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AN OVERVIEW OF BIOLOGICAL ACTIVITIES OF THIADIAZOLE DERIVATIVES

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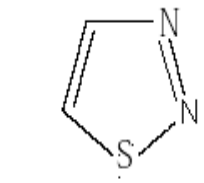
ABSTRACT

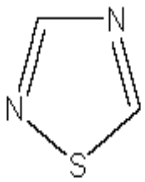
The chemistry of heterocyclic compounds has been an interesting field of study for a long time. Several five membered heterocyclic compounds having three hetero atoms such as thiadiazoles, oxadiazoles etc have been studied extensively owing to their interesting pharmacological activities. The synthesis of novel thiadiazole derivatives and investigation of their chemical and biological behaviour have gained more importance in recent decades Various substituted thiadiazole compounds are associated with diverse pharmacological activities such as anti-microbial, anti-inflammatory, anti-tubercular, anti-fungal, anti-malarial, anti-diabetic, diuretics, anti-depressant, anticonvulsant, antioxidant, anti-leishmanial, antidiabetic, antiviral activities. The present review highlights the recently synthesized thiadiazole derivatives possessing important biological activities.

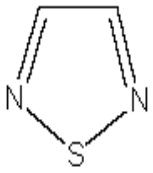
KEYWORDS: 1, 3, 4-Thiadiazole, antimicrobial, anti-tubercular, antifungal, anti-inflammatory and anticancer activities.

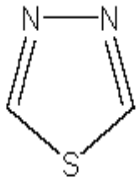
INTRODUCTION

The drugs containing thiadiazole moiety are the effective chemotherapeutic agents that are designed to inhibit/kill the infecting organisms and have minimal effect on the host. Thiadiazole is a 5-membered heterocyclic ring system containing two nitrogen and one sulphur atom. They occur in nature in four isomeric forms viz. 1,2,3-thiadiazole; 1,2,4-thiadiazole; 1,2,5-thiadiazole and 1,3,4-thiadiazole.


1,2,3 thiadiazole


1,2, 4 thiadiazole


1,2, 5 thiadiazole


1,3, 4 thiadiazole

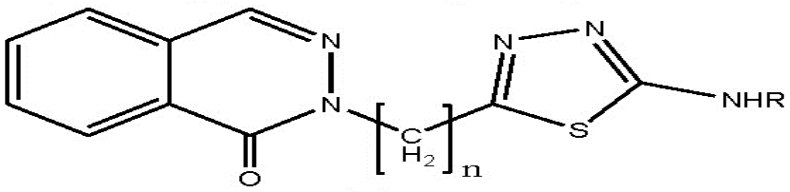
A review of literature shows that more work has been carried out on the 1,3,4-thiadiazole than all other isomers combined.. 1,3,4-Thiadiazole was first described in 1882 by Fischer and further developed by Busch and his coworkers .The advent of sulfur drugs and the later discovery of mesoionic compounds greatly accelerated the rate of progress in this field. [Stellings et. al, 1986] The literature review showed that the thiadiazole nuclei have various pharmacological activites .

1,3,4-Thiadiazole and its derivatives continue to be of a great interest to a large number of researchers owing to their great pharmaceutical and industrial importance. The specific pharmacological activities include antitubercular [1], anti-inflammatory [2], antibacterial [3] antifungiastic [4], anticonvulsant [5] , antioxidant activity [6] antitumoural [7], antileishmanial[8] antidepressant[9], and carbonic anhydrase inhibitor. [10] Thiadiazole moiety participates in binding either through hydrogen binding or by the donation of two electrons. Various substitutions are carried out at the thiadiazole ring in order to obtain the compounds with better pharmacological action and low toxicity. Compounds containing thiadiazole moiety are one of the most important category of drug that are prescribed in the treatment of very simple infection to the serious life threatening disease like cancer. Few examples of the drugs that contain thiadiazole moiety as a basic ring include, the thiadiazole SCH-202676 which was identified in 2001 as a promising allosteric modulator of G protein coupled receptors [11] and in 1998 KC 12291 showed the first evidence of its cardioprotective action. [12,13] More recently in 2002, the small heterocyclic thiadiazolidinones (TDZD) were described as the First non-ATP competitive GSK-3beta Inhibitors. [14] as potential drugs for the treatment of Alzheimer's disease.

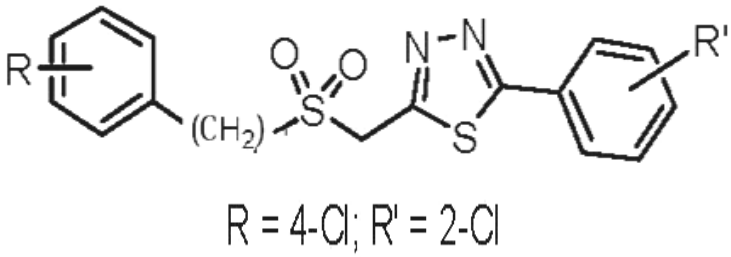
BIOLOGICAL ACTIVITY

Antimicrobial Activity: Onkol T and Co-workers [15] synthesized a new series of 2-[[1(2H)- phthalazinone-2-yl]methyl/ethyl]-5-arylamino-1,3,4- thiadiazole derivatives evaluated them in vitro for antimicrobial activity against bacterial and fungal species. The results showed that the tested compounds possessed weak antibacterial and antifungal activity

compared with standard drugs chloramphenicol and rifampicin for antibacterial and ketoconazole for antifungal activity.

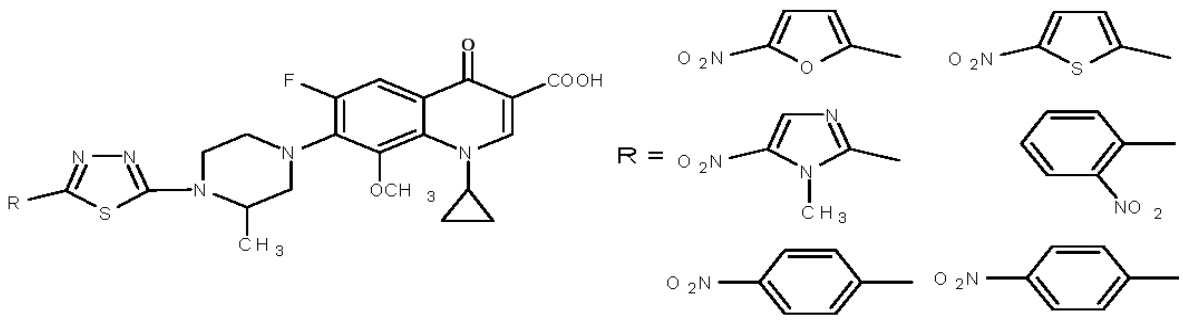


Padmavathi V and Co-workers[16] synthesized a few 2-(aryl-methanesulfonylmethyl)-5-aryl-1,3,4-thiadiazoles and tested for in vitro antimicrobial activity against Gram positive bacteria S. aureus, B. subtilis; Gram negative bacteria Klebsiella pneumoniae, Proteus vulgaris and Fungi Fusarium solania, Aspergillus niger, etc. and found them to be active with compound (a) having maximum activity. The presence of benzylsulfonyl group and chloro substituent enhances the activity of the compound.

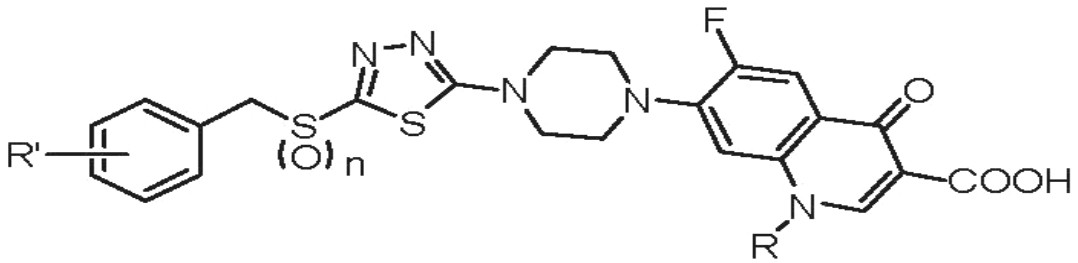


Compound (a)

Foroumadi A and Co-workers[17] synthesized a series of gatifloxacin analogues containing a nitroaryl-1,3,4-thiadiazole moiety attached to the piperazine ring at C-7 position and tested for in vitro antimicrobial activity against Gram positive and Gram negative bacteria. Among the synthesized compounds, nitrofuran analog exhibited more potent inhibitory activity against Gram-positive bacteria including Staphylococcus epidermidis, Bacillus subtilis, Enterococcus faecalis and Micrococcus luteus as compared to other synthesized compounds and reference drug gatifloxacin.

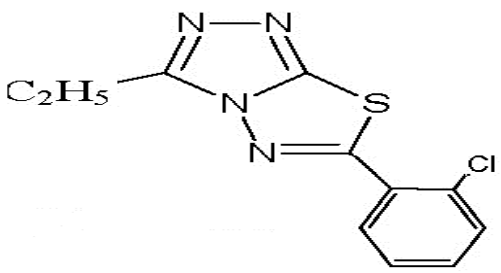


Foroumadi A and Co-workers [18] synthesized series of N-(5-benzylthio-1,3,4-thiadiazol-2-yl) and N-(5-benzylsulfonyl-1,3,4-thiadiazol- 2-yl) derivatives of piperazinyl quinolones and evaluated them for antibacterial activity against Gram positive and Gram negative microorganisms. Some of these derivatives exhibited high activity against Gram-positive bacteria S. aureus and S. epidermis, (MIC = 0.03-4 μg/mL) comparable or more potent than their parent _ piperazinyl quinolones norfloxacin and ciprofloxacin as reference drugs. The SAR indicates that both the structure of the benzyl unit and the S or SO_2 linker dramatically impact antibacterial activity.

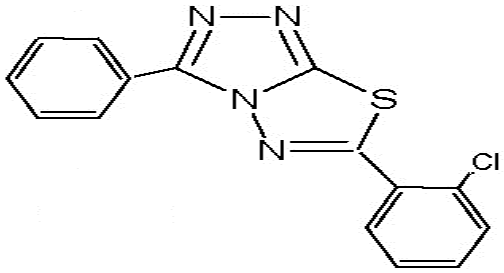


R = -C_2H_5, cyclopropyl; R' = H, NO_2; n = 0, 2

S. Nanjunda Swamy and Co-Workers[19] synthesized the two series of 4,6-disubstituted 1,2,4-triazolo-1,3,4-thiadiazole derivatives and checked for their efficacy as antimicrobials in-vitro against Bacillus subtilis, Escherichia coli, Pseudomonas fluorescens, Xanthomonas campestris pvs, Xanthomonas oryzae, Aspergillus niger, Aspergillus flavus, Fusariumoxysporum, Trichoderma sp. and Fusarium monaliforme. Compounds (b) and (c) and some other compounds showed significant inhibition against all the strains tested, when compared to standard drugs The compound-6-(2-chloro-phenyl)-3-ethyl-[1,2,4]triazole[3,4-b]thiadiazole **b** has been characterized by single crystal X-ray diffraction method.



Compound (b)



Compound (c)

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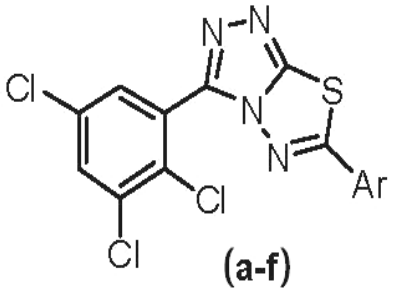
Karegoudar P and Co-workers[20] reported the successful synthesis and antimicrobial activity of new 1,2,4-triazolo thiadiazoles bearing 2,3,5-trichlorophenyl moiety. The antimicrobial activity study revealed that all the compounds (**a-f**) showed moderate to good

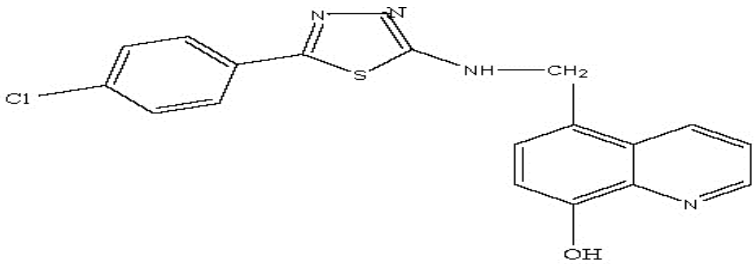
antibacterial and antifungal activities against pathogenic strains. SAR of title compounds showed that presence of 2,3,5-trichloro, -OCH3, 2,3-dichloro, 4-hydroxy- 3-amido, 4-chloro, -SCH3 groups attached to phenyl ring as well as pyridyl, and bromopyridyl groups attached to the thiadiazole ring of the title compounds are responsible for good antimicrobial activity.



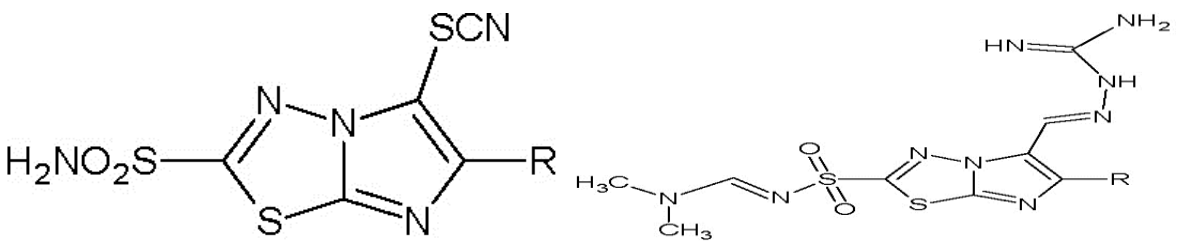
(a-f)

a = Ar = 4-$OCH_3C_6H_4$, **b** = Ar =3,5-$Cl_2C_6H_3$,
c = Ar = phenoxymethyl, **d** = Ar = 5-quinolyl,
e = Ar = pyridyl, **f** = Ar = 2-bromopyridyl

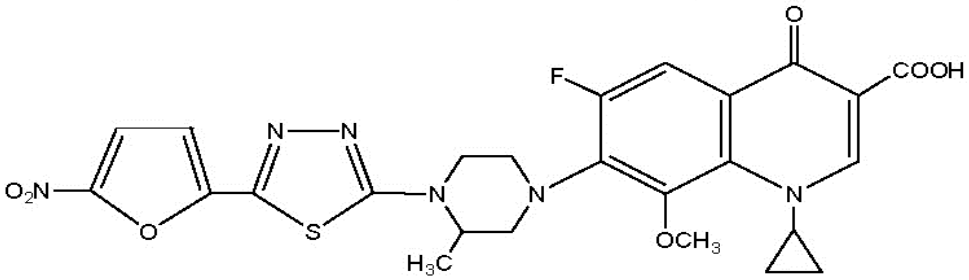
Divyesh K. Patel, and Co workers[21] have been Synthesise metal chelates of 5-[4 Chlorophenyl (1,3,4) thiadiazol-2-ylaminomethylene]-8-hydroxy quinoline , characterized and evaluated its anti-microbial activity .



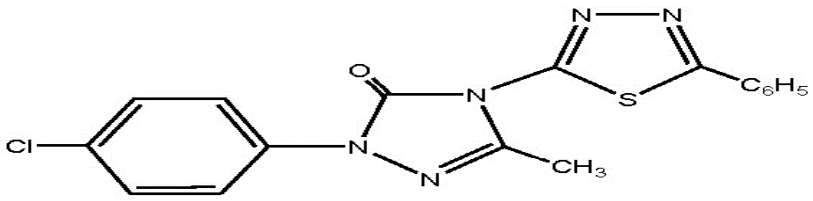
Andanappa K Gadad and Co-workers [22] synthesized a number of new 5-guanyl hydrazone/ thiocyanato-6-arylimidazo[2,1-b]-1,3,4-thiadiazole-2-sulfonamide derivatives derivatives were synthesized and evaluated for their antibacterial activity. Compounds showed a high degree of antibacterial activity against both Escherichia coli and Staphylococcus aureus comparable to that of sulfamethoxazole and Norfloxacin. However, they were found to show moderate activity against Salmonella typhi, Pseudomonas aeruginosa and Pneumococci.



Jazayeri S and Co-workers[23] synthesized studied antibacterial activity of number of gatifloxacin analogues containing a nitroaryl-1,3,4-thiadiazole moiety attached to the piperazine ring at C-7 position Among synthesized compounds, nitrofuran analog exhibited more potent inhibitory activity against gram-positive bacteria including Staphylococcus epidermidis (MIC=0.0078 microg/mL), Bacillus subtilis (MIC=0.0039 microg/mL), Enterococcus faecalis (MIC=0.125 microg/mL) and Micrococcus luteus (MIC=0.125 microg/mL), with respect to other synthesized compounds and reference drug gatifloxacin.

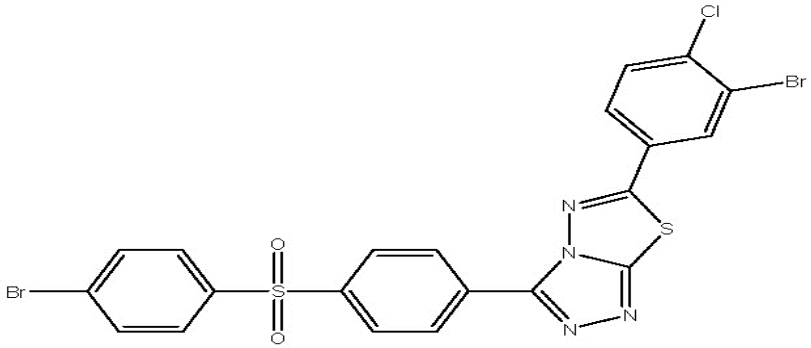


Bansode S and Co-workers[24] Synthesized novel 2-(3′-aryl-sydnon-4′-ylidene)-5′-substituted-[1,3,4]-thiadiazolylamines and [1,3,4]-thiadiazol-2′-yl-3-oxo-[1,2,4]-triazoles and evaluated for antimicrobial activity. Various combines biolabile molecules involving Schiff bases and 1,2,4-triazoles derivatized with the 1, 3, 4- thiadiazoles showed moderate to significant activity against bacteria at concentration of 100 µg/mL. Compounds with chloro group at the para-position of the aryl ring were shown to increase antibacterial activity (15.6 µg/mL) where the standard drug has shown MIC value at 12.5 µg/mL.

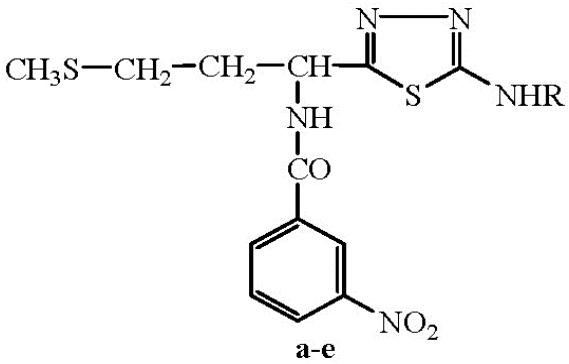


Almajan GL and Co-workers[25] synthesized some fused heterocyclic [1,2,4] triazolo[3,4-b][1,3,4]thiadiazole derivatives and evaluated them for their antimicrobial activities. The preliminary results revealed that some of the compounds exhibited promising antimicrobial activities against the Gram-positive bacteria (Staphylo-coccus aureus, Staphylococcus epidermidis,Enterococcus faecalis Bacillus cereus), Gram-negative bacteria (Escherichia coli; Enterobacter cloacae; Citrobacter freundii; Acinetobacter baumannii; Pseudomonas aeruginosa) and fungus Candida Albicans. It was found that the presence of one or more

halogen atom in the structure considerably increased the biological activity of the molecules. The best antibacterial effect was shown by 6-[(3-bromo-4-chloro)phenyl]-3-[4-(4 bromophenyl sulfonyl) phenyl]-[1,2,4]triazolo[3,4-b] [1,3,4] thiadiazole derivative .



Lenuta P and Co-workers[26] synthesized New 1,3,4-thiadiazole, a-e, possessing a D,L-methionine moiety by intramolecular cyclization of 1,4-disubstituted thiosemicarbazides in acidic media,. The potential antimicrobial effects of the synthesized compounds were investigated using the Staphylococcus aureus ATCC 25923, Bacillus antracis ATCC 8705, Bacillus cereus ATCC 10987, Sarcina lutea ATCC 9341 and Escherichia coli ATCC 25922 strains. The most active compounds was c containing a 4-methylphenyl susbtituent on the heterocyclic ring, which exhibited promising activities against Bacillus antracis and Bacillus cereus.

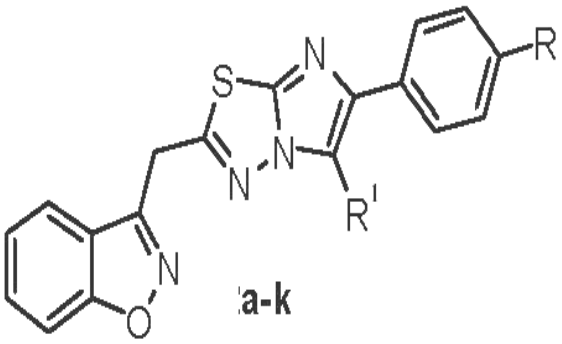


a-e

	R
a	—CH_3
b	—C_6H_5
c	—C_6H_4—CH_3 (4)
d	—C_6H_4—Br (4)
e	—CH_2—CH=CH_2

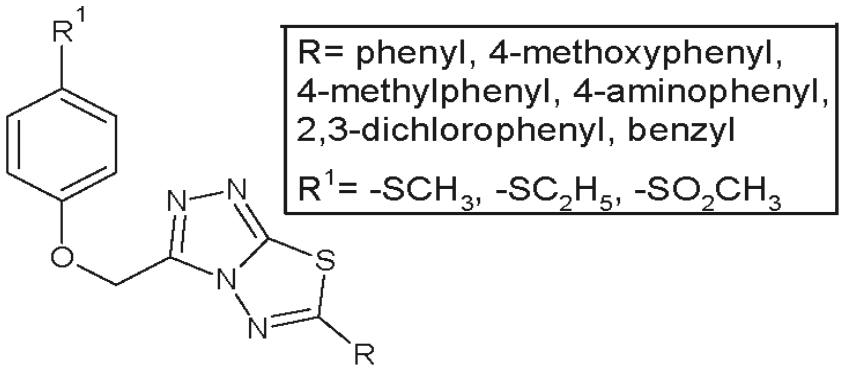
Lamani RS and Co-workers[27] synthesized novel methylene bridged benzisoxazolyl imidazo[2,1-b][1,3,4]thiadiazole derivatives and screened against two Gram-positive bacteria,Staphylococcus aureus-ATCC 25923, Bacillus subtilis-ATCC 6633 and Gram-negative bacteria Pseudomonas aeruginosa-TCC 10145, Escherichia coli-ATCC 35218 and compared against standard drug Ampicillin. Antifungal activity was screened against two fungal strain, Candida albicans and Aspergilus fumigatus using Clotrimazole as standard

drug. Some of the compounds displayed very good antibacterial (a-e) and antifungal activity (f-k).

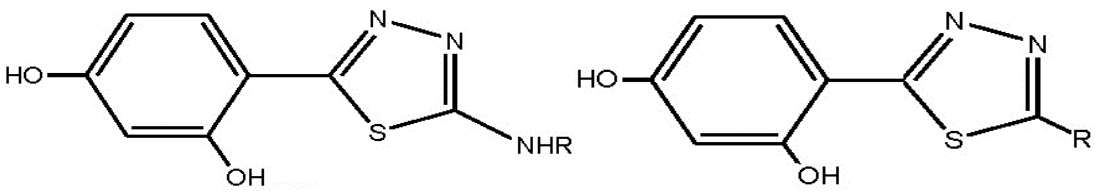


compd.	R	R'	compd.	R	R'
a	Cl	H	**g**	Br	H
b	Br	H	**h**	OMe	H
c	Cl	Br	**i**	3-coumarinyl	H
d	OMe	Br	**j**	OMe	SCN
e	Cl	SCN	**k**	3-coumarinyl	SCN
f	H	H			

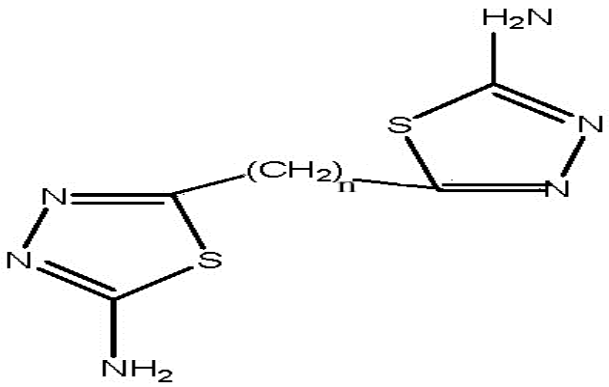
Karabasanagouda and Co-workers[28] synthesized some novel 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazoles and 1,2,4-triazolo[3,4-b]-1,3,4-thiadiazines carrying thioalkyl and sulphonyl phenoxy moieties and screened them for antimicrobial activity The antimicrobial activity study revealed that all the compounds tested showed moderate to good antibacterial and antifungal activities against pathogenic strains .



Matysiak J and Co-workers[29] synthesized a number of 5-substituted 2-(2,4-dihydroxyphenyl)-1,3,4- thiadiazole derivatives and evaluated them for antifungal activity against several clinical isolates of Candida albicans and non-albicans Candida spp. The compounds with methyl, phenyl, 4- ethoxyphenyl, and halogenophenyl groups at C-2 of thiadiazole ring showed higher antifungal activity. Amino-1,3,4-thiadiazole derivatives exhibited higher (than other analogues) antifungal effects against Candida no-albicans spp. than against C. albicans.

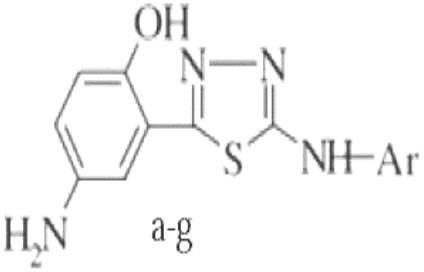


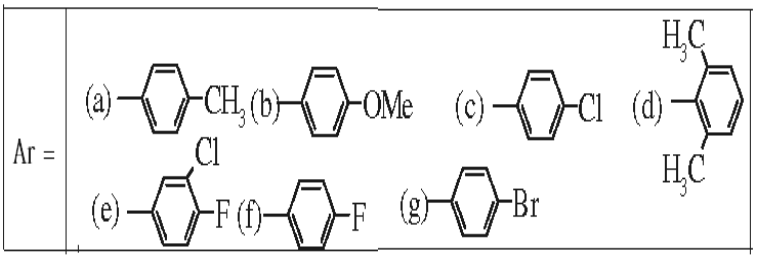
Barve A and Co-workers[30] synthesized a series of 1, 3, 4-Thiadiazol-2-Amine by using various dicarboxylic acids. The structures of these compounds were confirmed by IR, NMR spectroscopy and Mass spectrometry. The synthesized compounds were evaluated for in vitro antibacterial and antifungal activity against various Gram-positive bacterial strains: Bacillus Subtillis; Staphylococcus aureus, and Gram-negative bacterial strains: Escherichia coli; Pseudomonas aeruginosa and Fungal strains Saccharomyces cerevisiae; Aspergillus niger, Candida albicans. The results showed that compounds (a), (e), (f) and (h) exhibited comparable antibacterial and antifungal activity.



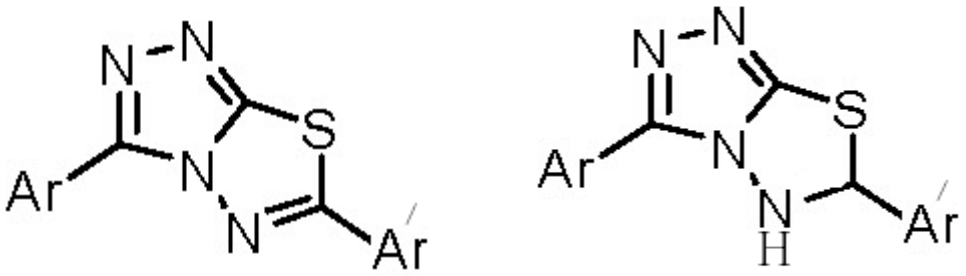
a	n = 1
b	n = 2
c	n = 3
d	n = 4
e	n = 5
f	n = 6
g	n = 7
h	n = 8

Hussain S and Co-workers[31] synthesized various 4-amino-2-{5-[(4-substituted phenyl) amino]-1, 3, 4- thiadiazole-2-yl} phenol a-g were synthesized and evaluated for their antibacterial and antifungal activity.The Compounds c, e & f were found to possess very good antibacterial activity against S. aureus (gram-positive) and E.coli (gram-negative) bacteria and antifungal activity against A. niger (MIC value 25µg/ml).

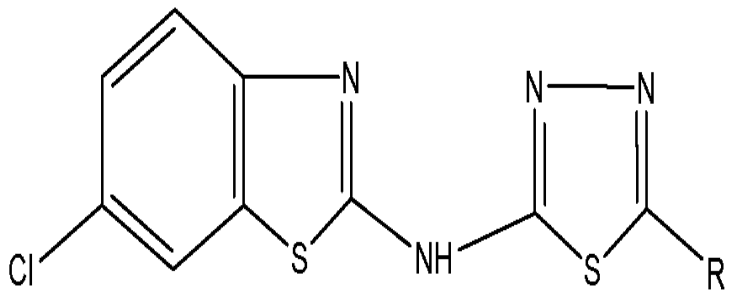




Methew V and Co-workers[32] synthesized several 3,6-disubstituted-1, 2,4-triazole [3,4-b]-1,3,4-thiadiazoles and their dihydro analogues.The synthesized compounds were studied for their antibacterial, antifungal, anti-inflammatory and analgesic activities. Some of the tested compounds showed significant pharmacological activity .It was observed that maximum antimicrobial activity was shown in the tested compounds having 2-flouro pyridine group at sixth position of the triazolothiadiazole system.

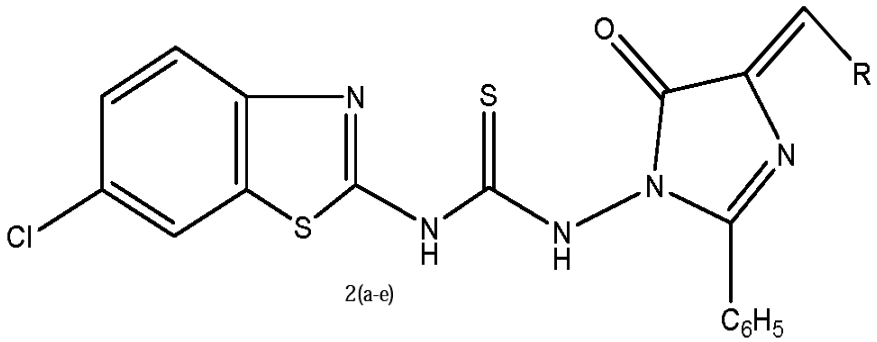


Amir M, and Co-workers[33] reported the synthesis and anti-microbial activity of new 2-aryl-5-(6/-chloro-1/,3/-benzothiazole-2yl-amino)-1,3,4-thiadiazoles (1a-j) and 4-(4/-arylidene)-2-phenyl-1-(6/-chloro-1/,3/-benzothiazol-2-yl-thiourido)-4,5- ihydroimidazolinones (2a-e). All the compounds showed significant antimicrobial activity.



1(a-j)

Ar=phenyl,4-Chiorophenyl,2,4-Dichlorophenyl, 4-Nitrophenyl, 2-Amir.opheny,2,4-Dichlorophenoxymethyl,2-Napthylmethyl,4-Methoxyphenyl,2-Acetoxyphenyl,3-Pyridyl.

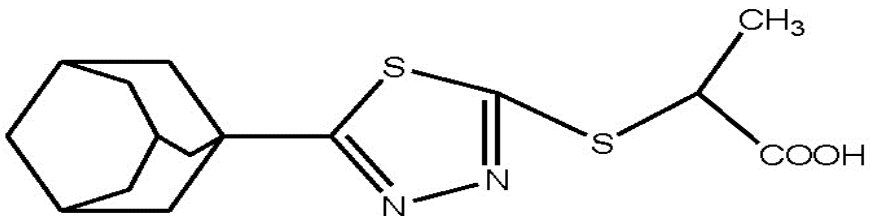


2(a-e)

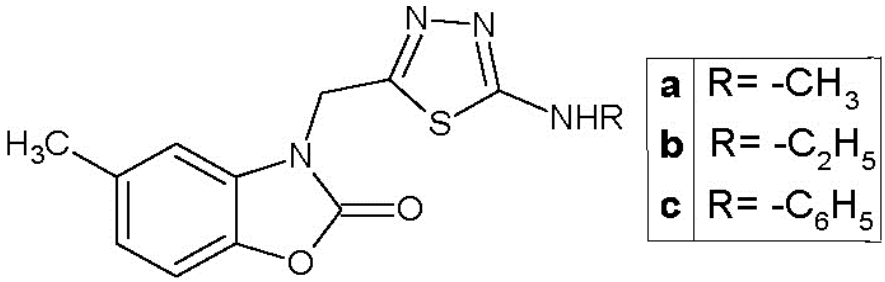
R= Phenyl,4-Chiorophenyl,4-Fluorophenyl, 4-N,N-dimethyl phenyl,3-Indolyl.

Anti-inflammatory Activity

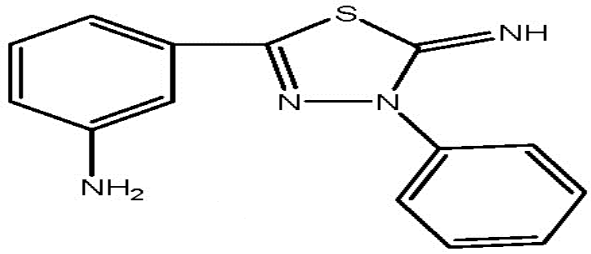
Kadi A.A. and Co-workers [34] synthesized and evaluated for anti-inflammatory and anti-microbial activity of new series of 5-(1-adamantyl)- 1,3,4-thiadiazole derivatives. The in vivo anti-inflammatory activity of the synthesized compounds was determined using the carrageenan-induced paw oedema method in rats. Interestingly, compound (±)-2-[5-(1-adamantyl)-2-thioxo-1,3,4-thiadiazolin-3-yl]propionic acid , showed almost equal anti-inflammatory activity at 20 mg/kg to that of Indomethacin (5 mg/kg). Replacement of 2-propionic acid with acetic and 3-propionic acid was slightly detrimental to the anti-inflammatory activity.



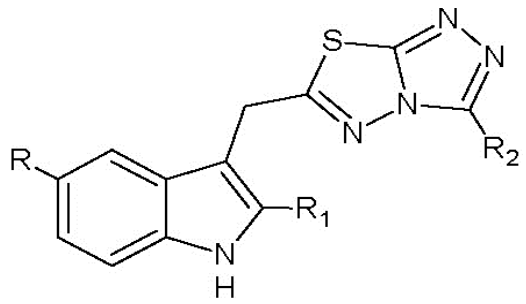
Goksen U.S. and Co-workers[35] synthesized and evaluated analgesic-anti-inflammatory and anti-microbial activity of 1,3,4-thiadiazoles bearing 5-methyl-2-benzoxazolinone moiety **(a-c)** Compound with phenyl substituent possessed the most prominent and consistent anti-inflammatory activity. An increase in the anti-inflammatory activity was observed with replacement of alkyl chain with phenyl ring.



Mohammad A. and Co-worker[36] synthesized 2, 4- Disubstituted-5-Imino-1, 3, 4-thiadiazole derivatives and evaluated their Anti-inflammatory activities. The acute anti-inflammatory activity of the synthesized compounds was screened using the carrageenan induced paw oedema method in rats. Diclofenac sodium was used as a reference drug. In the prepared thiadiazole series it But the compound, 2-p-aminophenyl-4-phenyl-5-imino-Δ^2-1, 3, 4-thiadiazole exhibited highest anti-inflammatory activity ($P < 0.0001$) with a percentage inhibition of 35.5.

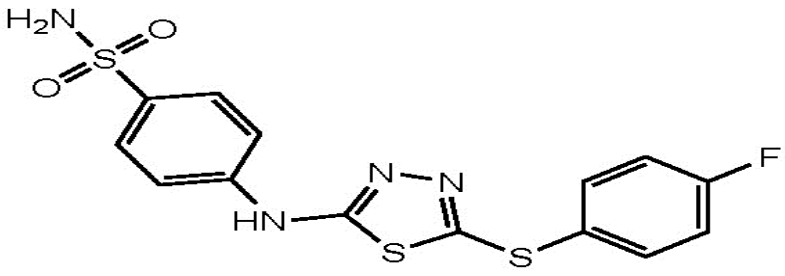


Mathew V and Co-workers[37] synthesized several 3,6-disubstituted1,2,4-triazolo [3,4b]1,3,4 thiadiazole and their dihydro analogues and evaluated their activity against the pathogenic strains. Results revealed that maximum anti-inflammatory activity was shown in the tested compounds having indole ring at the sixth position of the triazolothiadiazole system.



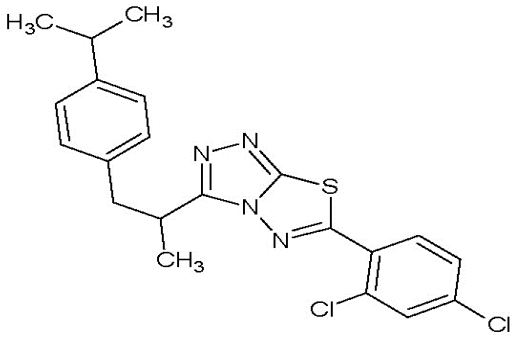
R= -H, -OCH_3; R_1= -H, -CH_3
R_2= 5-methoxy-3-indolylmethyl,
5-methoxy-2-methyl-3-indolylmethyl,
3-indolylmethyl

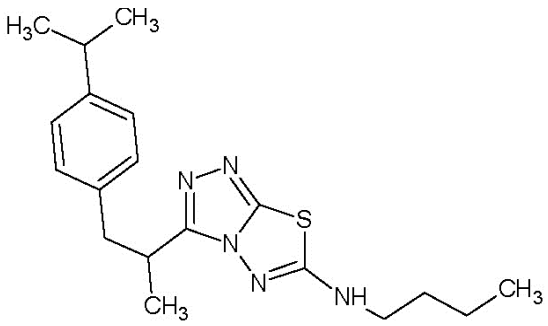
Sainy J and Co-workers [38] prepared several 2-amino-5-sulfanyl-1,3,4-thiadiazoles and concluded that the compounds were associated with lesser degree of anti-inflammatory activity when compared to indomethacin. Only compound 4-[5-(4-Fluorophenylsulfanyl) -[1,3,4]thiadiazol-2-ylamino] benzenesulfonamide showed 65.90% inhibition of paw edema after 3 h at 56 mg/kg (body weight) dose and 66.40% protection in acetic acid induced inflammation in mice.



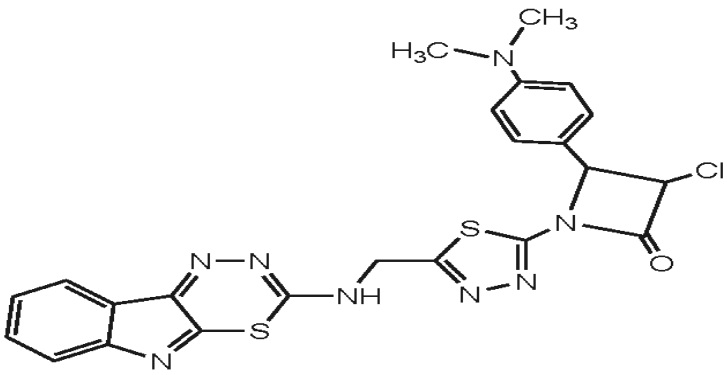
Amir M and Co-workers[39] synthesized and evaluated the anti-inflammatory activity of 1,2,4-triazolo [3,4-b]-1,3,4-thiadiazole derivatives of ibuprofen and biphenyl-4-yloxy acetic acid . The compounds (**a &b**) having 2,4-dichlorophenyl and nbutyl amino groups, respectively, was found to be the highest, being slightly less than ibuprofen, but equivalent to

flurbiprofen. In general the presence of 2,4-dichlorophenyl, 4- chloroprene, n-butyl amino and 4 aminophenyl groups at C-6 of triazolo-thiadiazole ringresulted in high anti-inflammatory activity.

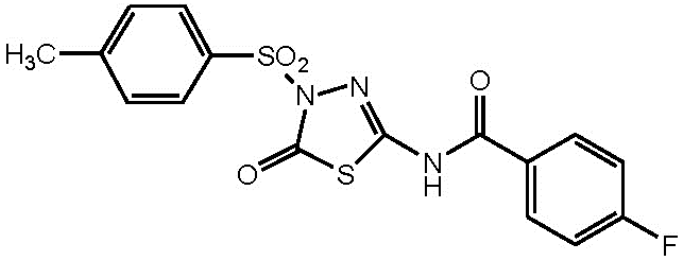




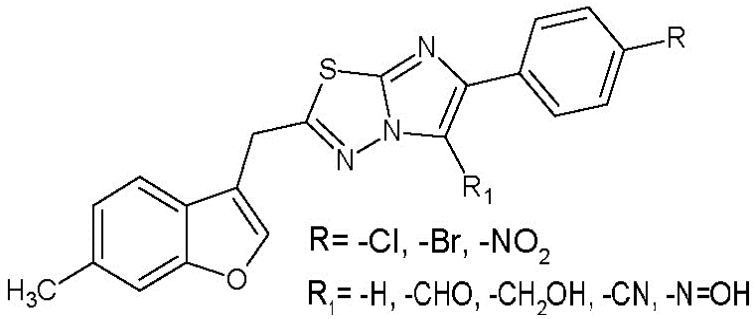
Bhati SK and Co-workers[40] synthesized and evaluated the anti-inflammatory activity of 2-aryl-3-{5-[([1,3,4] thiadiazino[6,5-b]indol-3-ylamino) methyl]- 1,3,4- thiadiazol-2-yl} -1,3-thiazolidin-4-one/azetidin-2-one using carrageenan induced rat's paw edema method. Compound with 2-chlorophenyl group at C-4 of azetidin-2-one ring as substituent exhibited the most potent anti-inflammatory (41.23%) and analgesic activity (38%) at a dose of 50 mg/kg than that of their corresponding thiazolidinone compounds.



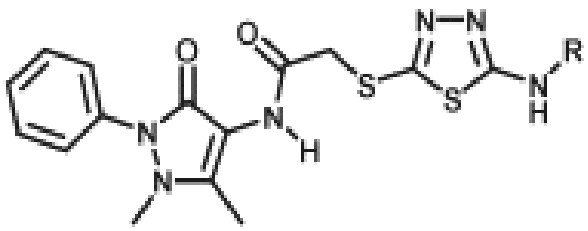
Schenone S and Co-workers[41] synthesized new 1,3,4-thiadiazole derivatives endowed with analgesic and anti-inflammatory activities. The presence of the tolyl substituent on the sulfonamide moiety on 4th position of 1,3,4-thiadiazole ring was found to be suitable for increasing the analgesic and anti-inflammatory activity. Compound with a p-fluoro phenyl substituent was the most active compound (51.4% of inhibition at 50 mg/kg) among the benzoyl sulfonamido derivatives .



Jadhav V. B. and Co-workers[42] synthesized a series of 6-substituted and 5,6-disubstituted 2-(6-methyl-benzofuran-3-ylmethyl)-imidazo[2,1-b][1,3,4]thiadiazoles and evaluated as anti-inflammatory agents. Qualitative SAR studies indicate that the chloro substitution in the imidazole ring and introduction of formyl group at C-5 position of the imidazole ring increased the anti-inflammatory and analgesic activity.

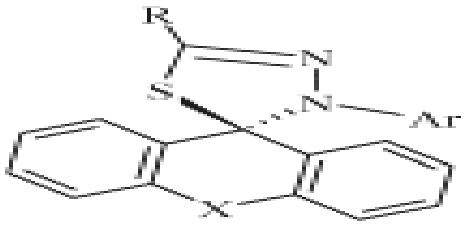


Rostom S.A.F., and Co-workers[43] synthesized 2,5-disubstituted-1,3,4-thiadiazole containing 5-methyl-2-benzoxazolinone derivatives and twelve out of the newly synthesized compounds were evaluated for their anti-inflammatory activity using two different screening protocols; namely, the formalin-induced paw edema and the turpentine oil-induced granuloma pouch bioassays, using diclofenac sodium as a reference standard. All the compounds exhibited anti-inflammatory activity (at the dose 50 mg/kg p.o.) of varying degree from 53.2% to 85.3% in inhibition of edema.



Hafez H.N. and Co-workers[44] performed a facile regioselective synthesis of novel spiro-thioxanthene and spiro-xanthene-9′,2-[1,3,4]thiadiazole derivatives and screened them for

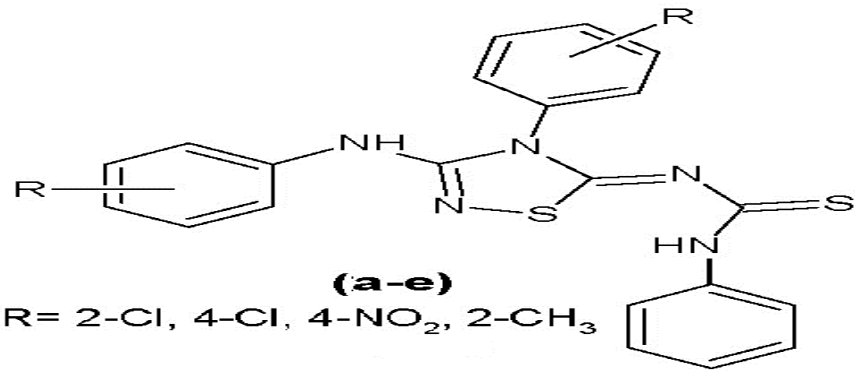
potential analgesic and anti-inflammatory agents. The 1,3-dipolar cycloaddition of nitrile imines to 9H-thioxanthone-9-thione and 9H-xanthone-9-thione afforded novel spiro-thioxanthene-9′,2-[1,3,4]thiadiazoles 1**a**–**g** and spiro-xanthene-9′,2-[1,3,4]thiadiazoles 2**a**–**g** in good yields. Some of the newly synthesized compounds were tested for anti-inflammatory and analgesic activities comparable to ibuprofen and showed significant activity compared to standard drug. The toxicity studies revealed that neither death nor other behavioral or toxicological changes were observed on rats up to a dose as high as 200 mg/kg.



1a–g , X = S
2a–g , X = O

Anticonvulsant Activity

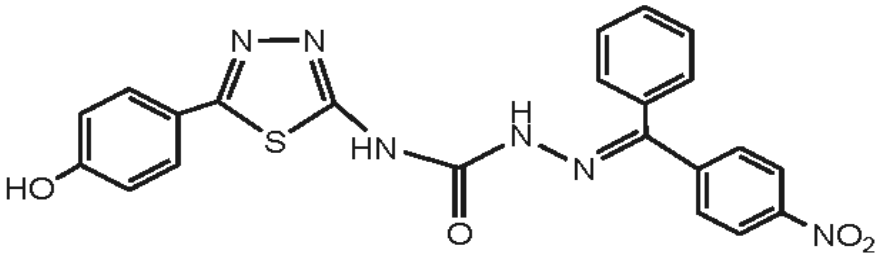
Siddiqui A and Co-workers[45] synthesized a series of 1,2,4-thiadiazoles (**a-e**) and evaluated for anticonvulsant activity . The compound with para-chloro substitution showed maximal activity in MES test and blocked strychnine seizures to some extent whereas other compounds of the series were less active.



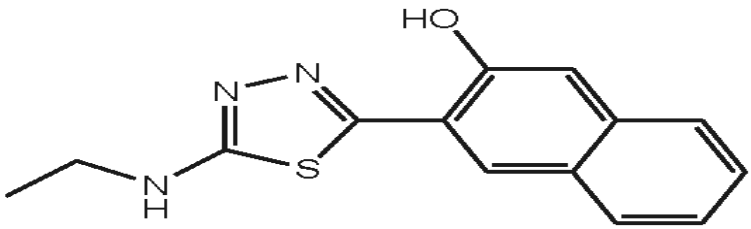
(a-e)
R= 2-Cl, 4-Cl, 4-NO_2, 2-CH_3

Rajak H and Co-workers[46] synthesized some 2,5-Disubstituted 1,3,4- Thiadiazoles and evaluated their potential anticonvulsant activity. The results showed that compound with 4-nitrophenyl-substituted semicarbazone were the most active compound comparable with carbamzepine. The SAR study suggested that [5-(4-substituted phenyl)- 1,3,4-thiadiazol-2-yl] moiety as hydrophobic portion, two-electron donor atom and another hydrophobic aryl ring

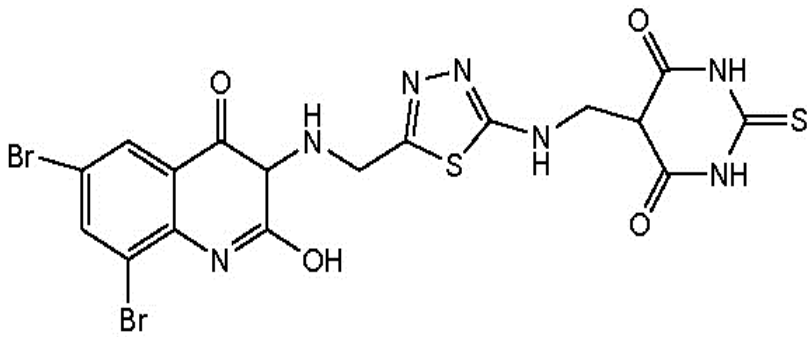
substituted with p-NO2 group responsible for metabolism, played a crucial role for its anticonvulsant activity.



Dogan H.N. and Co-workers[47] synthesized a series of 2-(N-alkyl/aryl-Nacetylamino)-5-(3-acetyloxy-2- naphthyl)-1,3,4-thiadiazole derivatives. Compound 2- ethylamino-5-(3-hydroxy-2-naphthyl)-1,3,4-thiadiazole showed degree of protection against PTZ-induced convulsions in mice ranging from 0 to 90%. Further, substitution of ethyl and acetylation of thiadiazoles resulted in loss of activity.

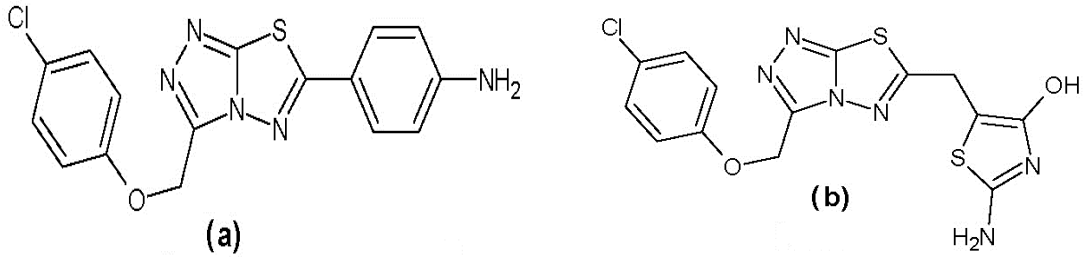


Srivastava VK and Co-workers[48] synthesized some newer derivatives of substituted quinazolinonyl-2-oxo/thiobarbituric acid as potent anticonvulsant agents. Compound 5-{2′-amino-5′-[3″-aminomethylene-2″-methyl- 6″,8″-dibromoquinazolin-4″ (3″H)-onyl]-1′,3′,4′-thiadiazol- 2′-yl}-2-thiobarbituric acid showed high percentage protection 90% (50 mg/kg ip) in both MES and PTZ models .

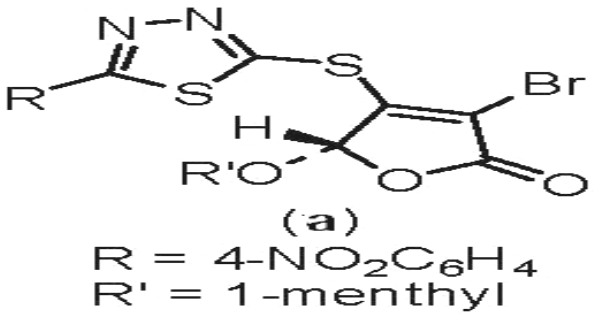


Anti-tumor / Anti-cancer Activity: Ibrahim, D.A. [49] synthesized a series of 3,6-disubstituted triazolo [3,4-b] thiadiazole derivatives. It was evaluated that compounds a and b

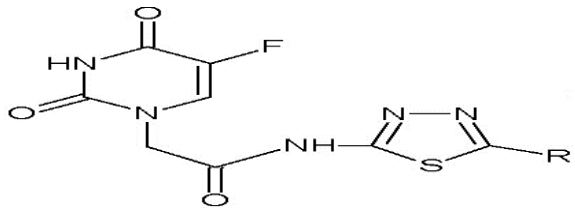
maintained the highest growth inhibition activity at micromolar concentrations in different human tumor cell lines. The compound **a** displayed high activity against NCI-H226 (log GI50 -5.14) cell line of non-small cell lung cancer subpanel and against CCRF-CEM (log GI50 -5.0) cell line of Leukaemia subpanel. Compound **b** exhibited the highest sensitivity against Renal, Colon and Melanoma Cancer cell lines, the best results being against Renal Cancer A498 cell line with log GI50 -7.27.



Wei M X and Co-workers[50] synthesized a new series of chiral 1,3,4-thiadiazole derivatives possessing g-substituted butenolide moiety and evaluated for in-vitro anticancer properties All the compounds showed good anticancer activities against Hella cell lines. Of all the studied compounds, compound (**a**) exhibited the best inhibitory activity with an IC50 of 0.9 mM. This might have relationship with the hydrophile ability of nitro group on the benzene ring. After being treated with 0.1 mg/mL compound **(a)** for 24 h, the growth inhibition rate of Hella cell lines was 59.2%.

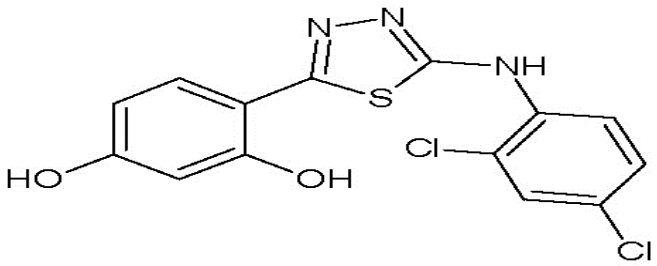


Zheng K B and Co-workers[51] synthesized and evaluated N1-acetylamino-(5-alkyl/aryl-1,3,4-thiadiazole-2-yl)-5-fluorouracil derivatives as novel class of potential anti-tumor agents against A-549 (human lung cancer cell) and Bcap-37 (human breast cancer cell) .While comparing activity with standard drug 5-fluorouracil; phenyl, 4-fluorophenyl, 4-methylphenyl, 3,5-dinitrophenyl substituted compounds showed higher activity against A-549 and 4-fluorophenyl, 4-methylphenyl, 3,5-dinitrophenyl substituted compounds showed higher activity against Bcap-37.

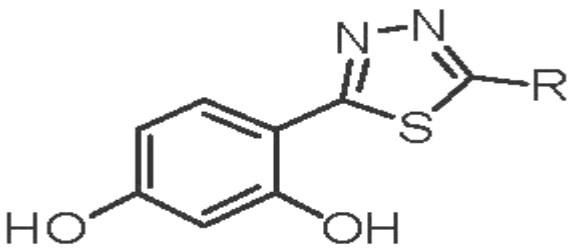


R= -CH_3, -C_2H_5, -C_3H_7, -$CH(CH_3)_2$, -C_6H_5, 4-ClC_6H_4, 4-FC_6H_4, 4-$CH_3C_6H_4$, 4-$OCH_3C_6H_4$, 3,5-$(NO_2)_2C_6H_3$

Matysiak J and Co-workers[52] synthesized a number of N-substituted 2-amino-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazoles and evaluated for their antiproliferative activity. The panel substitution included alkyl, aryl and morphinoalkyl derivatives. The cytotoxicity in-vitro against the four human cell lines: SW707 (rectal), HCV29T (bladder), A549 (lung) and T47D (breast) was determined. Alkyl and morphinoalkyl derivatives exhibited significantly lower effect than phenyl ones. The highest antiproliferative activity was found for 2-(2,4-dichlorophenylamino)-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole , with ID50 two times lower (SW707, T47D) than for cisplatin studied comparatively as the control compound.



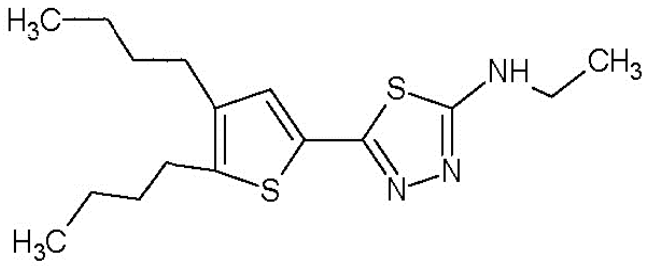
Matysiak J and Co-workers[53] synthesized a series of new 5-substituted 2-(2,4-dihydroxy phenyl)-1,3,4-thiadiazoles and evaluated for their antiproliferative activity The panel substitution included alkyl, alkoxy, aryl and heteroaryl derivatives. The highest antiproliferative activity was found with ID50 values comparable (HCV29T and SW707) or significantly lower (T47D) than for cisplatin. Compounds (**a**) and (**b**) proved to be most active. The presence of another atom of high electronegativity in the vicinity of C-5 ring probably causes formation of a strong electron gap at this atom of carbon which may be essential in ligand-receptor interactions.



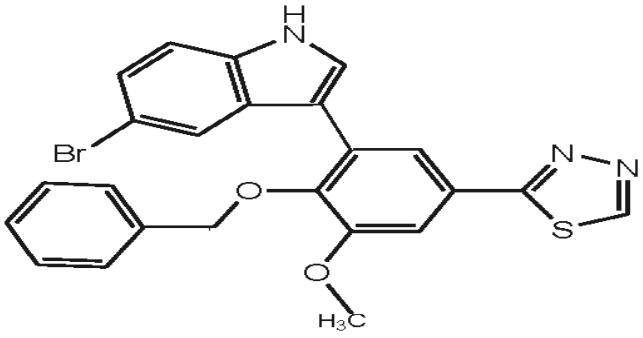
a = R = 4-$(CH_3)_3C$-C_6H_4

b = R = 4-OCH_3-C_6H_4-CH_2O

Mavrova A T and Co-workers[54] synthesized novel derivatives of 2,5-substituted-1,3,4-thiadiazoles and evaluated for their cytotoxicity. The biological study indicated that n-ethyl-5- (4,5,6,7-tetrahydro-1-benzothien-2-yl)-1,3,4-thiadiazole-2-amine possessed high cytotoxicity in-vitro against thymocytes. The corresponding IC50 being 5.2 x 10-6 □M. The derivatives containing ethyl-amino group at the second position of 1,3,4-thiadiazole cycle possessed good activity.

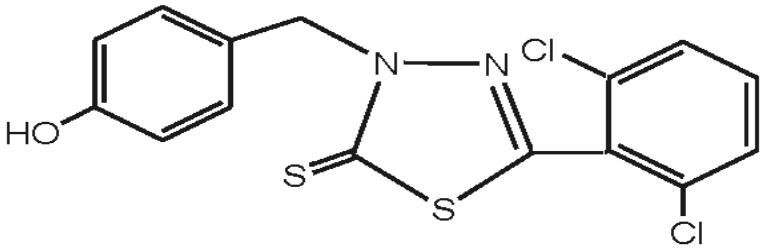


Kumar D and Co-workers[55] synthesized 5-(3-indolyl)-1,3,4-thiadiazoles and evaluated for anticancer activity. Primary screening was performed at a concentration ranging from 100 nM to 1 mM. Change in cell number and cell morphology in 96-well plates was observed at 24 and 48 h . Compounds that exhibited toxicity to cancer cell lines but not to normal cells were selected for the secondary confirmation assays. It was found that substitution on C-2 position of the 1,3,4-thiadiazole ring plays an important role in imparting the cytotoxic activity to the compound. Compound 2-(4-(Benzyloxy)-5-(5-bromo-3-indolyl)-3-methoxyphenyl)-1,3,4- was found to be the most potent compound of all.

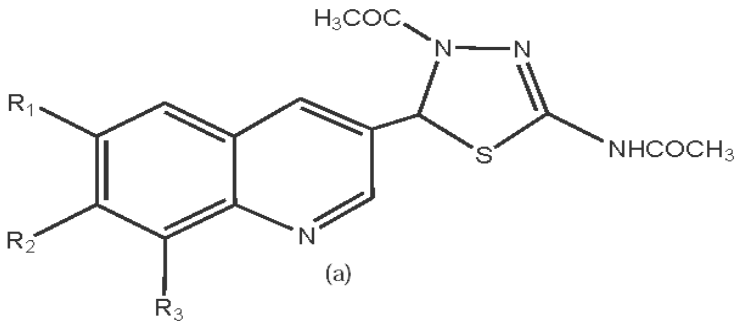


Bhole R. P. and Co-workers[56] Synthesized and evaluated antitumor activity of (4-hydroxyphenyl)[5-substituted alkyl/aryl)-2-thioxo-1,3,4-thiadiazol-3-yl]methanone and [(3,4-disubstituted)-1,3-thiazol-2ylidene]-4-hydroxybenzohydrazide. Compound (4-hydroxyphenyl)[5-(2,6-dichloro)-2-thioxo- 1,3,4-thiadiazol-3-yl]methanone showed broad spectrum of growth inhibition activity against human tumour cells and remarkable cytotoxic

activity on non small lung cancer (HOP 92) having log GI50 value at -6.49, colon cancer (HCC-2998) at GI50 value -5.31 and significant cytotoxic activity on prostate cancer (PC-3) having GI50 value -5.48. SAR study revealed that electron withdrawing group at position C-5 of thiadiazole was favorable for activity.

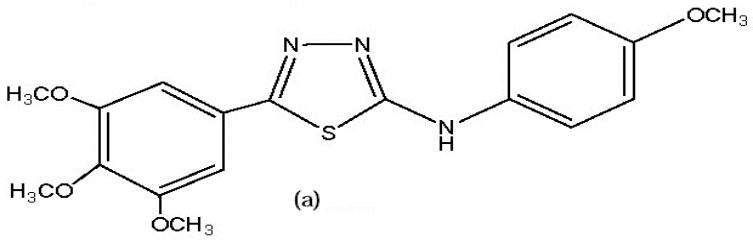


Marganakop S. B. and Co-workers[57] performed an efficient one-pot cyclization of quinoline thiosemicarbazones to quinolines derivatized with 1,3,4-thiadiazole as anticancer and anti-tubercular agents and investigated for their primary cytotoxic activity against cervical cancer cell line. Compounds **a** with methoxy at C- 6,7,8 of quinoline showed the potent anticancer activity and the cell lyses occurred only at 10 µg/mL.

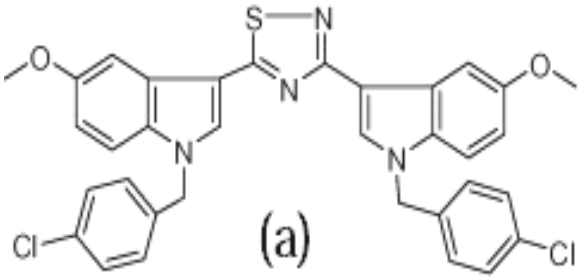


Kumar D and Co-workers synthesized[58] a series of 2-arylamino-5-aryl-1,3,4-thiadiazoles and screened for their anticancer activity against various human cancer cell lines. The novel one-pot synthesis of 1,3,4-thiadiazoles was achieved by refluxing aryl aldehydes, hydrazine hydrate, and aryl isothiocyanates in methanol followed by oxidative cyclization with ferric ammonium sulfate. Study of in vitro cytotoxic activity revealed a cytotoxic effect of individual compounds on cancer cells of prostate (PC3, DU145, and LnCaP), breast (MCF7 and MDA-MB-231), and pancrease (PaCa2). The SAR study showed that the 3,4,5-(OCH3)3C6H2 at C-5 position was responsible for binding to the Colchicine siteon tubulin and found to be favorable for activity. Further variation of C-2 arylamino group was associated with lesser degree of effect on the activity of 1,3,4-thiadiazoles. Most of the synthesized compounds were moderate in activity and compound (**a)** with

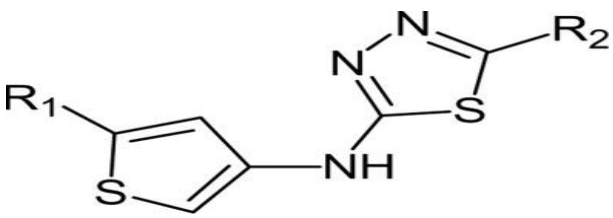
position trimethoxyphenyl at the C-5 displayed a greater potency toward pancreatic (PaCa2) cancer cell lines (IC50 = 4.3 lM).



Kumar D and Co-workers synthesized[59] a series of 3,5-bis(indolyl)-1,2,4-thiadiazoles and evaluated for their cytotoxicity against selected human cancer cell lines. The reaction of indole-3-thiocarboxamide with iodobenzene diacetate underwent oxidative dimerization to give 3,5-bis(indolyl)-1,2,4-thiadiazoles . Among the synthesized bis(indoly)-1,2,4-thiadiazoles, the compound **(a)** with 4-chlorobenzyl and methoxy substituents showed the most potent activity. (IC_{50}=14.6 μM) .

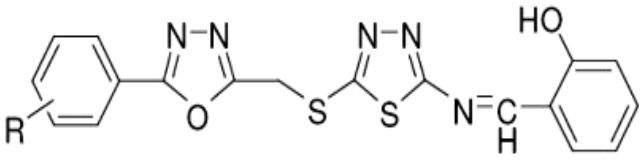


Revelant G and Co-workers[60] synthesized a series of 5-aryl-2-(3-thienylamino)-1,3,4-thiadiazoles in good yields in two steps starting from thiophen-3-isothiocyanates. Those compounds as well as the thiosemicarbazide intermediates were screened for their antiproliferative activity against a panel of six cancer cell lines. Among them, two 5-aryl-2-(3-thienylamino)-1,3,4-thiadiazoles have shown very interesting results with IC_{50}<10 μM on three cell line.



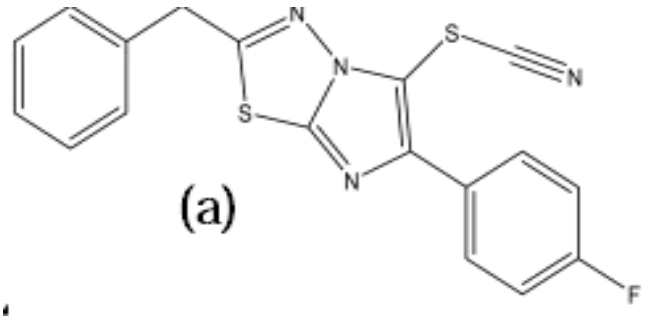
Zhang K and Co-workers[61] synthesized a series of novel hybrid molecules containing 1,3,4-oxadiazole and 1,3,4-thiadiazole bearing Schiff base moiety and evaluated for their in

vitro antitumor activities against SMMC-7721, MCF-7 and A549 human tumor cell lines by CCK-8 assay. The bioassay results demonstrated that most of the tested compounds showed potent antitumor activities, and some compounds exhibited stronger effects than positive control 5-fluorouracil (5-FU) against various cell lines. The pharmacological results suggest that the substituents of phenyl ring on the 1,3,4-oxadiazole are vital for modulating antiproliferative activities against various tumor cell lines.



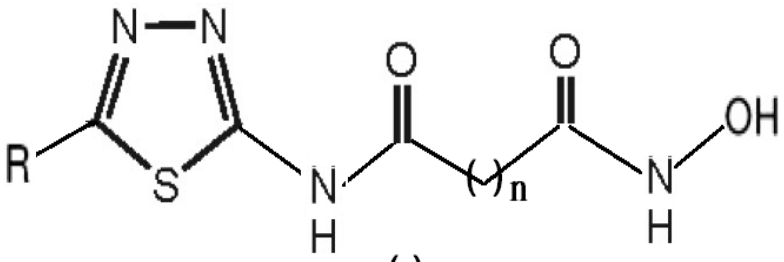
R= H, 4-F, 2-Cl, 4-Cl, 2-Br, 4-Br, 2-CH_3, 3-CH_3, 4-CH_3, 3-OCH_3, 4-OCH_3, 3,4,5-Tri-OCH_3, 3-NO_2, 4-NO_2

Karki S.S. and Co-workers[62] synthesized and evaluated biological activity of novel analogues of levamisole on leukemia cells. The cytotoxicity was studied using trypan blue and MTT assays and found that **some** exhibited strong cytotoxicity. Among these (a) (IC_{50}, 8 μM) was chosen for understanding the mechanism of cytotoxicity. FACS analysis in conjunction with mitochondrial membrane potential and DNA fragmentation studies suggested that **a** induced apoptosis, but not cell cycle arrest.



(a)

Guan P and Co-workers[63] synthersized , a series of 1,3,4-thiadiazole based hydroxamic acids as potent HDAC inhibitors. Some of them showed good inhibitory activity in HDAC enzyme assay and potent growth inhibition in some tumor cell lines. Among them, compound **(a)** (IC_{50} = 0.089 μM), exhibited better inhibitory effect compared with SAHA (IC_{50} = 0.15 μM).

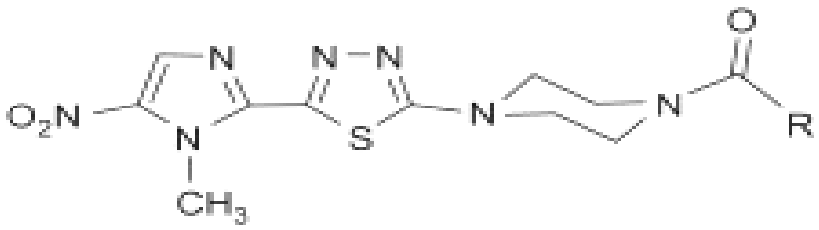


(a)

n = 0,2,3,4,5,6

Anti-leishmanial activity

Poorrajab F and Co-workers[64] synthesized a series of 1-[5-(1-methyl-5-nitro-1H-imidazol-2-yl)-1,3,4-thiadiazol-2-yl]-4-aroylpiperazines and evaluated in vitro against Leishmania major. Most of the target compounds exhibited good anti-leishmanial activity against the promastigote form of L. major at non-cytotoxic concentrations. The most active compound was 1-[(5-chloro-2-thienyl)carbonyl]-4-[5-(1-methyl-5-nitro-1H-imidazol-2-yl)-1,3,4-thiadiazol-2-yl]piperazine with an IC_{50} value of 9.35 ± 0.67 µM against L. major promastigotes. In addition, this compound was effective against intracellular L. major and significantly decreased the infectivity index.

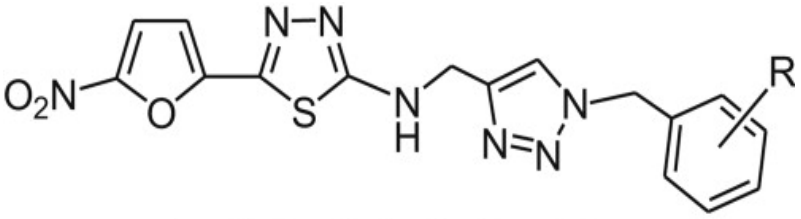


R = phenyl
R = 2-Cl-phenyl
R = 3-Cl-phenyl
R = 4-Cl-phenyl

R = thiophen-2-yl
R = 5-Cl-thiophen-2-yl
R = 5-Br-thiophen-2-yl

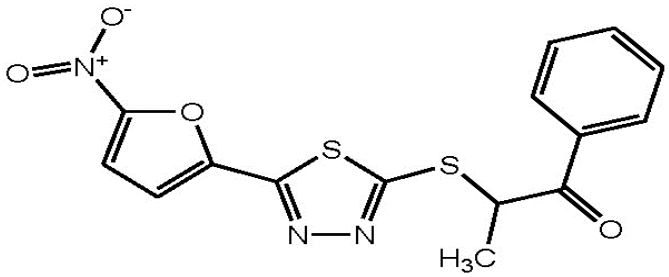
Tahghighi and Co-workers[65] synthesized a novel series of 5-(5-nitrofuran-2-yl)-1,3,4-thiadiazol-2-amines by introducing N-[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl] moiety as a new functionality on the C-2 amine of thiadiazole ring via click chemistry. The title compounds namely, N-[(1-benzyl-1H-1,2,3-triazol-4-yl)methyl]-5-(5-nitrofuran-2-yl)-1,3,4-thiadiazol-2-amines were characterized by IR, NMR and MS spectra. These compounds were evaluated for theirin vitro anti-leishmanial activity against promostigote form of the Leishmania major. Most compounds exhibited good anti-leishmanial activity against the promastigote form of L. major. The most active compound against promostigotes was found

to be 4-methylbenzyl analog , which significantly decreases the number of intracellular amastigotes per macrophage, percentage of macrophage infectivity and infectivity index.

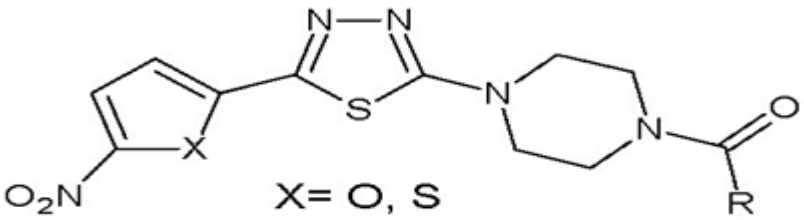


R= H, F, Cl, di-Cl_2, Me, NO_2

Navarro M and Co-workers[66] synthesized a large number of 1,3,4-thiadiazoles derivatives and evaluated for anti-leishmanial assays. Compound 2-(5-(5-nitrofuran-2- yl)-1,3,4-thiadiazol-2-ylthio)-1-phenylpropan-1-one showed IC50 of 1.11 µM against L. major promastigotes.



Fardmoghadam M.B. and Co-workers[67] carried out the synthesis and anti-leishmanial activity of nitroheteroaryl-1,3,4-thiadiazole-based compounds including 1-[5-(5-nitrofuran-2-yl)-1,3,4-thiadiazol-2-yl]-4-aroylpiperazines and 1-[5-(5-nitrothiophen-2-yl)-1,3,4-thiadiazol-2-yl]-4-aroylpiperazines were described. Most of the synthesized compounds exhibited potent anti-leishmanial activity against both promastigote and amastigote forms of Leishmania major at non-cytotoxic concentrations. In general, 5-nitrofuran derivatives were more active than the corresponding 5-nitrothiophene analogues

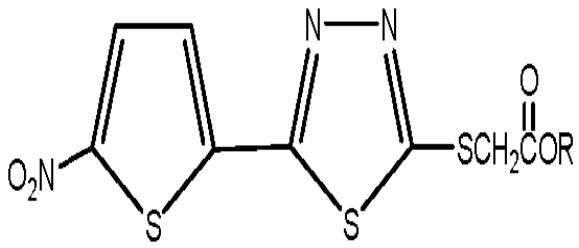


X= O, S

R= phenyl, Cl-phenyl, thio-2yl
5-Cl-thiophen-2yl, 5-Br-thiophen-2yl

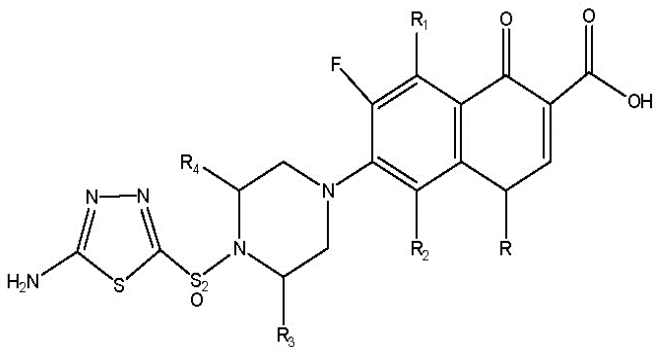
Anti-tubercular activity

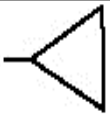
Foroumadi A and Co-workers[68] synthesized a series of alkyl a-[5-(5-nitro-2-thienyl)-1,3,4-thiadiazole-2-ylthio]acetic acid esters and evaluated them by in vitro antituberculosis activity. The antituberculosis activity of the synthesized thiadiazole derivatives against Mycobacterium tuberculosis strain data indicated that methyl, propyl, buthyl and benzyl esters showed a significant in vitro antimycobacterium tuberculosis activity (MIC-0.39- 0.78 µg/ml). The best activity was exhibited by propyl ester (MIC-0.39 mg/ml), but significant decrease in potency was observed by ethyl ester with inhibition percentage of 58 (MIC-6.25 µg /ml).



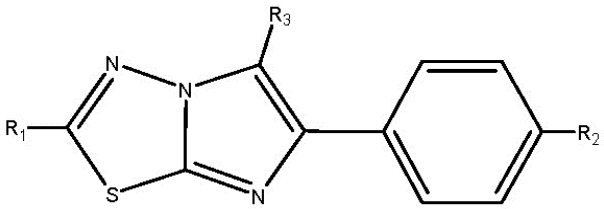
Compd	R
a	$-CH_3$
b	$-CH_3\,CH_2$
c	$-CH_3\,CH_2\,CH_2$
d	$-CH_3\,CH_2\,CH_2\,CH_2$
e	Benzyl

Talath S & Co-workers[69] synthesized a series of 7-[4-(5-amino-1,3,4 thiadiazole-2-sulfonyl)]-1-piperazinyl fluoroquinolonic derivatives. The in vitro antitubercular activity reports of selected compounds a, b against Mycobacterium tuberculosis strain $H_{37}Rv$ showed moderate activity at MIC of 10 µg ml^{-1}.



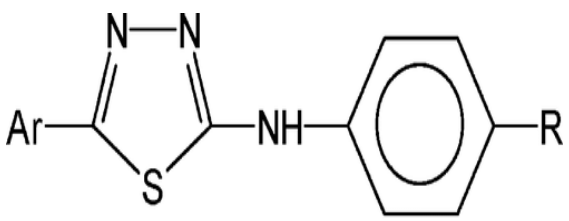
Compod.	R	R_1	R_2	R_3	R_4
a		-H	-H	-H	-H
b	$-CH_2\,CH_3$	-H	-H	-H	-H

Kolavi G and Co-worker[70] synthesized a series of 2,6-disubstituted and 2,5,6-trisubstituted imidazo [2,1-b][1,3,4] thiadiazole derivatives and the synthesized compounds were screened for antitubercular activity against Mycobacterium tuberculosis $H_{37}Rv$ using the BACTEC 460 radiometric system,antibacterial activity against Escherichia coli and Bacillus cirrhosis, and antifungal activity against Aspergillus niger and Penicillium wortmanni. Compounds (a) and (b) exhibited moderate antitubercular activity with percentage inhibition 36, 30, respectively, at a MIC of >6.25 µg/ml.



Compd	R1	R2	R3
a	Cyclohexyl	-H	-CHO
b	Cyclohexyl	-Br	-CHO

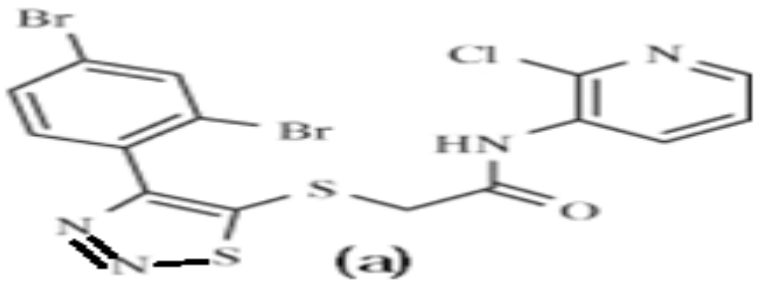
Oruc E E and Co-workers[71] synthesized a series of 2,5-disubstituted-1,3,4-thiadiazoles , the compounds structures were elucidated and screened for the antituberculosis activity against Mycobacterium tuberculosis H37Rv using the BACTEC 460 radiometric system. Among the tested compounds, 2-phenylamino-5-(4-fluorophenyl)-1,3,4-thiadiazole 22 showed the highest inhibitory activity. The relationships between the structures of compounds and their antituberculosis activity were investigated by the Electronic−Topological Method (ETM) and feed forward neural networks (FFNNs) trained with the back-propagation algorithm. As a result of the approach, a system of pharmacophores and anti-pharmacophores has been found that effectively separates compounds of the examination set into groups of active and inactive compounds.



Ar: C_6H_5, C_6H_4Br, C_6H_4Cl, C_6H_4F, $C_6H_4NO_2$, C_5H_5N
R: C_6H_5, C_6H_4Br, C_6H_4Cl, C_6H_4F, $C_6H_4CH_3$, $C_6H_4NO_2$

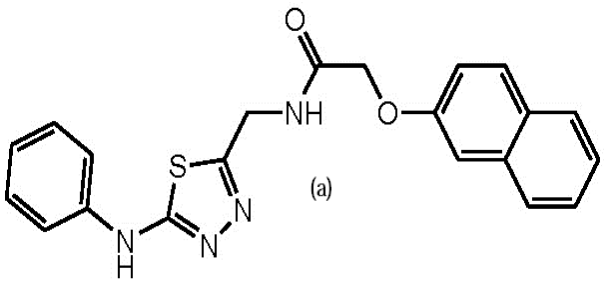
Antiviral activity & Anti HIV activity

Zhan P and Co-workers[72] devised a novel synthetic route and anti-HIV activity evaluation of a new series of 2-(4-(2,4-dibromophenyl)-1,2,3-thiadiazol-5-ylthio)acetamide derivatives). Bioactivity assay indicated that most of the title compounds showed good activities against HIV-1. In particular, compound **(a)** displayed the most potent anti-HIV-1 activity (EC_{50} = 36.4 nM), inhibiting HIV-1 replication in MT-4 cells more effectively than NVP (by sevenfold) and DLV (by eightfold).



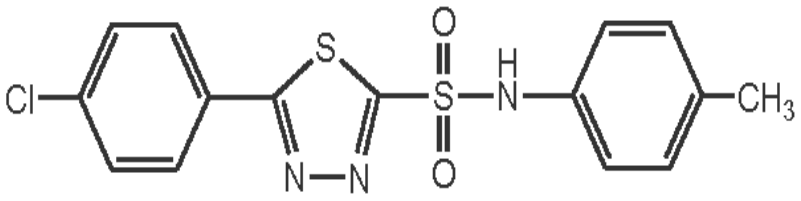
(a)

Hamad N.S. and Co-workers[73] synthesized 2-(naphthalen-2-yloxy)-N-((5-(phenylamino)-1,3,4- thiadiazol-2-yl)methyl) acetamide (a) and tested it in vitro anti-HIV-1 (strain IIIB) and anti-HIV-2 (strain ROD) activity by the inhibition of the virus induced cytopathic effect in the human T-lymphocyte (MT-4) cells, based on MTT assay. All the compounds were found to be inactive except for (a) which showed EC50 values of 0.96 µg/mL.

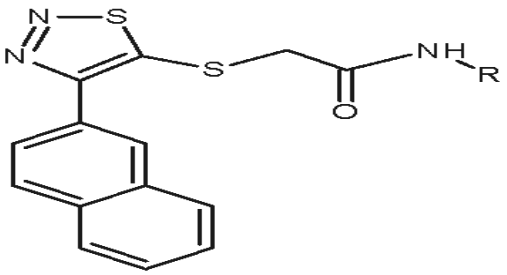


(a)

Chen Z and Co-workers[74] synthesized and evaluated 5-(4-chlorophenyl)-1,3,4- thiadiazole sulfonamides for antitobacco mosaic virus activity. It was found that some of the compounds with sulfonamide moiety were effective inhibitors of tobacco mosaic virus with less cytotoxicity. 5-(4-chlorophenyl)-N-p-tolyl-1,3,4-thiadiazole-2-sulfinamide (a) showed inhibitory activity of about 42%.



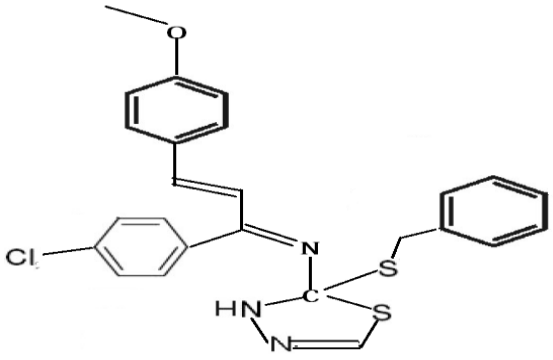
Zhan P and Co-workers[75] synthesized a series of 2-(4-(naphthalen-2-yl)-1,2,3-thiadiazol-5-ylthio)acetamide (TTA) derivatives were synthesized and evaluated as potent inhibitors of HIV-1 Amongst the tested compounds, **a**, **b** and **c** were the most potent inhibitors of HIV-1 replication of the series (EC50=0.17±0.02, 0.36±0.19 and 0.39±0.05 mM, respectively).



a	R= 2-chloropyrin-3-yl
b	R= 4-acetyl-2-bromophenyl
c	R= 2-nitrophenyl

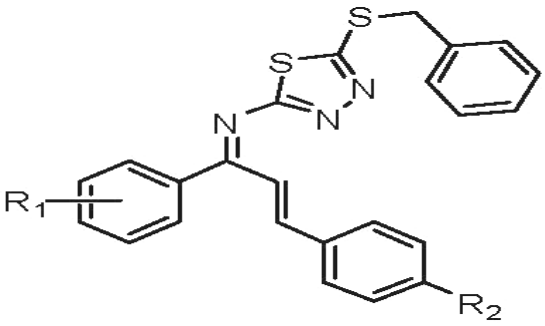
Anti-Depressant Activity

Ahmed B and Co-workers[76] synthesized a number of new imine derivatives of 5-amino-1,3,4- thiadiazole- 2-thiol and their anti-depressant activity was tested using imipramine as reference drug. Compound namely 5-{[1-(4-chlorophenyl)-3-(4-methoxyphenyl) prop-2-en-1-ylidene]- amino}-5 benzylthio- 1,3,4-thiadiazole (24) has shown significant anti-depressant activity.



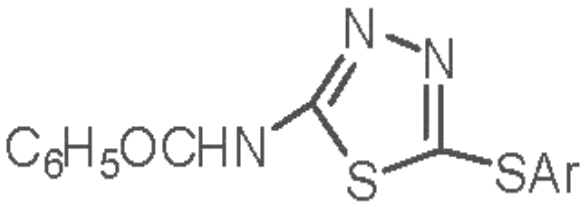
Yusuf M and Co-workers[77] synthesized a number of new imine derivatives of 5-amino-1,3,4-thiadiazole-2-thiol and their antidepressant activity was tested using imipramine as reference drug. Two compounds namely 5-{[1-(4-chloroprene)-3-(4-methoxyphenyl)prop-2-en-1-ylidene]-amino}-5-benzylthio-1,3,4-thiadiazole (**a**) and 5-{[1-(4-chloroprene)-3-(4-

dimethyl-aminophenyl)prop-2-en-1-ylidene]-amino}-5-benzylthio-1,3,4-thiadiazole (**b**) have shown significant antidepressant activity.



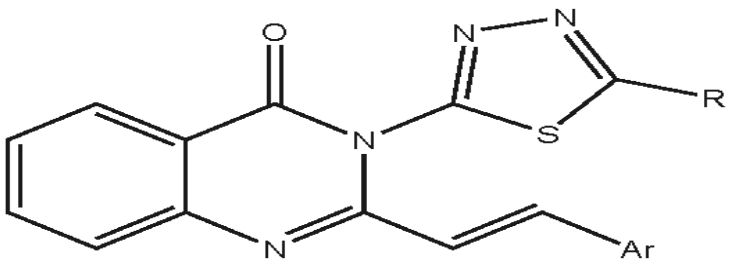
a	$R_1 = OCH_3$, $R_2 = Cl$
b	$R_1 = (CH_3)_2N$, $R_2 = Cl$

Pattanayak P and Co-workers[78] evaluated newly synthesized 2-amino-5-sulfanyl-1,3,4-thiadiazole for antidepressant activity. Three of the tested compound (**a**), (**b**) and (**c**) exhibited excellent antidepressant activity in comparison to reference drugs.



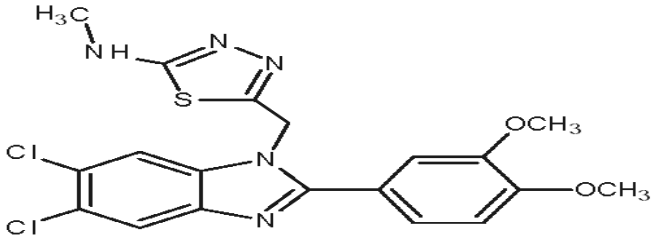
a	Ar = 4-$C_6H_4SO_2Cl$
b	Ar = 4-$C_6H_4SO_2NH_2$
c	Ar = 4-$C_6H_4CF_3$

Jatav, V and Co-workers[79] synthesized a series of novel 3-[5-substituted phenyl-1, 3, 4-thiadiazole-2-yl]-2-styryl quinazoline-4(3H)-ones were synthesized and evaluated for anticonvulsant, sedative-hypnotic and CNS depressant activities.

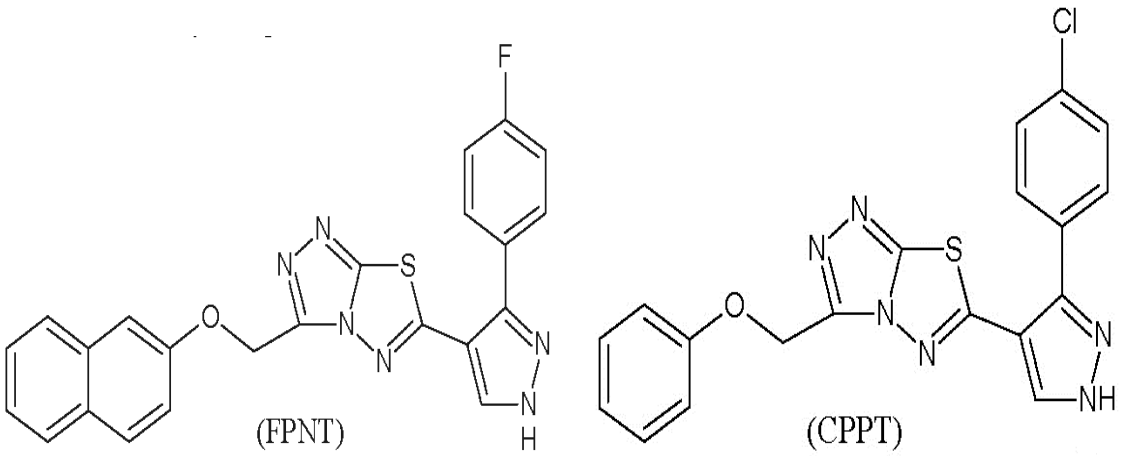


Antioxidant/ Radio-protective Activity

Kus C and Co-workers[80] synthesized Some novel 5-[(2-(substituted phenyl)-1H-benzimidazole -1-yl)methyl]-_-methyl-1,3,4-thiadiazole-2-amines were synthesized and tested for antioxidant properties using various in vitro systems. Compound (**a**), which is the most active derivative inhibited lipid peroxidation slightly at 10^{-3} M concentration.

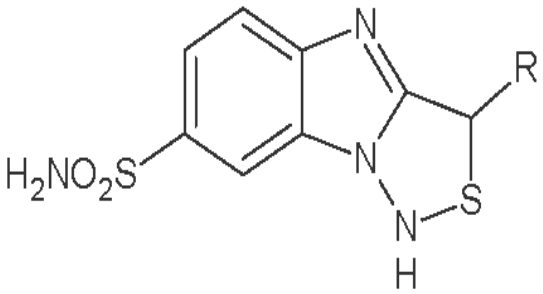


Sunil D and Co-workers [81] had investigated the in vitro antioxidant property of two triazolo- thiadiazoles, 6-[3-(4-fluorophenyl)-1H-pyrazol-4-yl]-3-[(2-naphthyloxy) methyl][1,2,4] triazolo [3,4-b]-[1,3,4] thiadiazole (FPNT) and 6-[3-(4-chlororophenyl)-1H-pyrazol-4-yl]-3-[(phenyloxy)methyl]-[1,2,4] triazolo [3,4-b][1,3,4]thiadiazole (CPPT) by spectrophotometric DPPH and ABTS radical scavenging methods as well as by lipid peroxide assay. The significant antioxidant activity of FPNT with low IC50 values when compared to standard is clearly evident from DPPH, ABTS free radical scavenging and in vitro lipid peroxidation assays. The in vitro lipid peroxidation assay also proved FPNT to be an excellent antioxidant.



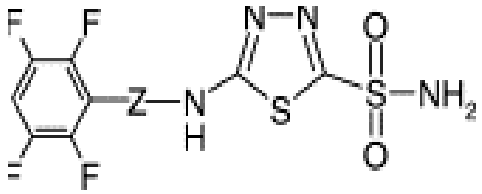
Carbonic anhydrase inhibitors

Matulis D and Co-workers[82] synthesized a series of Benzimidazo[1,2c][1,2,3]thiadiazole sulfonamides as human carbonic anhydrase I (hCAI) and bovine carbonic anhydrase II (bCAII). The strongest binder to both isozymes of carbonic anhydrase was compound (a) with the observed Kd of about 0.04 lM. The most specific binder of hCAI was compound (b) that bound about fourfold stronger to hCAI than to bCAII. The (c) compound bound threefold tighter to bCAII than to hCAI.



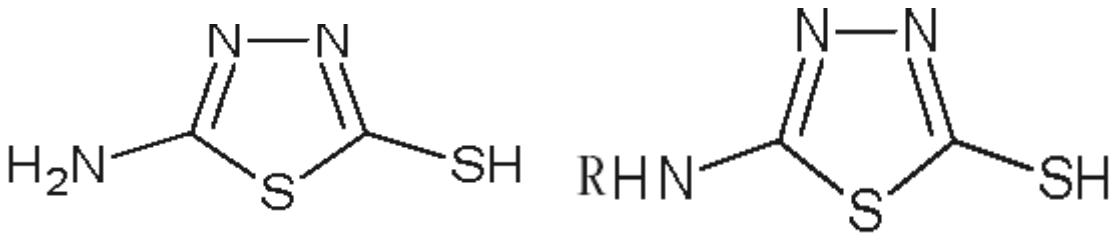
Compd	R
a	-Cl
b	$-SO_2CH_3$
c	$-N(CH_2CH_3)_2$

Vullo D and Co-workers[83] synthesized a series of such compounds has been obtained by attaching 2,3,5,6-tetrafluorobenzoyl- and 2,3,5,6-tetrafluorophenylsulfonyl- moieties to aromatic/heterocyclic sulfonamides possessing derivatizable amino moieties. Some of these compounds showed excellent CA IX inhibitory properties and also selectivity ratios favorable to CA IX over CA II, the other physiologically relevant isozyme with high affinity for sulfonamide inhibitors. The first subnanomolar and rather selective CA IX inhibitor has been discovered, as the 2,3,5,6-tetrafluorobenzoyl derivative of metanilamide showed an inhibition constant of 0.8 nM against hCA IX, and a selectivity ratio of 26.25 against CA IX over CA II. Several other low nanomolar CA IX inhibitors were detected among the new derivatives reported here. The reported derivatives constitute valuable candidates for the development of novel antitumor therapies based on the selective inhibition of tumor-associated CA isozymes.



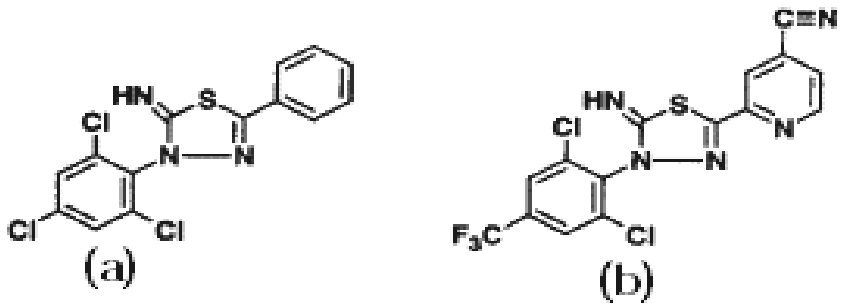
Z = CO; SO_2

Almajan G. L. and Co-workers[84] synthesized a series of heterocyclic mercaptans incorporating 1,3,4-thiadiazole- and 1,2,4-triazole rings have been prepared and assayed for the inhibition of three physiologically relevant carbonic anhydrase (CA, EC 4.2.1.1) isozymes, the cytosolic human isozymes I and II, and the transmembrane, tumor-associated hCA IX. Against hCA I the investigated thiols showed inhibition constants in the range of 97 nM to 548 μM, against hCA II in the range of 7.9–618 μM, and against hCA IX in the range of 9.3–772 μM. Thiadiazoles were generally more active than triazoles against all investigated isozymes. Generally, the best inhibitors were the simple derivative 5-amino-1,3,4-thiadiazole-2-thiol and its N-acetylated derivative,



Anthelmintic Activity

Lee B H and Co-workers[85] following their discovery of the strong binding of thiadiazole **(a)** to the AF-2 neuropeptide receptor of gastrointestinal nematodes (e.g., Ascaris suum), prepared two series of analogs. Only the series containing the thiadiazole ring had potencies comparable to that of compound **(a)**. Analog **(b)** exhibited an apparent potency in the AF-2 binding assay 300 times that of compound **(a)**.



CONCLUSIONS

This review gives an overview of the wide spectrum of pharmacological activities exhibited by thiadiazoles The pharmacological activities of thiadiazoles derivatives has attracted considerable attention owing to the usefulness of this moiety in the field of medicinal chemistry. Further development can be carried out by making slight alterations leading to drastic changes to yield better drug The importance of thiadiazole moiety can be magnified by carrying out further studies on its possible substitution. Thus this paper proves to be significant for further research work on the bioactive thiadiazole ring and biological profiles of these new generations of thiadiazoles would represent a fruitful matrix for further development of better medicinal agents.

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