WORLD JOURNAL OF PHARMACY AND PHARMACEUTICAL SCIENCES
SJIF Impact Factor 7.421
Volume 8, Issue 6, 218-240 Review Article ISSN 2278 – 4357

# 2, 5- DISUBSTITUTED 1,3,4-THIADIAZOLES: MOLECULES OF MANIFOLD APPLICATIONS – A REVIEW

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Article Received on
07 April 2019,

Revised on 28 April 2019,
Accepted on 19 May 2019

DOI: 10.20959/wjpps20196-13798

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## ABSTRACT

1,3,4-thiadiazole is an example for motley moiety, which on substitution with its bioisosteres such as oxadiazole, oxazole and benzene leads to increase n its pharmacological activity. The unique chemical properties and biological activity of 1,3,4-thiadiazoles make them as attractive targets for the medicinal chemists. 1,3,4-thiadiazole nucleus represent an excellent pharmacophore with diverse activititessuch as antimicrobial, anti-tubercular, anticancer, CNS depressant, antioxidant, antiviral, antidiabetic and hypertensive etc. The review presents a brief summary of the chemistry, synthesis and a broad view on the various pharmacological activities possessed by different compounds substituted with 1,3,4-thiadiazole nucleus.

**KEYWORDS:** 2,5-disubstituted 1,3,4-thiadiazoles, Reactivity, Methods, Pharmacological activity.

## INTRODUCTION

Thiadiazoles[1] are an important class of heterocyclic compounds that exhibit diverse applications in organic synthesis, pharmaceutical and biological applications. They also known to useful as oxidation inhibitors, cyanine dyes, metal chelating agents, anti-corrosion agents. Attracted by their broad spectrum of applications; scientists across the globe are working on this moiety and consequently have been instrumental in the advancement of thiadiazole chemistry.

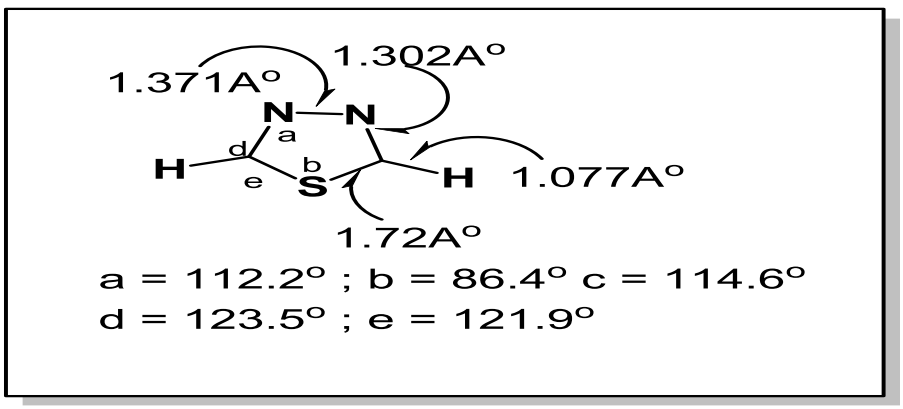
Among the different thiadiazoles available the synthesis and applications of 1,3,4-thiadiazoles and 1,2,4- thiadiazoles is more available in the literature and relatively less about of 1,2,5-thiadiazoles, But there is a scanty of information about 1,2,3-thiadiazoles.

Thiadiazole is a very multifaceted moiety that shows a wide range of pharmacological activity. Thiadiazoles are bioisosteres of heterocycles such as oxadiazole, oxazole and benzene. Substitution of thiadiazoles with their bioisosteres increases activity.

1,3,4-Thiadiazole was first given in 1882 by Fischer and further developed by Busch and his coworkers But the legitimate nature of the thiadiazole ring system was authenticated first in 1956 by Goerdal et.al.

Unlike benzene, pyridine and thiophene, 1,3,4-thiadiazole molecule does not display true aromatic behavior. Microwave spectra of t1,3,4-thiadiazole molecule have been analysed by *Bak* et.*al* and bond lengths, bond angles, Dipole moment and bond orders were calculated. The dipole moment was Reported as 3.25D for 1,3,4-thiadiazole and 1.61D for thiazole. They concluded that π-electron delocalization which is measurement of the aromatic character decreases in the order of 1,2,5-thiadiazole > thiophene > thiazole > 1,3,4-thiadiazole.

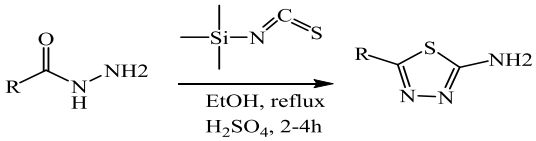
M.O. calculations were made by **Zahardnik and Koutechy** using Longuet Higgins model for the sulfur atom of thiadiazole isomers (highest molecular orbital method) which showed increased delocalization in 1,2,5-isomer than in thiazole and 1,3,4-thiadiazole. 1,3,4-thiadiazole is a polar symmetric molecule exhibiting pseudoaromatic character. The molecular geometry figure for 1,3,4-thiadiazole is shown here, calculated on the bases of M.O. method.



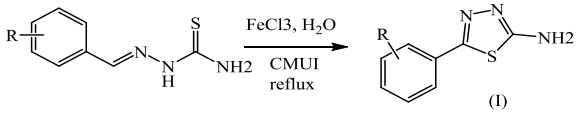
1,3,4-Thiadiazoles are mesoionic, a poly-hetroaromatic system with five membered heterocyclic ring combined with conjugated π and p electrons and distinct regions of positive and negative charges (scheme). Mesoionic systems[4] cannot be satisfactorily represented by anyone covalent or dipolar structure, but only as hybrids of polar structures and they possess a sextet of electrons. These systems are dense and highly polarisable, with a net neutral electron charge. The distinct properties of mesoionic compound and improved lipophilicity due to presence of sulphur atom make it to get across cellular membranes and Interact with biological targets with sharp-cut affinities.

**Synthesis of 2,5 disubstituted 1,3,4-thiadiazole**

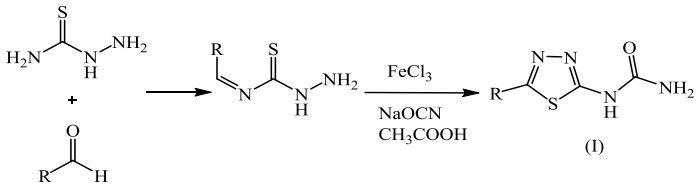
Guda, Dinneswara Reddy[2] *et al.* developed one pot synthesis of 2-amino-1,3,4-thiadiazoles in good yields using trimethylsilyl isothiocyanate.



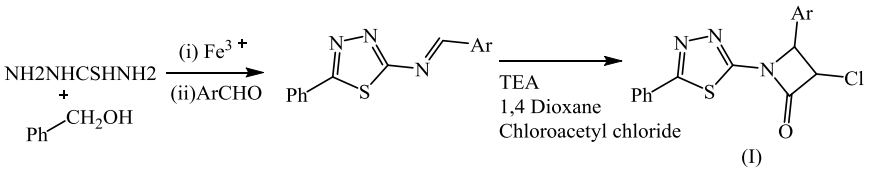

Feng, Huangdi[3] *et al.* Reported eco-friendly aqueous heterogeneous approach promoted synthesis of 1,3,4-thiadiazoles from schiffs bases of thiosemicarbazides in presence of microwave and ultra violet in presence of ferric chloride.



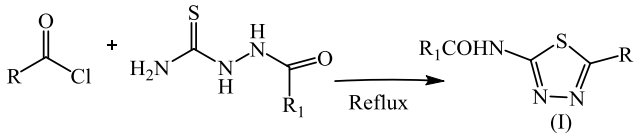

Gowramma, B[4] *et al* submitted synthesis of 1-(5-aryl-1,3,4-thiadiazol-2-yl)urea (I) obtained by oxidative cyclization of thiosemicarbazone using ferric chloride as oxidative agent which on reaction with sodium cyanate in glacial acetic acid gave target compound (I).



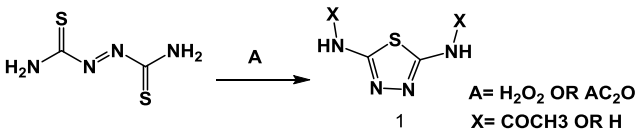

Babu, M Narayana[5] *et al.* Reported multistep method for synthesis of 3-Chloro-4-(substituted)-1-(5-phenyl-1,3,4-thiadiazol-2-yl)azetidin-2-ones by Staudinger imine reaction of schiffs base of 2-amino 5-aryl-1,3,4-thiadiazole.



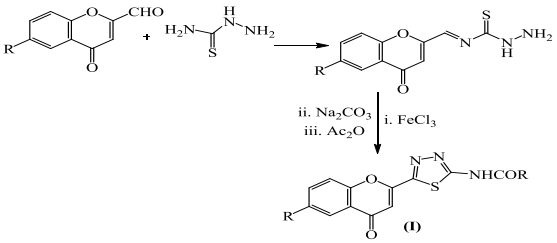

Singh, Arvind K.[6] *et al.* Reported synthesis of 2,5disubstituted thiadiazoles (I) obtained from cyclisation and condensation of acyl chloride and thiobezoyl semicarbazide.



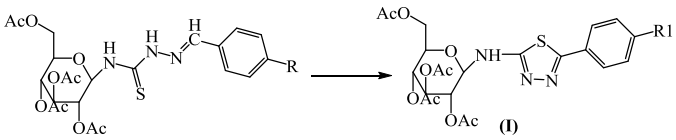

Desai, vignesh[7] *et al.* Reported synthesis of 2-Amino-5-(substituted)-1,3,4-thiadiazoles obtained by treating bithiourea with 3% hydrogen peroxide.




Ibrahim, S. S[8] *et al.* Reported synthesis of 4-oxo-4H-1-benzopyran derivatives (I) from aldehydes with Oxobenzopyrancarboxamides.

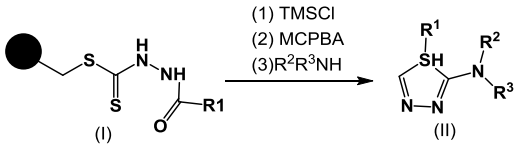



Valentiny, M[9] *et al.* discussed preparation of N-glucosyl derivatives of 5-substituted 2-amino-1,3,4-thiadiazole by oxidative cyclization of 4- (2,3,4,6-tetra-O-acetyl-β-D-glucopyranosyl)thiosemi -carbazones with ferric chloride.

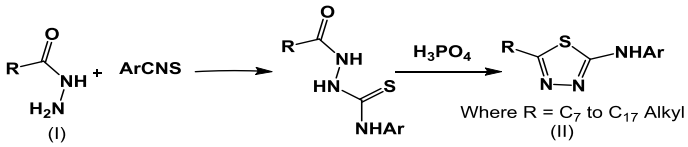



Stolle[10] *et* al. Reported synthesis of 2,5 Diphenyl-1,3,4 Thiadiazole obtained by treating benzoyl hydrazine or N,N dibenzoyl hydrazine with phosphorus pentasulphide.

Hweng, J. Y[11] *et al.* 1,3,4-S thiadiazole (II) can be synthesized selective, reagent-based cyclization of acyldithiocarbazate resins, (I) in presence of trimethylsiliyl chloride (TMSCl), meta-chloro peroxy benzoic acid (MCPBA) and secondary amine.



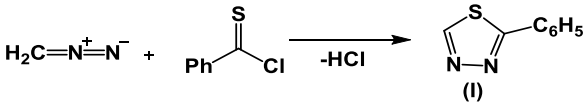

Udapudi[12] *et al.* 1,3,4-thiadiazoles (II) containing long alkyl side chain can be synthesized by reacting alkyl substituted thiosemicarbazide (I) with arylisothiocyanate in presence of phosphoric acid.



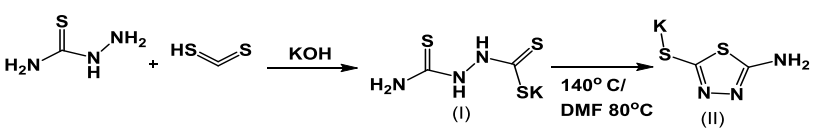

Kurzer, F.[13] Reported 1,3,4-thiadiazoles by reaction of aminoguinidine salts and aroylisothiocyanates followed by acid catalysis and cyclisation of acylthiosemicarbazides obtained.

Ruhlmall, K.[14] Reported dehydrogenation of thiazolidineones with sulphur in boiling pyridine gave 2,5 dialkyl 1,3,4-thiadiazole. Thiazolidineones was prepared from aliphatic aldehyde, hydrazine and hydrazine sulphide.

Sartorelli[15] *et* al. Reported synthesis of 2-Aryl-1,3,4-thiadiazole (I) in good yield by addition of diazomethane to substituted thiobenzoyl chloride.




Guha[16] *et al.* Reported 2-amino 5-mercapto-1,3,4-thiadiazole(II) by treatment of thiosemicarbazide with carbon disulphide in presence of potassium hydroxide followed by heating to 140°C or treatment with dimethyl formamide at 80°C to get target compound.

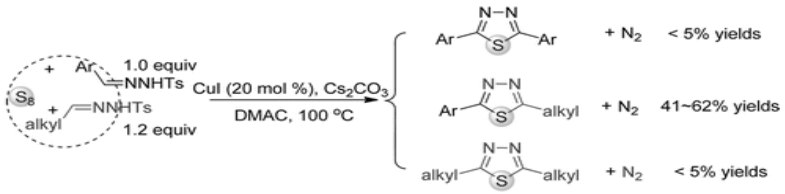


Mahmoud R Mahmoud[17] *et al*. Reported synthesis of 2,5 disubstituted -1,3,4-thiadiazole by cyclisation of corresponding thiosemicarbide followed by the reaction with electrophilic agents such as aromatic aldehydes, isatin, phenyl isothiocyanate and carbon disulfide in a good yield.

Zi- Ninq cui[18] et *al*. Reported synthesis of 2,5 disubstituted -1,3,4-thiadiazole by using lawesson's reagent by an efficient approach under microwave irradiation in good yield.

Nitin Deshmukh[19] *et al*. Reported thiosemicarbide of phenyl hydrazine on cyclization with different aromatic carboxylic acid in $POCl_3$ gives 2 –(substituted phenyl)-5-(2-phenyl hydrazinyl)-1,3,4 thiadiazole.

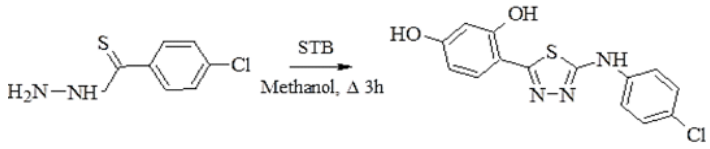
Zhen Zhou[20] *et al*. Reported a copper-mediated, three component reaction between two different N-Tosyl hydrazones and elemental sulfur yields a series of unsymmetric 2,5-disubstituted 1,3,4 thiadiazoles in moderate yields with good functional group compatibility.




Jinfeng Kang[21] *et al*. Reported the synthesis of 2-amino substituted 1,3,4 thiadiazoles via condensation of semicarbide/thiosemicarbide and the corresponding aldehydes followed by $I_2$ mediated oxidative bond formation.

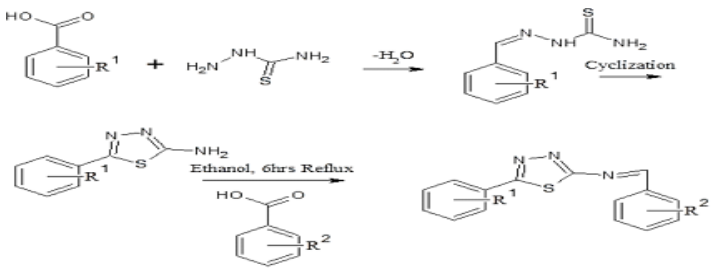
Sobhi M Gomha[22] *et al.* Reported the synthesis of 5-(thiophen-2-yl)-1,3,4-thiadiazole derivative by heterocyclization of n-(4-nitrophenyl)thiophene-2-carbohydrazonoyl chloride with hydrazine-carbodithioate derivatives.

Geogeta S[23] *et al*. Reported the synthesis of 2-R-5-formyl -1,3,4-thiadiazole derivative from the aromatic and heterocyclic amines treated with carbon disulfide in ammonium hydroxide followed by refluxing with hydrazine hydrate in ethanol after treated with monochloracetyl chloride. Malgorzata J.[24] et *al*. synthesized 2-(4-chlorophenylamino)-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole. The compound was obtained from sulfinylbis (2,4-dihydroxythiobenzoyl) and 4-(3-chlorophenyl)-3-thiosemicarbazide or 4-(4-chlorophenyl)-3-thiosemicarbazide via cyclization process.




MR Mahendrasinh Raj[25] *et al*. synthesized thiadiazole derivatives by the reaction between benzoic acid 2-hydroxy benzoic acid with thiosemicarbazide using conc H2SO4 as oxidising agent.

MS Yar[26] *et al*. Reported the synthesis of 2,5 –disubstituted 1,3,4 thiadiazole derivative by the reaction between isoniazid and various substituted isothiocyanates A Naskar[27] *et al*. synthesized 2-amino-5- aryl -1,3,4- thiadiazoles by oxidative cyclization of thiosemicarbazones using $FeCl_3$ catalyst and from this Schiff bases were prepared by condensation with aldehyde.

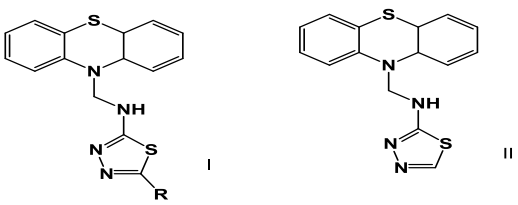



M Asif[28] *et al*. Reported the synthesis 2,4- diphenyl-5-imino-1,3,4-thiadiazole derivatives by cyclization of α-chlorobenzalphenylhydrazone derivatives using potassium thiocyanate. A-chlorobenzalphenylhydrazone derivatives were synthesized by chlorination of hydrazonyl derivatives using PCl5 which in turn was synthesized from benzoyl chloride and phenyl hydrazine in pyridine.

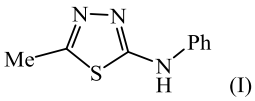
**2,5- Disubstituted1,3,4-thiadiazole derivatives of pharmacological interest**

**Antibacterial and antifungal activity**

Yin[29] *et al.* Reported synthesis of phenothiazainyl compounds (I) in good yields by addition of phenothiazine, formaldehyde and 1,3,4-thiadiazole as antibacterial agents.

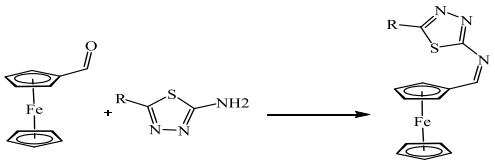


Siddiqui, Shadab Miyan[30] *et al.* Reported few 1,3,4-thiadiazoles (I) as potent inhibitors of Entamoeba histolytica. The compounds had good anti amoebic profile compared to metronidazole.



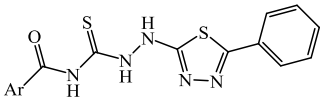

(I)

Yin, Dawei[31] *et al.* Reported synthesis and antibacterial activity of Ferrocene-based with thiadiazole (I). The compounds were found to have increased antibacterial activity against one or more species.



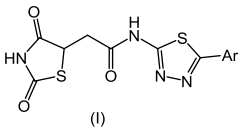

R = -H, -$CH_3$, -$CH_2CH_3$, -$CH{=}CH_2$, -SH, -Ph,-Pridyl

Joshi, S.D[32] *et al.* Reported 2-(substituted benzoylthiocarbamido)-5-(phenylsulfon -amido) -1,3,4-thiadiazoles (I) as potent antibacterials and antivirals.



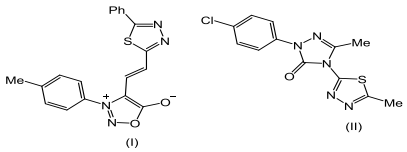

(I)

Alegaon, Shankar G[33] *et al.* investigated synthesis, anti microbial and cytotoxic properties of thiazolidinedione-5-acetic acid amide derivatives (I).




(I)

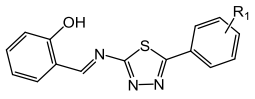
Bansode, Soujanya[34] *et al.* synthesised and screened 2-(3'-aryl-sydnon-4'-ylidene)-5'-substituted-[1,3,4]-thiadiazolylamines (i) and [1,3,4]-thiadiazol-2'-yl-3-oxo-[1,2,4]-triazoles (ii) for anti microbial acivity.




(I) (II)

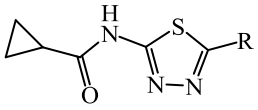
Mathew, Bijo[35] *et al.* submitted 2-amino,5-(phenyl substituted) 1,3,4-thiadiazole derivatives as potent anti microbials.

Salimon, Jumat[36] *et al.* presented 2-N-salicylidene-5-(substituted)-1,3,4-thiadiazole obtained by cyclisation and condensation of thiosemicarbazide, 4-substituted benzoates in $POCl_3$ and salicylaldehyde as potent anti microbials.



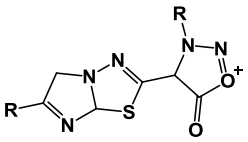

(I)

Liu, Xing-Hai[37] *et al.* Reported synthesis, 3D-QSAR and fungicidal activity of N-(5-substituted-1,3,4-thiadiazol-2-yl)cyclopropanecarboxamides (I).



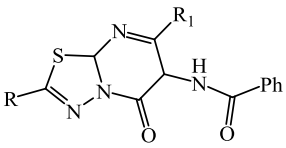

(I)

Zang, Yan[38] *et al.* Reported synthesis, mechanism and antibacterial activity of imidazolo[2,1-b]-1,3,4-thiadiazoles and S-triazole[3,4-b]-1,3,4-thiadiazoles (I).



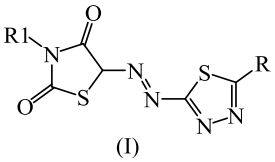

Khan, Mukhtar Hussain[39] *et al.* Reported synthesis of 5-aryl-2-[spiro(1,3-dithiolane)-2,4'-(3'-chloro-2'-azetidinon)-1'-yl]-1,3,4-oxa(thia)diazoles from 5-aryl-2-(1,3ditholan-2-yl) imino-1,3,4-thiadiazoles with chloroacetyl chloride as antimicrobial agents.

Singh, Harendra[40] *et al.* Reported synthesis and anti fungal activity of 6,7-dihydro-5H-thiadiazolo[3,2-a]pyrimidin-5-ones prepared by Michael addition and cyclocondensation.



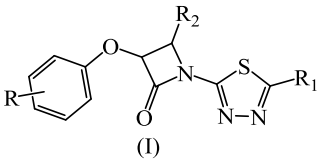

(I)

Singh, S[41] *et al.* synthesized and carried out anti fungal activity of thiadiazolylazorhodanines (I) by cyclodehyration of acyl thiosemicarbazide followed by diazotsation and coupling with arylrhodanines.



(I)

Osman, A. M.[42] et al. Reported Molluscicidal and bactericidal activity for phenoxy heterocyclic compounds (I) obtained by reaction of phenoxyacetyl chlorides with 2-aminothiazoles.



(I)

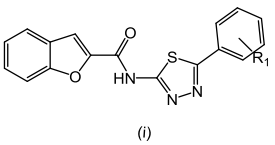
Bhoomedra A Bhongade[43] *et al.* Reported the evaluation of imidazo [2,1] [1,3,4]-thiadiazoles for the anti-bacterial and anti- fungal activity against the several Gram positive and Gram negative microbes.

Abhishek Kumar Jain[44] *et al.* Reported the anti- bacterial and anti- fungal activity of 2-[1(2H)-phthalazinone-2-yl]-maehyl/ethyl]-5-arylamino-1,3,4-thiadiazole derivatives against the bacteria and fungal species(candida albicans).

**Anti inflammatory and Anti Viral activity.**

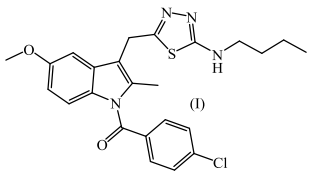
Singh, Arvind K.[45] *et al.* Reported synthesis and evaluation of in vitro anti microbial and in vitro anti inflammatory activity of 2,5disubstituted thiadiazoles (I) obtained from cyclisation and condensation of acyl chloride and thiobezoyl semicarbazide.

Bari, S. B[46] *et al.* Reported 2-Aryl-5-(1,3,4-thiadiazole-2-carboxamido)benzofurans (I) from benzofuran-2-carbonyl chloride possessing analgesic and antiinflammatory activity.



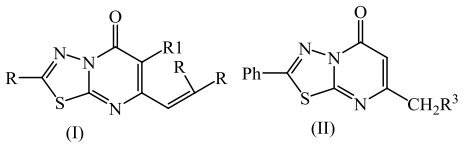
(i)

Amir[47] et *al.* designed series of indomethacin by replacing COOH with amino-1,3,4-thiadiazole(I) as anti inflammatory and analgesics.



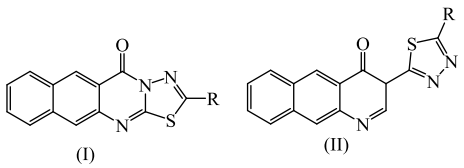
(I)

Doria, Gianfederico[48] *et al.* Reported on 1,3,4-thiadiazolo[3,2-a] pyrimidines derivatives (I) /(II) obtained by cyclocondensation of ethyl chloroacetoacetate with 2-amino-5-phenyl-1,3,4-thiadiazole as unti ulcer and anti-inflammatory agents.



(I) (II)

Benzo[g]quinozolin-4-one (II) obtained by condensation for antiinflammatory and analgesic activity.

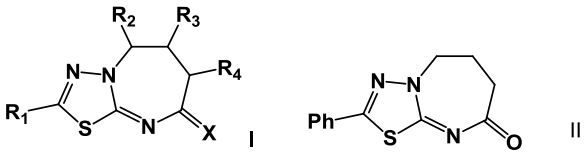


(I) (II)

M Asif[49] *et al*. synthesized 2,4- diphenyl-5-imino-1,3,4-thiadiazole derivatives and screened for in vivo anti-inflammatory activity by carrgeenan induced paw oedema and a few of them showed promising activity when compared to standard drug diclofenac sodium.

**Anti convulsant Activity**

Gowramma, B[50] *et al* submitted synthesis and anticonvulsant activity of 1-(5-aryl-1,3,4-thiadiazol-2-yl)urea (I).

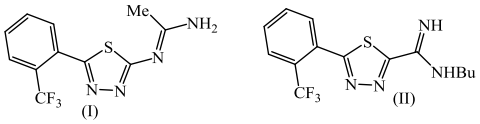


I II

Mullick, Pooja[51] *et al.* Reported synthesis of novel 1,3,4-thiadiazoles (I) with good anti convulsant activity.

Singh, Hemendra Pratap[52] *et al.* Reported microwave assisted synthesis, in- silico and evaluation of anti convulsant activity for thiadiazole derivatives.

Chapleo, Christopher B[53] *et al.* synthesized and evaluated two series of 2-aryl-1,3,4-thiadiazole amidines for anti convulsant activity.

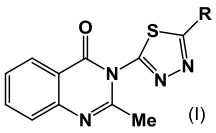



**Anti-Cancer activity**

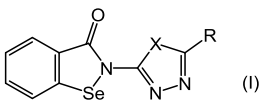
Yang, Xian-Hui[54] *et al.* Reported synthesis, molecular docking studies and anti proliferative activity of 1,3,4-thiadiazol-2-amide derivatives (I). The compounds were found to be potent FAK inhibitors.

Taher, Azza T[55] *et al*. Reported Synthesis and in-vitro antitumor activity of 1,3,4-heterodiazole analogues.

Joseph, Alex[56] *et al.* Reported synthesis and anti cancer activity of 3-(1,3,4-thiadiazol-2-yl)-quinazolin-4(3H)-ones (I).



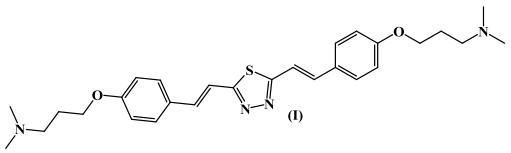

Chen, Baoquan[57] et al. Reported anti tumor activity of 1,3,4-thiadiazole and 1,3,4-oxadiazole derivatives (I) obtained by heterocyclization of 2-(chloroseleno)-benzoyl chloride with 1,3,4-thiadiazol-2-amine.




Zheng, Kai Bo[58] *et al.* Reported N1-acetylamino-(5-alkyl/aryl-1,3,4-thiadiazole-2-yl)-5-fluorouracil derivatives exhibited good anti-tumor activity compared to 5-flurouracil.

Busch, Brett[59] *et al.* Reported use of 3 -phenyl-N-(1,3,4-thiadiazol-2-yl)acrylamide derivatives in the treatment of cancer, rheumatoid arthritis or neurological disorders.

Chou[60] *et al.* synthesized 1,3,4-thiadiazoles (I) and tested for cytotoxicity on human lung cancer by mtt assay.



(I)

Mishra, Lallan[61] *et al.* Reported ferrous and ferric complex obtained from heterocyclic compounds as anti tumor and anti microbial agents.

Miyamoto, Kenichi[62] *et al.* discussed anti tumor activity of 5-substituted 2-amino-1,3,4-thiadiazole analogs against L1210 leukemia, B16 melanoma and Lewis lung carcinoma.

Baby Ramana Mutchu[63] *et al*. Reported the synthesis and evaluation of cytotoxic activity of 2-(5-methyl_2-nitrophenyl)-5-(substituted)-1,3,4-thiadiazole.

Gowramma Byran[64] *et al*. Reported the synthesis and evaluation of of 2-(bis(2-chloroethyl)amino)-N-(5-substituted-phenyl)-1,3,4-thiadiazole-2-yl)acetohydrazide showed anti-cancer activity against Hep-2 cell lines.

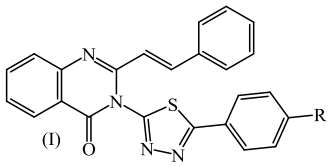
Raj, Vinit Raj[65] *et al*. discussed the anti tumour activity of 2-amino-5-(substituted)-1,3,4-thiadizole derivatives for colon cancer treatment.

S Banerjee[66] *et al*. Reported the synthesis and evaluation of thiadiazole derivatives and Screened for *in vitro* anticancer activity was carried out using MTT (3-[4,5- dimethylthiazol-2-yl]-2,5-diphenyl terazolium bromide) assay on HT-29 colorectal cancer cell line. The compounds had shown significant activity at very less concentration.

A Naskar[67] *et al*. synthesized and evaluated the 2-amino-5- aryl -1,3,4- thiadiazoles has anti cancer activity in Ehrlich's Ascites carcinoma cells.

**CNS depressant activity**

Jatav, Varsha[68] *et al.* Reported on screening of CNS depressant and sedative –hypnotic activity activity for 3-[5-substituted 1,3,4-thiadiazole-2-yl]-2-styryl quinazoline-4(3H)-ones (I).



(I)

Mishra, Pradeep[69] *et al.* Reported synthesis and evaluation of 2-methyl-3-(1,3,4-thiadiazol-2-yl)-4(3H)-quinazolinones for anticonvulsant and CNS depressant activity.

Francesca Clerici[70] *et al.* Reported the synthesis and evaluation of 2-amino-5-sulfonyl-1,3,4-thiadiazole derivatives for their anti-depressant and anxiolytic activity.

**Anti Tubercular activity**

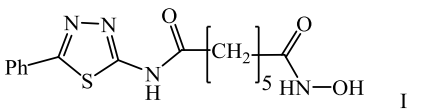
Patel, Manishkumar B[71] *et al.* Reported screening of Calix[4]arene based 1,3,4-oxadiazole and thiadiazole derivatives for their antitubercular activity against Mycobacterium tuberculosis $H_{37}Rv$.

George, Sonia[72] *et al.* Reported synthesis and evaluation of N-(1, 3, 4-thiadiazole)pyrrole carboxamide derivatives for anti tubercular activity.

Naveen Polkam[73] *et al.* Reported the anti cancer and anti mycobacterial activity of 5-(2,5-dimethoxyphenyl)1,3,4-thiadizole-2-amino derivative against cancer cell lines HT-29, MDA-MB-231 and Mycobacterium smegmatis.

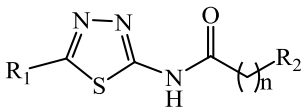
**Enzyme Inhibitors**

Guan, Peng[74] *et al.* Reported a series of 1,3,4-thiadiazole hydroxamic acid derivatives as novel histone deacetylase inhibitors. Compound (I) was found to have more activity than vorinostat.



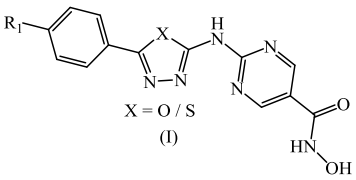
I.

Fang, Hao[75] *et al.* Reported method of preparation and application of thiadiazole-like compound (I) as histone deacetylase (HDAC) inhibitor.

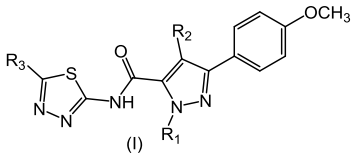


(I)

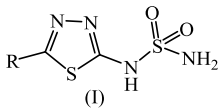
Rajak, Harish[76] *et al.* Reported design and synthesis of hydroxamic acid based 2,5-Disubstituted-1,3,4-oxadiazoles/thiadiazole (i)as histone deacetylase inhibitors.




An, Yue[77] *et al.* submitted auxin activities of 3-(4-Methoxyphenyl)-1H-pyrazole-5-carboxamide derivatives obtained by condensation of 4-(4-methoxyphenyl)-1-methyl-1H-pyrazole-5-carbonyl chloride with 1,3,4-thiadiazol-2-amine derivatives.

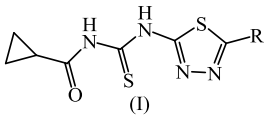



Smaine, Fatma-Zohra[78] *et al.* 2-Substituted-1,3,4-thiadiazole-5-sulfamides (I) as potent Carbonic anhydrase inhibitors.

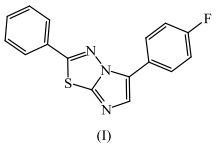



Li, Shao-hua[79] *et al.* designed and synthesized peptide-like derivatives (I) as inhibitors of aminopeptidase N and matrix metalloproteinase.

Liu, Xing-Hai[80] *et al.* Reported N'-(5-substituted-1,3,4-thiadiazol-2-yl)-N-cyclopropylformyl-thioureas as KARI inhibitors.

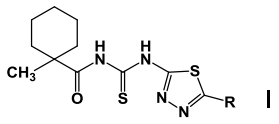



Pevarello, Paolo[81] *et al.* synthesized and evaluated imidazolothiadiazole derivatives (I) as protein kinase inhibitors.

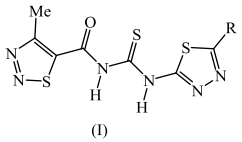


**Other Pharmacological activities**

Tan, Chengxia[82] *et al.* Reported acylthiourea-1,3,4-thiadiazoles (I) as herbicides.

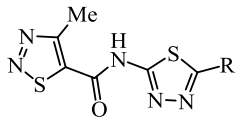


Liu, Xinghai[83] *et al.* Reported synthesis of thiadiazolyl thiourea (I) as plant growth.



(I)

Liu, Xinghai[84] *et al.* showed N-(1,3,4-thiadiazol-2-yl)-4-methyl-1,2,3-thiadiazole-5-carboxamide derivatives (I) to have plant anti fungal activity.



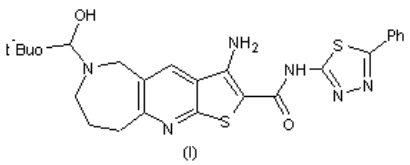
(I)

Amal Smali[85] *et al.* examined the 2,5-bis(pyridinyl)-1,3,4-thiadiazole derivative has their ability to elicit the tomato defence responses against Verticillium wilt and crown gall diseases.

Yamina Baba Ahmed[86] *et al.* Reported the the effect of 2,5-bis(2-pyridyl)-1,3,4-thiadizole on T-lymphocyte proliferation (Th-1 and Th-2)cytokine secretion and the intracellular oxidant/anti –oxidant status.

Mathew, Bijo[87] *et al.* concentrated on synthesis of Schiff bases of 5-Ph substituted, 2-amino 1, 3, 4 thiadiazoles as effective anthelmentics.

Byrd, Chelsea M.[88] *et al.* Reported synthesis of thienopyridine derivatives (I) as preventors of dengue virus infection.



(I)

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