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A Review on Chemistry and Biological Activities of Thiadiazole Derivatives

Harinder Kaur[1]*, Harmandeep Kaur[1], Payal Chawla[1], Amit Chawla[1], U.S. Baghel[1]

1. Khalsa College of Pharmacy, Amritsar,

ABSTRACT

Several five membered aromatic systems having three heteroatoms at symmetrical positions such as thiadiazoles have been studied extensively owing to their interesting pharmacological activities. Compounds containing thiadiazole moiety possess interesting biological activity due to strong aromaticity of this ring system that leads to great in vivo stability and lack toxicity. Thiadiazoles are an important class of heterocyclic compounds that exhibit diverse applications in organic synthesis, pharmaceutical and biological applications that exhibits a wide variety of biological activities like antimicrobial, anti-inflammatory activity, antitubercular activity, antidiabetic activity, diuretics, antidepressant & cytotoxic activity. Modification of the thiadiazole ring has proven highly effective with improved potency and lesser toxicity. The present review highlights the recently synthesized thiadiazole possessing important biological activities.

Keywords: Thiadiazole ring, Antitubercular activity, Antidiabetic activity

*Corresponding Author Email: amitchawla84@gmail.com

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INTRODUCTION

In the last few decades, the chemistry of five membered heterocyclic rings has received considerable attention owing to their synthetic and effective biological importance. Nitrogen containing heterocyclic systems has been attracting increasing interest over the past decade because of their utility in various applications. Thiadiazole is a versatile moiety that exhibits a wide variety of biological activities. Thiadiazole moiety acts as "hydrogen binding domain" and "two-electron donor system". It also acts as a constrained pharmacophore.[1,2] There are four isomeric forms of thiadiazole 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 1,3,5 Thiadiazole

Although currently the only commercial 1,2,4- thiadiazole drug present is the antibiotic cefozopram, there are a number of synthetic products related to this system with a broad range of biological activities such as antiinflammatory, antitubercular , antifungiastic, antibacterial , antitumoural ,anticonvulsant , antileishmanial , antidepressant , antioxidant activity.[3]

Pharmacological Activities of Five Membered Heterocylic Rings

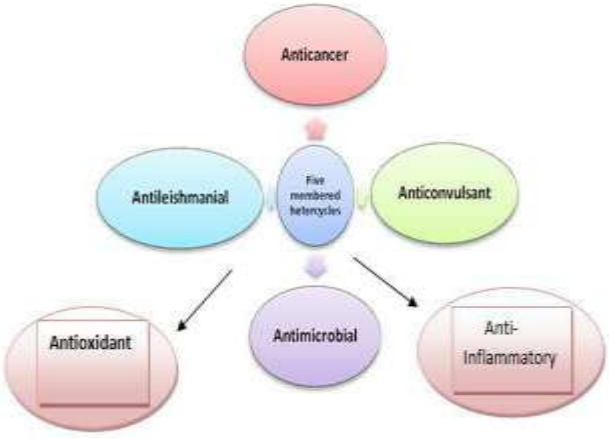


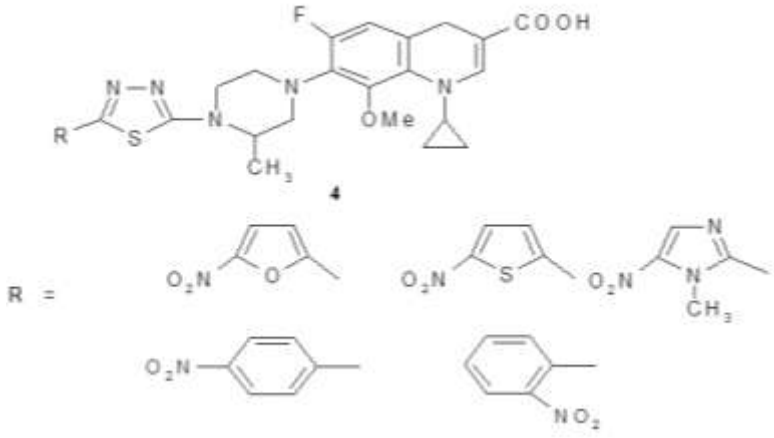
Figure 1. Various pharmacological activities of five membered rings.

This review provides a brief summary of the medicinal chemistry of thiadiazole system and highlights some examples of recent drug containing these moieties in the current literature.

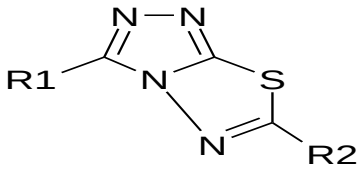
Antimicrobial Activity

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 synthesized compounds, nitrofuran analog exhibited more potent inhibitory activity against Gram-positive bacteria including *Staphylococcus epidermidis*, *Bacillus subtilis*, *Enterococcus faecalis* and *Micrococcus luteus* with respect to other synthesized compounds and reference drug gatifloxacin.[4]



Some of the novel condensed heterocyclic 4, 6-disubstituted-1,2,4-triazolo-1,3,4-thiadiazole derivatives were synthesized and checked for their efficacy as antibacterial in vitro. Compounds **5b**, **5c** and **5d** showed significant inhibition against all the strains tested, when compared to standard drugs.[5]

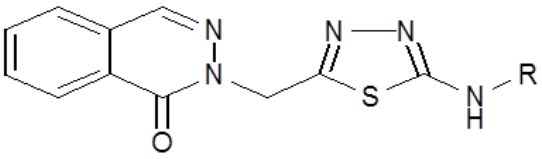


5(a-j)

	R1	R2
5a	$-CH_3$	$-2-Cl-C_6H_5$
5b	$-C_2H_5$	$-2-Cl-C_6H_5$
5c	$-C_6H_5$	$-2-Cl-C_6H_5$
5d	$-4-Cl-C_6H_4$	$-2-Cl-C_6H_5$
5e	$-4-CH_3-C_6H_4$	$-2-Cl-C_6H_5$
5f	$-CH_3$	$-CH_3(C_3H_7)$
5g	$-C_2H_5$	$-CH_3(C_3H_7)$
5h	$-C_6H_5$	$-CH_3(C_3H_7)$
5i	$-4-Cl-C_6H_5$	$-CH_3(C_3H_7)$
5j	$-4-CH_3-C_6H_4$	$-CH_3(C_3H_7)$

Some new 2-[[1(2*H*)-phthalazinone-2-yl] methyl/ethyl]-5-aryl amino-1,3,4-thiadiazole derivatives were synthesized with promised antimicrobial activity. Antimicrobial properties of the titled compounds were investigated against two Gram-positive bacteria (*S. aureus* and *B.*

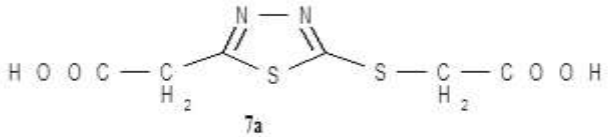
subtilis), two Gram-negative bacteria (*P. aeruginosa*, *E. coli*) and two yeast-like fungi (*C. albicans* and *C. parapsilosis*). Generally the compounds were found to be active against *B. subtilis* and the fungi.[6]



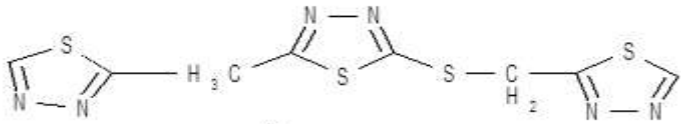
R = phenyl , benzyl, phenethyl, 4-Chlorophenyl, 4-methylphenyl, 4-methoxyphenyl

6

Successful synthesis of some new 2,5- (dithioacetic acid)- 1,3,4- thiadiazole **7a** and 2,5 di – (5-amino -1,3,4 – thiadiazole-2- thiomethyl) – 1,3,4 – thiadiazole **7b** which were screened for their invitro antibacterial activities against gram positive (*S. aureus , S. cervisiae and C. diptheriae*) and gram negative (*E.coli and P. aeruginosa)* bacteria.[7]

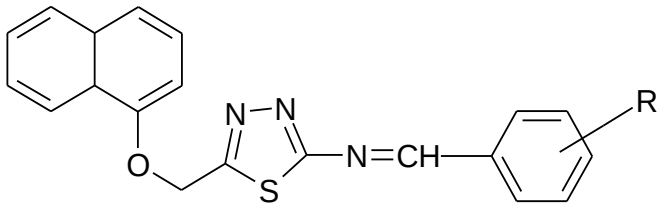


7a



7b

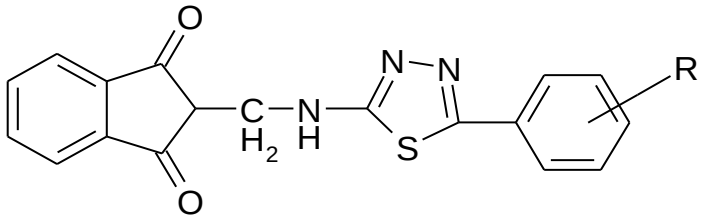
A series of new 2- (substituted benzalamino)- 5- (8 – quinolinoxy methyl) – 1,3,4 – thiadiazole were synthesized as antimicrobial agents . Compound **8g** (R = 4-NO_2) has maximum inhibitory efficiency against four strains of bacteria followed by compound **8f** (R= 2-Cl). Rest of the compounds was mild to moderately effective.[8]



8

R = 3- OCH_3 4-OH, 2- OH, 4- OCH_3, 3- OCH_3 4-OCH_3, 4- N-N- dimethyl, 2-Cl, 4- NO_2, -H 2-[(1',3'-dioxo-1',3'-dihydro-(2'H)-isoindol-2'-yl)- amino methyl]-5 aryl/(2''/3''/4''/3'',5''-substituted aryl)- 1,3,4-thiadiazoles **9(a-i)** compounds were synthesized and screened for their antimicrobial activity. Antimicrobial screening of the title compounds was done following the

disc diffusion technique. All the compounds were screened for their in vitro antibacterial activity against *E. coli, S. auerus* and *S. typhi* at 250 µg/disc with Streptomycin as the standard drugs. Antifungal activity was conducted against *Aspergillus niger, Penicillium sp.* and *Candida albicans* at a concentration of 500 µg/disc using Gentamycin as the standard drug. The zone of inhibition was recorded in mm after incubation of plates for 24 hrs. (antibacterial) and 72 hrs. (antifungal) at 37 °C.[9]

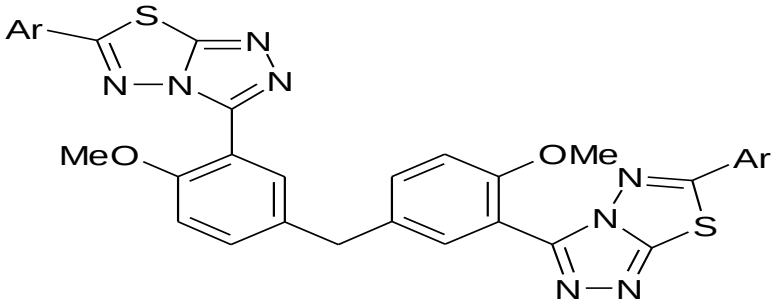


9(a-l)

9 a) R=H, b) R=2-Cl, c) R=3-Cl, d) R=4-Cl,e) R=2-Br, f) R=3-Br, g) R=2-NO2, h) R=3-NO2, i) R=4-NO2, j) R=3,5-NO2,k) R=4-OH l) R=3,5-OH.

Antifungal Activity

Bis [4-methoxy-3-[4-amino-5-sulfanyl-4*H*-1,2,4-triazol-3- yl]phenyl] methane compounds were synthesized and were evaluated for their antifungal activity against various fungal strains.



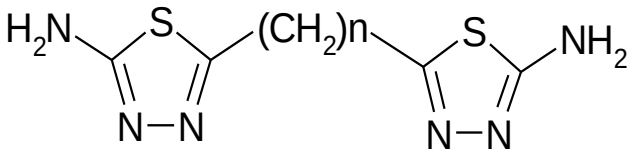
10(a-l)

Ar = a) phenyl; b) 2-chlorophenyl; c) 4-chlorophenyl; d) 4-methylphenyl; e)4-hydroxyphenyl; f) 4- methoxyphenyl; g) 3-nitrophenyl; h) 4-nitrophenyl; i) benzyl; j) 4-chlorobenzyl; k) 3-pyridyl; l) 2- pyrazinyl

Compounds **10(a-l)** were also evaluated *in vitro* antifungal activity against four fungi *viz. Candida albicans* (ATCC 10231), *Aspergillus fumigatus* (HIC 6094), *Trichophyton rubrum* (IFO 9185) and *Trichophyton mentagrophytes* (IFO 40996) by agar diffusion method. For the antifungal assay Sabourands agar media was used. Results of antifungal activity showed that most of the new **10(a–l)** were active with moderate to good activity. The compounds **10k** and **10l** bearing heterocyclic ring on the carbon of N–C–S fragment of the thiadiazole ring showed

highest activity against all the fungi tested. The activity of these compounds is almost equal to the standard. Compounds **10h** and **10i** bearing 4-nitrophenyl and benzyl moieties also showed good inhibition towards *A. fumigatus* and *T. mentagrophytes.*[10]

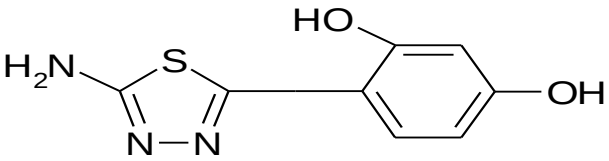
A series of eight novel 1,3,4 thiadiazole- 2 – amine **11(a-h)** derivatives were synthesized and investigated for invitro antifungal activity against various fungal strains S. cervisiae , A. niger , C. albicans. It shows that compound **11a**, **11e**, **11f**, **11h** exhibited antifungal activity.[11]



11(a-h)

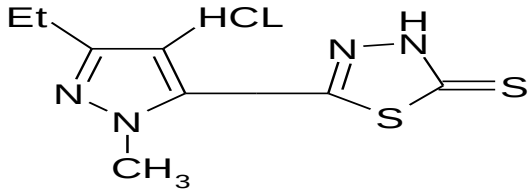
n = 1, 2, 3…….8

A series of [2-(2, 4-Dihydroxyphenyl)-1, 3, 4- thiadiazole analogues were synthesized and evaluated them for their *in vitro* antifungal activity against *Candida nonalbicans* spp. than against *C. alhicans.* Some compounds exhibit higher activities than the comparatively studied antifungal drugs. 2-Amino-1, 3, 4- thiadiazole derivatives exhibited higher (than other analogues) antifungal effects.[12]

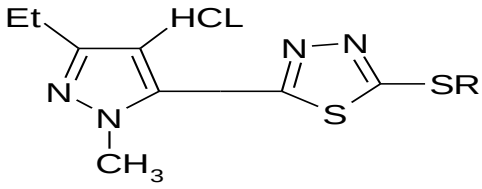


12

Pyrazolyl-Substituted 1, 3, 4-Thiadiazole derivative were synthesized for their antifungal avtivity.. The most active compound was 5-pyrazolyl-1,3,4-thiadiazole-2-thione **13a** and 2-alkylthio-5-pyrazolyl-1,3,4-thiadiazole **13b** and possess fungicidal activity against *Rhizoctonia solan (Sheath blight on rice).*[13]



13 a

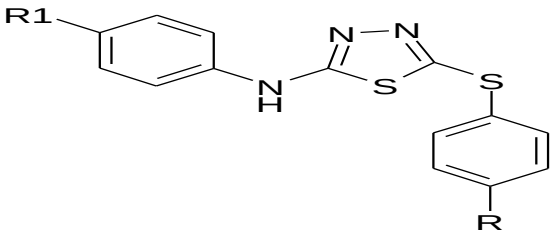


13b

Anti-Inflammatory Activity

A new series of selective cox-2 inhibitors with 2-amino-5-sulfanyl-1, 3, 4-thiadiazole Derivatives **14(a-d)** were synthesized. These compounds were selective inhibitiors of COX-2

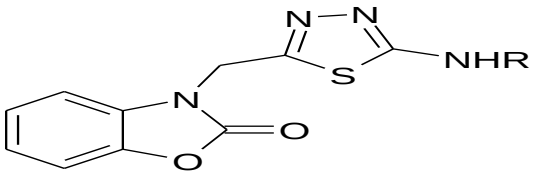
and potentiated the activity of COX-1 enzyme. The presence of sulphonamide group is a required pharmacophore for selective inhibition of COX-2 enzyme.[14]



14(a-d)

	R	R_1
a	-F	$-SO_2NH_2$
b	$-CH_3$	$-SO_2NH_2$
c	$-CF_3$	$-SO_2NH_2$
d	$-SO_2NH_2$	$-SO_2NH_2$

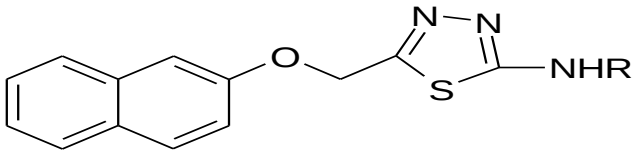
Various condensed 2-benzoxazolinone and substituted thiadiazoles were synthesized by and screened for anti-inflammatory activity. Compound with phenyl substituent possessed the most prominent and consistent anti-inflammatory activity. An increase in the anti-inflammatory activity was observed with replacement of alkyl chain to phenyl ring.[15]



15

R= $-CH_3$, $-C_2H_5$, $-C_6H_5$

2-(2-naphthyloxymethyl)-5-substitutedamino-1, 3, 4-thiadiazole derivatives was synthesized and evaluated for their anti-inflammatory activity by carrageenan hind-paw edema test. All the compounds were found to exhibit weak anti-inflammatory activity.[16]

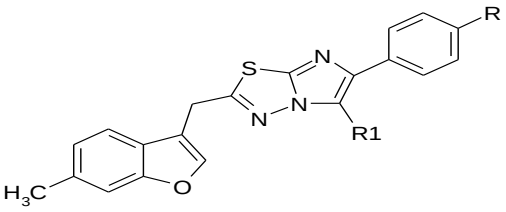


16

R= $-CH_3$, C_2H_5, $-CH_2CH=CH_2$, $-C_6H_5$

A series of 6-substituted and 5,6-disubstituted 2-(6-methyl-benzofuran-3-ylmethyl)-imidazo[2,1-b][1,3,4]thiadiazoles was synthesized and evaluated as anti-inflammatory agents. Amongst the substituents at R1, formyl and hydroxymethyl substituted compounds showed best

effects.[17]



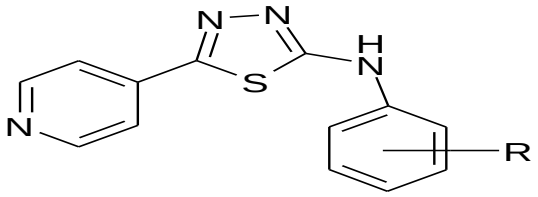
17

R= -Cl, -Br, -NO_2

R1= -H, -CHO, -CH_2OH, -CN, -N=OH

Anticonvulsant Activity

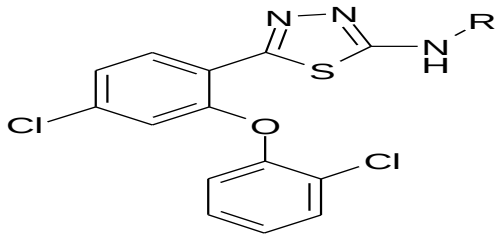
2-(Substituted phenyl) amino-5-(4-pyridyl)- 4H-1,3,4-thiadiazoles **18(a-f)** were synthesized with anticonvulsant activity. Anticonvulsant activity of the synthesized compounds was evaluated by MES method. All the compounds showed activity in the range of 33-100 % in comparison to phenytoin which completely inhibited the convulsions produced by electroconvulsometer in albino mice. Compound **18f** showed maximal activity whereas compound **18a** showed good activity.[18]



18(a-f)

R= a) H, b) *o*- CH3, c) *p*- CH3, d) *o*- OCH3, e) *p*- OCH3, f) *p*- Cl

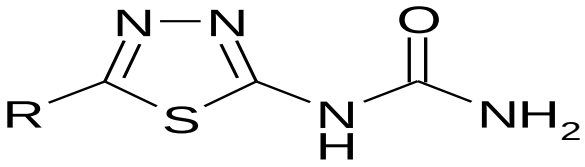
A number of 2-amino-5-(4-chloro-2-(2-chlorophenoxy) phenyl-1, 3, 4-thiadiazole derivatives **19(a-d)** were synthesized and tested for anticonvulsant activity. Compound 5-(4-chloro-2-(2-chlorophenoxy) phenyl)-N-ethyl-1, 3, 4-thiadia-zol-2-amine **19a** was the most active compound in both MES (ED_{50}=20.11) and PTZ (ED_{50}=35.33) tests.[19]



19(a-d)

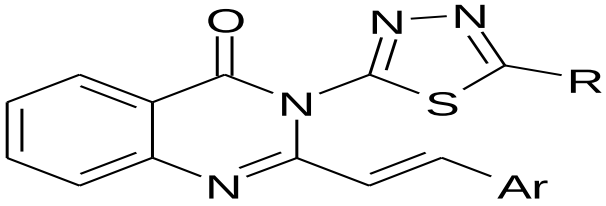
19a R= H, 19b R = Me, 19c R = Et, 19d R = Ph

1-(5-aryl-1, 3, 4-thiadiazol-2-yl) urea compounds are synthesized and were screened for their anticonvulsant activity by Pentylene Tetrazol Method (PTZ). Some of the synthesized compounds exhibited prominent anticonvulsant activity.[20]



20

Series of new 3-[5-substituted phenyl-1, 3, 4-thiadiazol-2-yl]-2-styryl quinazoline-4(3*H*)-ones were synthesized and evaluated for anticonvulsant activity. Compounds were examined in the maximal electroshock (MES) induced seizures and subcutaneous pentylenetetrazole (scPTZ)-induced seizure models. Compound showed good anticonvulsant activity in the test models.[21]



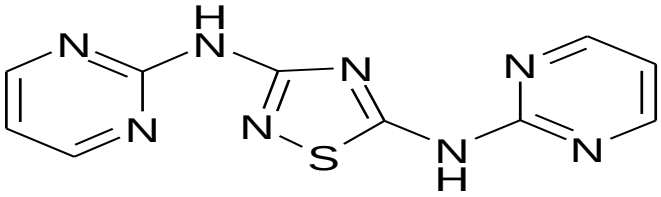
21(a-c)

a = R = C_6H_5; Ar =4 - Cl C_6H_4

b = R = 3 - Cl C_6H_4; Ar = 4 -Cl C_6H_4

c = R = 4 - Cl C_6H_4; Ar = Pyridyl

The synthesis of series of substituted 1, 2, 4-thiadiazoles and their anticonvulsant activity. Their study indicated that all the compounds showed protection against MES (maximal electroshock-induced seizures) screen after 0.5 h and was concluded that the synthesized compounds were potent against MES-induced seizures than ScPTZ induced and showed low potency as sedative-hypnotic agent which is advantageous.[22]

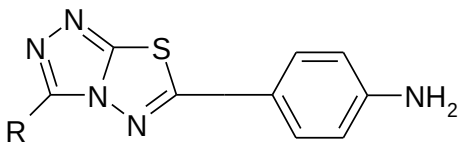


22

Anticancer Activity

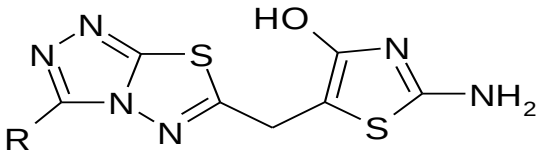
3, 6- disubstituted triazolo [3,4-b] thiadiazole derivatives was evaluated that compounds **23a** and **23b** maintained the highest growth inhibition activity at micromolar concentrations in different

human tumor cell lines. The compound **23a** 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 **23b** 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.[23]



23a

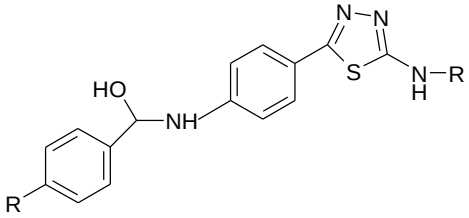
R = -CH_2O - Ph (p - Cl)



23b

R = - CH_2O - Ph (p-Cl)

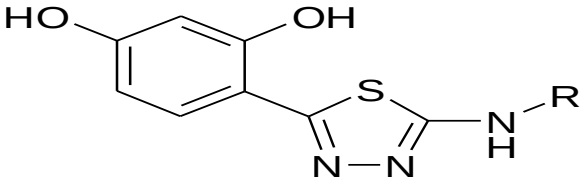
5-[-4-(4fluorobezoylolamino) phenyl]-2-subsitutedamino-1, 3, 4-thiadiazole derivatives were synthesized and evaluated for the cytotoxic activity.[24]



24

R = Ar

A series of N-substituted 2-amino-5-(2, 4-dihydroxyphenyl)-1,3,4-thiadiazoles were synthesized and evaluated for their antiproliferative activities against human cancer cell lines. The cytotoxicity in vitro against the four human cell lines: SW707 (rectal), HCV29T (bladder), A549 (lung), and T47D (breast) was determined. 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.[25]

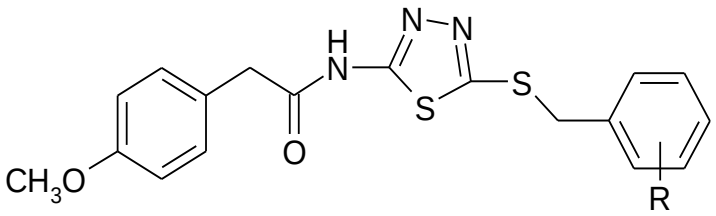


25

R = alkyl, aryl, morpholinoalkyl

A series of N-(5-Mercapto-1,3,4-thiadiazol-2-yl)-2-(4-methoxyphenyl) acetamide **26(a-l)** was synthesized. All compounds **26(a-l)** demonstrated a higher cytotoxic activity against MDA-MB-

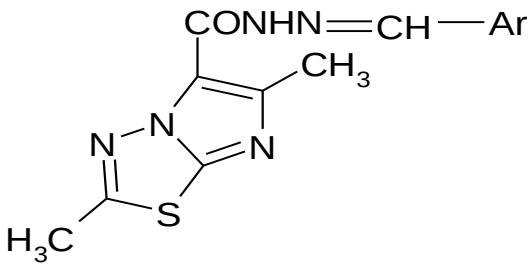
231 breast cancer cell line in comparison with other cell lines. Compounds **26h** (IC50= 11 ± 0.18 μM), **26j** (IC50= 10 ± 0.39 μM), **26k** (IC50= 11 ± 0.77 μM) and **26l** (IC50= 8 ± 0.69 μM) exhibited higher cytotoxic activity against MDA-MB-231 cell line compared to imatinib (IC50= 20 ± 0.69 μM) as the reference drug.[26]



26(a-l)

26a	2-Cl	26g	3-OCH3
26b	3-Cl	26h	4-OCH3
26c	4-Cl	26i	2-F
26d	2-NO2	26j	3-F
26e	3-NO2	26k	4-F
26f	4-NO2	26l	H

Some novel 2, 6-dimethyl-N'-substituted phenylmethylene-imidazo [2,1-b][1,3,4]thiadiazole-5-carbohydrazides were synthesized . The newly synthesized compounds **27(a-h)** were evaluated in the National Cancer Institute's 3-cell line, one dose in vitro primary cytotoxicity assay Compounds **27c** and **27 h** which passed the criteria for activity in this assay (20-29% growth percentages) were scheduled automatically for evaluation against the full panel of 60 human tumor cell lines at a minimum of five concentrations at 10- fold dilutions. 2, 6-Dimethyl-N'-(2-hydroxyphenylmethylidene)imidazo[2,1-b][1,3,4]thiadiazole-5 carbohydrazide **27 c** showed the most favorable cytotoxicity.[27]

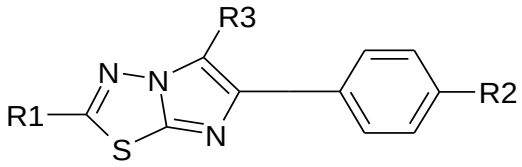


27(a-h)

27a	C_6H_5	27e	$4\text{-}BrC_6H_4$
27b	$4\text{-}CH_3C_6H_4$	27f	$4\text{-}ClC_6H_4$
27c	$2\text{-}HOC_6H_4$	27g	$4\text{-}FC_6H_4$
27d	$4\text{-}CH_3OC_6H_4$	27h	$4\text{-}NO_2C6H_4$

Antitubercular Activity

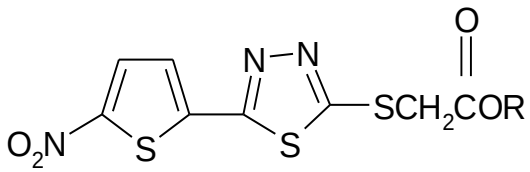
A series of 2,6- disubstituted and 2,5,6-trisubstituted imidazo [2,1- b][1,3,4] thiadiazole derivatives were synthesized. Compounds were screened for antitubercular activity against *Mycobacterium tuberc*ulosis H37Rv using the BACTEC 460 radiometric system, Compounds **28a** and **28b** exhibited moderate antitubercular activity with percentage inhibition 36, 30, respectively, at a MIC of >6.25 µg/ml.[28]



28(a-b)

	R1	R2	R3
28a	Cyclohexyl	-H	-CHO
28b	Cyclohexyl	-BR	-CHO

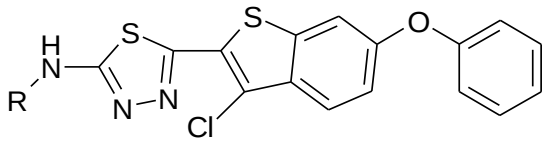
Series of alkyl a-[5-(5-nitro-2-thienyl)-1,3,4-thiadiazole-2- ylthio]acetic acid esters were evaluated for in vitro antituberculosis activity. The antituberculosis activity of the synthesized thiadiazole derivatives against *Mycobacterium tuberculosis* strain data indicated that methyl, propyl, buthyl 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).[29]



29(a-e)

29a	Methyl	29b	Ethyl
29c	n -Propyl	29d	n-Buthyl
29e	Benzyl		

1,3,4-thiadiazole derivatives bearing Benzo [b] thiophene nucleus were screened for antimicrobial activity against mycobacterium tuberculosis (H37 RV) .The antimycobacterial activity data were compared with standard drug Rifampin at 0.25 µg/ml concentration which showed 98% inhibition. Compounds having 2-(3′- chloro- 5′-phenoxy-benzo[b]thiophen-2′-yl)-5-(p methoxyphenyl) amino-1, 3, 4-thiadiazole derivatives showed higher activity than the others.[30]

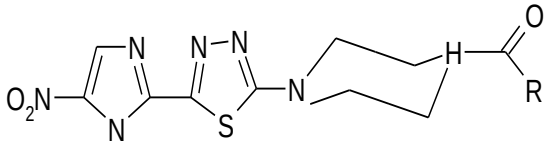


30

R = Aryl

Antileismanial Activity

Various Nitroimidazolyl-1, 2, 3-thiadiazole agents were evaluated for their antileishmanial activity against the promastigote form of *L. major* at non-cytotoxic concentrations. The anti-leishmanial screening was performed using direct counting and MTT assay. The most potent compounds against the promastigote form of *L. major* were found to be N-(5-chloro-thiophen-2-yl)carbonyl derivative **31f** and N-benzoyl analog **31a** with IC50 values of 9.35 ± 0.67 and 10.39 ±0.95 mM, respectively.[31]



31(a-g)

31a - Phenyl

31b -2-Cl-phenyl

31c -3-Cl-phenyl

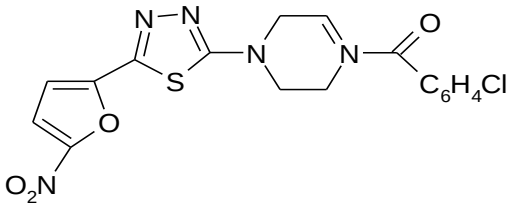
31d -4-Cl-phenyl

31e -Thiophen-2-yl

31f -5-Cl-thiophen-2-yl

31g -5-Br-thiophen-2-yl

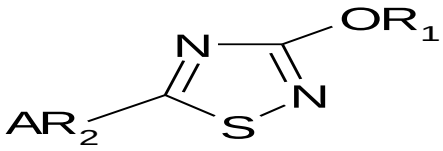
A series of 1-[5-(5-nitrofuran-2-yl)-1, 3, 4-thiadiazol-2-yl] and 1-[5-(5-nitrothiophen-2-yl)-1, 3, 4-thiadiazol-2-yl] - 4-aroylpiperazines and their in-vitro leishmanicidal activity was evaluated against promastigote and amastigote forms of *Leishmania*. It was concluded that 5-nitrofuran derivatives were more active than the corresponding 5- nitrothiophene analogues.[32]



32

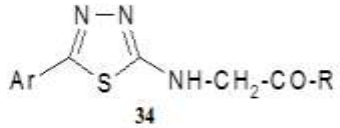
Antidiabetic Activity

A novel l, 2, 4-thiadiazole compound represented by the formula: 1, 2, 4-thiadiazole compound Wherein, R1 represents C3-C7 alkynyl that may be substituted with halogen; R2 represents C3-C8 cycloalkyl which may be substituted with C1-C4 alkyl, halogen atom and tritluoromethyl or the like; A represents a single bond, C1-C2 alkylene or C2-C3 alkylidene. The following sulfonylurea derivatives were synthesized and screened for antidiabetic activity.[33]

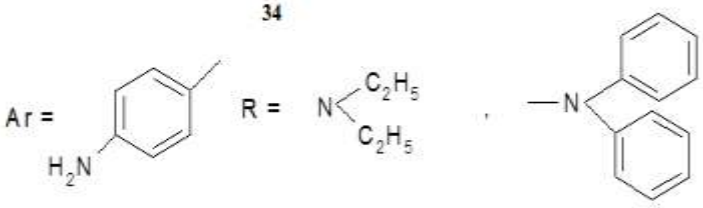


33

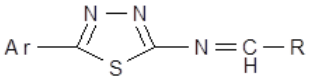
Some 1, 3, 4- thiadiazoles derivatives were synthesized and these compounds acts as a potential anti-diabetic agents.[34]



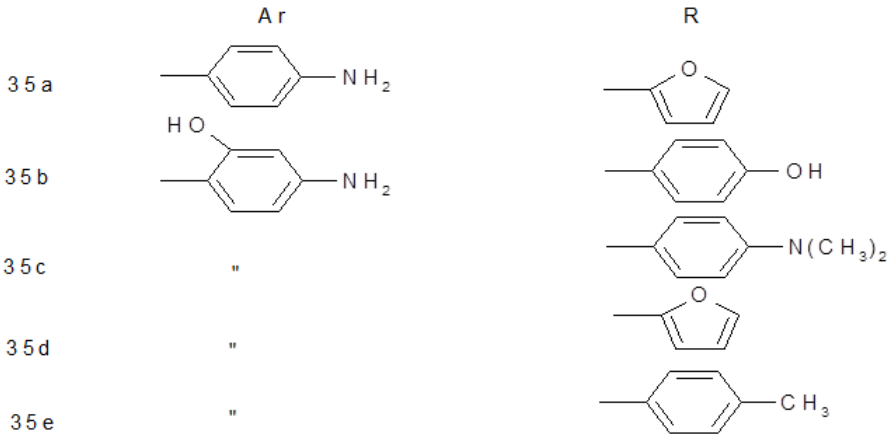
34



A new series of 1, 3, 4 thiadiazole derivatives were synthesized and evaluated for antidiabetic activity. All these compounds show significant antidiabetic activity. These results were calculated by measuring the mean SE ± and *'P'* value.[35]

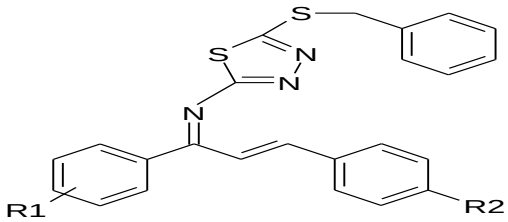


35



Antidepressant Activity

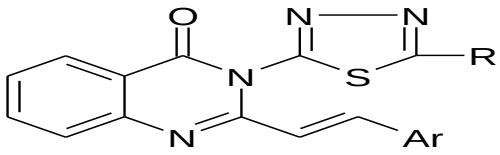
A number of new imine derivatives of 5-amino-1, 3, 4-thiadiazole-2-thiol, and their anti-depressant activity was tested using imipramine as reference drug. Two compounds namely 5-{[1-(4- chlorophenyl)-3-(4-methoxy-phenyl)prop-2-en-1-ylidene]-amino}- 5-benzylthio-1, 3,4 – thiadiazole **36a** and 5-{[1-(4-chlorophenyl)-3-(4-dimethyl-aminophenyl)-prop-2-en-1-ylidene]amino}-5-benzylthio-1,3,4-thiadiazole **36b** have shown significant anti-depressant activity, which decreased immobility time by 77.99% and 76.26% compared to the standard imipramine (82%).[36]



36

36a R1= OCH_3, R2=Cl, 36b R1= $(CH_3)_2N$, R2=Cl

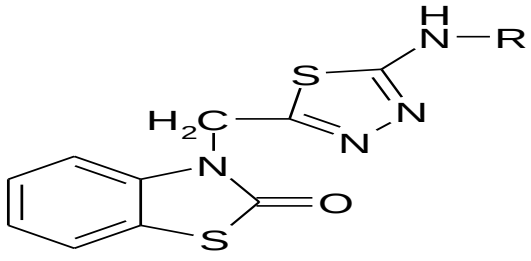
A series of novel 3-[5-substituted phenyl-1, 3, 4-thiadiazole-2-yl]-2-styryl quinazoline-4(3*H*)-ones were synthesized and evaluated for anticonvulsant, sedative-hypnotic and CNS depressant activities.[37]



37

Antihistaminic Activity

2-Oxobenzothiazoline derivatives bearing substituents at position 3 with thiadiazole moiety have reported to exhibit antihistaminic activity. Compounds **38a, 38b, 38d, 38e** and **38h** were more potent than others and the standards in tail flick test.[38]

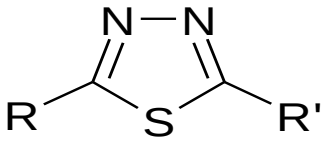


38(a-j)

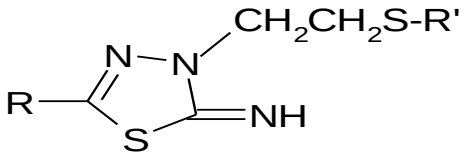
38a. methyl, 38 b. ethyl, 38 c. allyl, 38d. cyclohexyl, 38 e. phenethyl, 38f. phenyl, 38 g. 4-methylphenyl, 38 h. 4-clorophenyl, 38 i. 4-methoxyphenyl, 38 j. 4-nitrophenyl.

Radioprotective Activity

Thiol and aminothiol compounds are among the most efficient chemical radioprotectors. Synthesized thiol and aminothiol compounds derived from thiadiazole structures **39a**, **39b** examined for their ability to scavenge free radicals (DPPH·, ABTS·+, ·OH). Thiol derivatives with a thiadiazole structure are the most active compounds scavenging DPPH· and ABTS·+ free radicals, with an IC50 of 0.053 ± 0.006 and 0.023 ± 0.002 mM, respectively, for the derivative 39a. Moreover compound **39a** at 60 mM gave 83% protection against 2- deoxyribose degradation by ·OH. In both the test thiol derivatives were most efficient. Compound **39a** totally inhibits DNA strand breaks at the concentration of 50 mM.[39]



39a

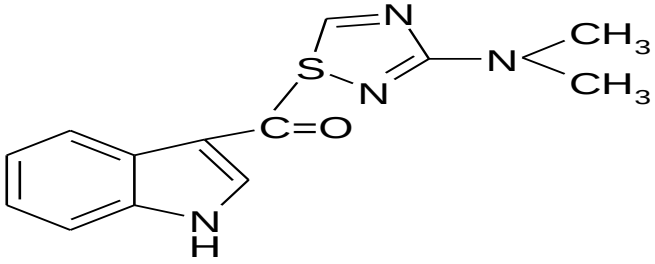


39b

R = -SCH_2CH_3, -CH_2CH_3 R'= -SH, -$NHCH_2CH_2SH$ R = -SCH_2CH_3, -CH_2CH_3, R'= -SO_3H, -$PO(OH)_2$

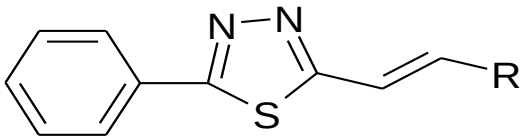
Antioxidant Activity

Dendrodoine (5-[(3-N-dimethylamino)-1, 2, 4- thiadiazolyl]-3-indanyl methanone) is an alkaloid extracted from the marine algae Dendrodoa grossularia. It possesses a 1, 2, 4- thiadiazole unit, a rarity among natural products. It is use as antioxidant.[40]



40

2-arylamino-5-phenyl 1,3,4- thiadiazole derivatives were synthesized and screened for in vitro antioxidant activity by various methods as Scavenging of hydrogen peroxide, Scavenging of nitric oxide radical, Lipid peroxidation inhibitory activity. Compounds **41b** and **41a** have shown more promising antioxidant activity as compare to standard, ascorbic acid.[41]



41

41a = 4-F-C_6H_4, 41b = 4-OH-C_6H_4

CONCLUSION

This review indicates a wide spectrum of pharmacological activities exhibited by various thiadiazoles derivatives. Various research subscribed in this review exhibiting 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 establishing slight alterations in the structure of thiadiazole compounds that would lead to drastic changes to yield better drug. The importance of thiadiazole moiety can be magnified by carrying out further studies on its possible substitution. The review article will be fruitful base for further development of better medicinal agents for the researchers across the world.

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