had considerable action, with percentage inhibitions of 36, 30, 15, and 20, respectively. The compounds with the strongest (100%) inhibitory action were 2-(2-furyl)-6-phenylimidazo[2,1- b][1,3,4] thiadiazole-5 carbaldehyde **(25)** and 2- cyclohexyl-6-phenylimidazo[2,1- b][1,3,4]thiadiazol-5-yl)methanol **(26)**.[43] Foroumadi et al. synthesised a novel series of 2-(5-nitro-2-furyl)-1,3,4-thiadiazole derivatives **(27)** as a possible antituberculosis agent in vitro against Mycobacterium tuberculosis. The most potent activity was reported in an analogue with an ethylthio moiety linked at thiadiazole, with a minimum inhibitory concentration (MIC) of 0.78 µg/mL.[44] Unusual 7-[4-(5-amino-1,3,4 thiadiazole-2-sulfonyl)] seriesTalath et al. synthesised and assessed the preliminary in vitro antibacterial efficacy of -1-piperazinyl fluoroquinolonic derivatives **(28)** against a variety of Gram-positive and Gram-negative bacteria. Compared to reference medications, certain synthesised compounds demonstrated less action against Gram-negative bacteria but superior activity against Gram-positive bacteria, such as S. aureus, E. faecelis, and Bacillus species, with MIC values of 1–5 µg/mL.[45] Oruç et al. created a variety of 2,5-disubstituted-1,3,4-thiadiazole derivatives and tested them against Mycobacterium tuberculosis to determine their antituberculosis activity. 2-phenylamino-5-(4-fluorophenyl)-1,3,4-thiadiazole **(29)** was the most active compound and had the highest level of inhibitory action.[46] Foroumadi et al. synthesised a novel series of 2-(1-methyl-5-nitro-2- imidazolyl)-1,3,4-thiadiazole-5-alkylsulfides **(30),** alkylsulfoxides, and alkylsulfones, and evaluated them for antitubercular action. Compounds with a main alkylthio substitution showed good antituberculosis action at MIC of 3.13-6.25 µg/mL, according to the data. The antituberculosis action of methyl and propyl derivatives was eliminated upon oxidation to sulfone, according to a SAR analysis of titled; however, the ethylsulfonyl counterpart remained active, with a MIC value of 1.56 µg/mL.[47] N-[5-(3- Chlorobenzo[b]thiophen-2-yl)-1,3,4-thiadiazol-2- yl] is a novel series ofAly et al. developed and synthesised -1H-benzo[d]imidazol-2-yl-amine derivatives, and assessed their antibacterial efficacy in vitro against Bacillus cereus, Escherichia coli, Aspergillus niger, and Penicillium notatum at MIC of 125, 250, and 500 µg/cm3. Comparing compound **(31)** to other strains, it exhibited modest action against E. coli and moderate activity against them. Compound **(32)** has a strong anti-A. niger effect and a modest anti-other strain effect.[48] The biological activities of 2-(furoyl amino)-5-(substituted aryl)-1,3,4-thiadiazole (33a-d) and 2-(substituted benzoyl amino)-5-(furyl)-1,3,4-thiadiazole derivatives (34a-d) were synthesised and assessed by Dabholkar et al. When compared to conventional reagent Ampicilli, it can be stated that the perchloric acid salt of compound **(33–34)** had substantial anti-microbia activity against E. coli, S. typhi, S. aureus, and B. subtilus bacteria at a concentration of 250 µg/m.[49] In order to determine the minimum inhibitory concentration (MIC) of the newly synthesised subsituted-2,4 diphenyl-5-imino-1,3,4-thiadiazole derivatives (**35a–h),** Asif et al. tested the derivatives' in vitro antibacterial activity against two Gramme negative strains (Escherichia coli and Pseudomonas aeruginosa) and two Gramme positive strains (Bacillus cereus and Staphylococcus aureus). The recently created substances showed encouraging antibacterial properties.[50] A series of 2-aminosubsituted-5-[(4-nitro-1H-imidazol-1-yl)methyl]-1,3,4-thiadiazole derivatives **(36a–f)** were synthesised by Vosooghi et al. and tested for antimicrobial activity against Clostridium difficile, Aspergillus niger, Cryptococcus neoformans, Staphylococcus aureus, and Staphylococcus epidermidis. Compounds **(36a)** and **(36d)** with a 200 µg/mL MIC value shown similar activity against S. aureus as Cefotaxime, the reference medication, at a 20 µg/mL MIC value.[51] Vedavathi et al. synthesised fluorobenzothiazole combined with 1,3,4-thiadiazole derivatives **(37, 38**) and assessed its antimicrobial efficacy. Members of this series exhibited significant antibacterial activity in comparison to the reference medication.[52] The new 2-amino,5-(phenyl substituted)1,3,4-thiadiazole derivatives **(39a-j)** were synthesised and evaluated by Mathew et al. for their antibacterial activity against a range of microbial strains, including Staphylococcus and E. Coli, as well as fungal strains, including Candida albicans. Bacillus cerevisea the standard medication gentamycin demonstrated a zone of inhibition of 14 and 16 mm at a dose of 100 µg/ml against the bacteria Bacillus and E. Coli, respectively, in terms of antibacterial activity. Among the compounds that were synthesised, **39c, 39e, 39f,** and **39i** shown favourable activity against E. coli. Compounds such as **39e, 39f, 39i, and 39j** demonstrated favourable action against the Bacillus species. The conventional medicine griseofulvin demonstrated antifungal effectiveness against Candida albicans and Saccharomyces cervisea, with a 15 and 21 mm zone of inhibition at 100µg/ml concentration, respectively. Three of the synthetic compound's components, **39f, 39i**, and **39j**, showed substantial action against the two organisms. They created an effective antibacterial antibiotic from these synthesised compounds by applying the appropriate chemical change.[53]

CONCLUSION

The literature review has highlighted the significant therapeutic potential of thiodiazoles and their derivatives as effective bacteriocidal, antimicrobial, and antibacterial agents. These compounds demonstrate promising efficacy in combating bacterial and microbial infections. Their broad-spectrum activity and ability to target resistant strains make them valuable candidates for the development of novel antimicrobial therapies. Further research and development in this area hold promise for the advancement of treatments against various infectious diseases, addressing the pressing need for effective antimicrobial agents in healthcare.

FUNDING
NONE

CONFLICT OF INTEREST
The authors declare no conflict of interest, financial or otherwise.

DECLARATION
None

ACKNOWLEDGEMENT
Authors would like to express gratitude to Faculty of Pharmacy, Swami Vivekananad Subharti University for their support during work. I am thankfull to Dr. Ganesh Prasad Mishra, Professor, Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Swami Vivekananad Subharti University for their continuous support.

REFERENCES

1. Newton CG, Ramsden CA. Meso-ionic heterocycles (1976 1980) Tetrahedron. 1982;38:2965–3011. [Google Scholar]
2. Salimon J, Salih N, Hameed A, Ibraheem H, Yousif E. Synthesis and antibacterial activity of some new 1, 3, 4-oxadiazole and 1, 3, 4-thiadiazole derivatives. J Appl Sci. 2010;6:866–870. [Google Scholar]
3. Kumar D, Kumar NM, Noel B, Shah K. A series of 2-arylamino-5-(indolyl)-1,3,4-thiadiazoles as potent cytotoxic agents. Eur J Med Chem. 2012;55:432–438. [PubMed] [Google Scholar]
4. Liesen AP, de Aquino TM, Carvalho CS, Lima VT, de Araújo JM, de Lima JG, et al. Synthesis and evaluation of antitoxoplasma gondiiand antimicrobial activities of thiosemicarbazides, 4-thiazolidinones and 1, 3,4-thiadiazoles. Eur J Med Chem. 2010;45:3685–3691. [PubMed] [Google Scholar]
5. Küçükgüzel ŞG, Küçükgüzel İ, Tatar E, Rollas S, Şahin F, Güllüce M, et al. Synthesis of some novel heterocyclic compounds derived from diflunisal hydrazide as potential antiinfective and antiinflammatory agents. Eur J Med Chem. 2007;42:893–901. [PubMed] [Google Scholar]
6. Jiang, S., Su, S., Chen, M., Peng, F., Zhou, Q., Liu, T., Liu, L., & Xue, W. (2020). Antibacterial activities of novel dithiocarbamate-containing 4H-chromen-4-one derivatives.. Journal of agricultural and food chemistry. https://doi.org/10.1021/acs.jafc.0c01652.
7. Wang, P., Wang, M., Zeng, D., Xiang, M., Rao, J., Liu, Q., Liu, L., Wu, Z., Li, Z., Song, B., & Yang, S. (2019). Rational Optimization and Action Mechanism of Novel Imidazole (or Imidazolium)-Labeled 1,3,4-Oxadiazole Thioethers as Promising Antibacterial Agents against Plant Bacterial Diseases.. Journal of agricultural and food chemistry, 67 13, 3535-3545 . https://doi.org/10.1021/acs.jafc.8b06242.
8. Muğlu, H., Yakan, H., & Shouaib, H. (2020). New 1,3,4-thiadiazoles based on thiophene-2-carboxylic acid: Synthesis, characterization, and antimicrobial activities. Journal of molecular structure, 1203, 127470. https://doi.org/10.1016/j.molstruc.2019.127470.
9. Smith, C., Cataldo, V., Dimke, T., Stephan, I., & Guterman, R. (2020). Antibacterial and Degradable Thioimidazolium Poly(ionic liquid). ACS Sustainable chemistry & Engineering, 8, 8419-8424. https://doi.org/10.1021/acssuschemeng.0c02666.
10. Ghasemi, B., Beyzaei, H., & Majidiani, H. (2016). A Comparative Study on the Antibacterial Effects of Some Newly Synthesized Thiazole, Imidazolidine and Tetrahydropyrimidine Derivatives Against Bacillus cereus and Salmonella typhimurium. Pharmaceutical sciences, 22, 142-142. https://doi.org/10.15171/PS.2016.10.
11. Fan, Z., Shi, J., Luo, N., Ding, M., & Bao, X. (2019). Synthesis, Crystal Structure, and Agricultural Antimicrobial Evaluation of Novel Quinazoline Thioether Derivatives Incorporating the 1, 2, 4-Triazolo[4,3-a]pyridine Moiety.. Journal of agricultural and food chemistry. https://doi.org/10.1021/acs.jafc.9b04733.
12. Tenover, F. (2006). Mechanisms of antimicrobial resistance in bacteria.. The American journal of medicine, 119 6 Suppl 1, S3-10; discussion S62-70 . https://doi.org/10.1016/J.AMJMED.2006.03.011.
13. Song, X., Li, P., Li, M., Yang, A., Yu, L., Luo, L., Hu, D., & Song, B. (2017). Synthesis and investigation of the antibacterial activity and action mechanism of 1,3,4-oxadiazole thioether derivatives.. Pesticide biochemistry and physiology, 147, 11-19 . https://doi.org/10.1016/j.pestbp.2017.10.011.

14. Wang, P., Zhou, L., Zhou, J., Wu, Z., Xue, W., Song, B., & Yang, S. (2016). Synthesis and antibacterial activity of pyridinium-tailored 2,5-substituted-1,3,4-oxadiazole thioether/sulfoxide/sulfone derivatives.. Bioorganic and medicinal chemistry letters, 26 4, 1214-7 . https://doi.org/10.1016/j.bmcl.2016.01.029.
15. Mohamed, H., Ammar, Y., Elhagali, G., Eyada, H., Aboul-Magd, D., & Ragab, A. (2022). In Vitro Antimicrobial Evaluation, Single-Point Resistance Study, and Radiosterilization of Novel Pyrazole Incorporating Thiazol-4-one/Thiophene Derivatives as Dual DNA Gyrase and DHFR Inhibitors against MDR Pathogens. ACS Omega, 7, 4970 - 4990. https://doi.org/10.1021/acsomega.1c05801.
16. Cui, P., Li, X., Zhu, M., Wang, B., Liu, J., & Chen, H. (2017). Design, synthesis and antimicrobial activities of thiouracil derivatives containing triazolo-thiadiazole as SecA inhibitors.. European journal of medicinal chemistry, 127, 159-165 . https://doi.org/10.1016/j.ejmech.2016.12.053.
17. Li, Y., Sun, N., Ser, H., Long, W., Li, Y., Chen, C., Zheng, B., Huang, X., Liu, Z., & Lu, Y. (2020). Antibacterial activity evaluation and mode of action study of novel thiazole-quinolinium derivatives. RSC Advances, 10, 15000 - 15014. https://doi.org/10.1039/d0ra00691b.
18. Ghasemi, B., Beyzaei, H., & Majidiani, H. (2016). A Comparative Study on the Antibacterial Effects of Some Newly Synthesized Thiazole, Imidazolidine and Tetrahydropyrimidine Derivatives against Bacillus cereus and Salmonella typhimurium. Pharmaceutical sciences, 22, 142-142. https://doi.org/10.15171/PS.2016.10.
19. Ghasemi, B., Beyzaei, H., & Majidiani, H. (2016). A Comparative Study on the Antibacterial Effects of Some Newly Synthesized Thiazole, Imidazolidine and Tetrahydropyrimidine Derivatives against Bacillus cereus and Salmonella typhimurium. Pharmaceutical sciences, 22, 142-142. https://doi.org/10.15171/PS.2016.10.
20. Bahram L., Negar M., Ali A., Alireza F., Synthesis and In Vitro antibacterial activity of new 2-(1-methyl-4-nitro-1Himidazol- 5-ylsulfonyl)-1,3,4-thiadiazoles, E-Journal of Chemistry 2011; 8: 1120- 1123.
21. Salimon J., Salih N., Hameed A., Ibraheem H., Yousif E., Synthesis and antibacterial activity of some new 1,3,4- oxadiazole and 1,3,4-thiadiazole derivatives, Journal of Applied Sciences Research 2010; 6(7): 866-870.
22. Parmar K., Prajapati S., Patel R., Joshi, S. Patel P., Efficient synthesis and biological evaluation of 3-(phenyl)-6-(4-amino phenyl)[1,2,4]triazolo[3,4- b][1,3,4]thiadiazole and their schiff base derivatives, Inter. J. Chem. Tech. Res. 2011; 3(2): 761-765.
23. Dabholkar V.V., Ansari F.Y., Synthesis and biological studies of bis (thiadiazole/triazole) by sonication. Acta. Pol. Pharma. Drug Res.2008; 65: 521-526.
24. Cherkupally S.R., Chandrashekar R., Dasari C.R., Vookanti Y., Adki N., Synthesis and antimicrobial study of bis- [thiadiazol-2-yltetrahydro-2Hpyrazolo[3,4 d][1,3]thiazole]methanes, Org. Commun. 2010; 3: 57-69.
25. Palekar V.S., Damle A.J., Shukla S.R., Synthesis and antibacterial activity of some novel bis- 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles and bis-4-thiazolidinone derivatives from terephthalic dihydrazide, Eur. J. Med. Chem. 2009; 44: 5112-5116.
26. Tehranchian S., Akbarzadeh T., Fazeli M.R., Jamalifar H., Shafiee A., Synthesis and antibacterial activity of 1-[1,2,4- triazol-3-yl] and 1-[1,3,4-thiadiazol-2-yl]- 3-methylthio-6,7- dihydrobenzo[c]thiophen-4(5H)ones Bioorg. Med. Chem. Lett. 2005; 15: 1023- 1025.
27. Liu X.H., Shi Y.X., Ma Y., Zhang C.Y., Dong W.L., Synthesis, antifungal activities and 3D-QSAR study of N-(5-substituted-1,3,4-thiadiazol-2- yl)cyclopropanecarboxamides, Eur. J. Med. Chem. 2009; 44: 2782-2786.
28. Kumar G.V.S., Rajendraprasad Y., Mallikarjuna B.P., Chandrashekar S.M., Kistayya C., Synthesis of some novel 2- substituted-5-[isopropylthiazole] clubbed 1,2,4-triazole and 1,3,4-oxadiazoles as potential antimicrobial and antitubercular agents, Eur. J. Med. Chem., 2010; 45: 2063-2074.
29. Chen H.S., Li Z.M., Feng Y.F.Y., Wang Z.W., New fungicidally active pyrazolylsubstituted 1,3,4-thiadiazole compounds and their preparation, Chinese Chemical Letters 1999; 10(5): 365-366.
30. Kadi A.A., El-Brollosy N.R., Al-Deeb O.A., Habib E.E., Ibrahim T.M., El-Emam A.A., Synthesis, antimicrobial, and anti-inflammatory activities of novel 2-(1- adamantyl)-5-substituted-1,3,4-oxadiazoles and 2-(1-adamantylamino)-5- substituted-1,3,4-thiadiazoles, Eur. J. Med. Chem. 2007; 42(2): 235-242.
31. Sharba A.H.K., Al-Bayati R.H., Aouad M.M., Rezki N., Synthesis of oxadiazoles, thiadiazoles and triazoles derived from benzo[b]thiophene, Molecules 2005; 10: 1161-1168.
32. Camoutsis C., Geronikaki A., Ciric A., Sokovic M., Zoumpoulakis P., Zervou M., Sulfonamide-1,2,4-thiadiazole derivatives as antifungal and antibacterial agents: synthesis, biological evaluation, lipophilicity, and conformational studies, Chem. Pharm. Bull. 2010; 58: 160-167.
33. Matysiak J., Malinski Z., 2-(2,4- Dihydroxyphenyl)-1,3,4-thiadiazole analogues: antifungal activity in vitro against Candida species, Bioorg. Khim 2007; 33(6): 640-647.
34. Liu F., Luo X.Q., Song B.A., Bhadury P.S., Yang S., Jin L.H., Xue W., Hu D.Y., Synthesis and antifungal activity of novel sulfoxide derivatives containing trimethoxyphenyl substituted 1,3,4- thiadiazole and 1,3,4-oxadiazole moiety, Bioorg. Med. Chem., 2008; 16: 3632- 3640.

35. Hayat F., Salahuddin A., Zargan J., Azam A., Synthesis, characterization, antiamoebic activity and cytotoxicity of novel 2-(quinolin-8-yloxy) acetohydrazones and their cyclized products (1,2,3-thiadiazole and 1,2,3- selenadiazole derivatives). Eur. J. Med. Chem. 2010; 45: 6127-6134.
36. Jazayeri S., Moshafi M.H., Firoozpour L., Emami S., Rajabalian S., Haddad M., Pahlavanzadeh F., Esnaashari M., Shafiee A., Foroumadi A., Synthesis and antibacterial activity of nitroaryl thiadiazole-gatifloxacin hybrids, Eur. J. Med. Chem. 2009; 44: 1205-1209.
37. Thomasco L.M., Gadwood R.C., Weaver E.A., Ochoada J.M., Ford C.W., Zurenko G.E., Hamel J.C., Stapert D., Moerman J.K., Schaadt R.D., Yagi B.H., The synthesis and antibacterial activity of 1,3,4-thiadiazole phenyl oxazolidinone analogues, Bioorg. Med. Chem. Lett. 2003; 13(23): 4193-4196.
38. Lamani R.S., Shetty N.S., Kamble R.R., Khazi I.A., Synthesis and antimicrobial studies of novel methylene bridged benzisoxazolyl imidazo[2,1- b][1,3,4]thiadiazole derivatives, Eur. J. Med. Chem. 2009; 44(7): 2828-2833.
39. Khalaj A., Nakhjiri M., Negahbani A.S., Samadizadeh M., Firoozpour L., Rajabalian S., Samadi N., Faramarzi M.A., Adibpour N., Shafiee A., Foroumadi A., Discovery of a novel nitroimidazolyl-oxazolidinone hybrid with potent anti Gram-positive activity: Synthesis and antibacterial evaluation, Eur. J. Med. Chem. 2011; 46(1): 65-70.
40. Prathap K.J., Himaja M., Mali S.V., Karigar A.A., Sikarwar M.S., Synthesis of new 3-aryl-1-(5-(pyridin-3-yl)-1,3,4- thiadiazol-2-yl)-1H-pyrazole-4- carbaldehydes as antitubercular agents, Drug Invention Today 2011; 3(3): 10-11.
41. Vasoya A.S.L., Paghdar D.J., Chovatia P.T., Joshi H.S., Synthesis of some new thiosemicarbazide and 1,3,4-thiadiazole heterocycles bearing benzo[b]thiophene nucleus as potent antitubercular and antimicrobial agents, Journal of Sciences, 2005; 16(1): 33-36.
42. Gadad A.K., Noolvi M.N., Karpoormath R.V., Synthesis and anti-tubercular activity of a series of 2-sulfonamido/trifluoromethyl-6-substituted imidazo[2,1-b]-1,3,4-thiadiazole derivatives, Bioorg. Med. Chem. 2004; 12: 5651-5659.
43. Kolavi G., Hegde V., Khazi I., Gadad P., Synthesis and evaluation of antitubercular activity of imidazo[2,1- b][1,3,4]thiadiazole derivatives, Bioorg. Med. Chem. 2006; 14(9): 3069-3080.
44. Foroumadi A., Asadipour A., Mirzaei M., Karimi J., Emami S., Synthesis, evaluation of in vitro antituberculosis activity and cytotoxicity of some 2-(5- nitro-2-furyl)-1,3,4-thiadiazole derivatives, Farmaco. 2002; 57(9): 765- 769.
45. Talath S., Gadad A.K., Synthesis, antibacterial and antitubercular activitiesof some 7-[4-(5-amino-[1,3,4]thiadiazole- 2-sulfonyl)-piperazin-1-yl] fluoroquinolonic derivatives, Eur. J. Med. Chem. 2006; 41(8): 918-924.
46. Oruc E.E., Rollas S., Kandemirli F., Shvets N., Dimoglo A.S., Synthesis, structure elucidation, and structureantituberculosis activity relationship investigation, J. Med. Chem. 2004; 47(27): 6760-6767.
47. Foroumadi A., Mirzaei M., Shafiee A., Antituberculosis agents II: Evaluation of in vitro antituberculosis activity and cytotoxicity of some 2-(1-methyl-5-nitro- 2-imidazolyl)-1,3,4-thiadiazole derivatives, Farmaco. 2001; 56(8): 621- 623.
48. Aly A.A., EL-Sayed R., Synthesis and biological activity of new 1,3,4- thiadiazole derivatives, Chem. Pap. 2006; 60; 56-60.
49. Dabholkar V.V., Parmar B.M., Synthesis and biological activities of 2-(furoyl amino)-5-(substituted aryl)-1,3,4- thiadiazole and 2-(substituted benzoyl amino)-5-(furyl)-1,3,4 thiadiazole, Hetero. Lett. Org. 2011; 1: 136-145.
50. Asif M., Asthana C., 2,4-Substituted diphenyl-5-imino-2-1,3,4-thiadiazole derivatives: synthesis and evaluation of antimicrobial properties, Acta. Pharmaceutica. Sciencia. 2010; 52: 442- 450.
51. Vosooghi M., Akbarzadeh T., Fallah A., Fazeli M.R., Jamalifar H., Shafiee A., Synthesis of substituted 1,3,4-oxadiazole, 1,3,4-thiadiazole and 1,2,4-triazole derivatives as potential antimicrobial agents, Journal of Sciences 2005; 16: 145- 151.
52. Vedavathi M., Somashekar B., Sreenivasa G.M., Jayachandran E., Synthesis, characterization and anti-microbial activity of Fluorobenzothiazole incorporated with 1,3,4-thiadiazole, J. Pharm. Sci. & Res. 2010; 2(1): 53-63.
53. Mathew B., Jerad S.A., Mathew G.E., Shankar S., Shayam S., Kumar S.S., Synthesis, characterisation, and antimicrobial screeninig of some 2-amino,5- (phenyl substituted)1,3,4-thiadiazole derivatives, Inter. J. Chem. Tech. Res. 2011; 3: 364-368.