A REVIEW ON 1, 3, 4-THIADIAZOLE DERIVATIVES

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ABSTRACT

1,3,4-thiadiazole nucleus is a versatile nucleus. It has attracted the attention of medicinal chemists in the development of newer compounds in the recent years at a large scale. This nucleus exhibits a wide variety of biological activities. The main activities include anticancer, antimicrobial, anti-inflammatory, anti-oxidant, anti-HIV, anti-tubercular, anti-carbonic anhydrase etc. This nucleus due to presence of three heteroatoms acts as a hydrogen binding domain and consists of two electron donor systems. Various substitutions on this nucleus and condensation of this nucleus with other compounds leads two newer compounds with modified activity. In the present review we have presented the various methods of synthesis of 1,3,4-thiadiazole derivatives along with their biological activities.

Keywords: Thiadiazole, Biological activities, Heterocyclic compounds.

INTRODUCTION

Heterocyclic compounds are cyclic compound with the ring containing carbon and other element, the component being oxygen, nitrogen and sulphur. The simplest of the five membered heterocyclic compounds are pyrrole, furan and thiophene, each of which contains single heteroatoms. The five membered ring containing more than one or two heteroatoms also such as azole, pyrrole, thiazole, thiadiazole, oxadiazole, triazene etc. Thiadiazole is a heterocyclic compound featuring both two nitrogen atom and one sulfur atom as part of the aromatic five-membered ring. Thiadiazole and related compounds are called 1, 3, 4-thiadiazole (two nitrogen and one other heteroatom in a five-membered ring). Thiadiazole and related compounds are called 1, 3, 4-thiadiazole (two nitrogen and one other heteroatom in a five-membered ring). They occur in nature in four isomeric forms as. 1,2,3-thiadiazole; 1,2,5-thiadiazole; 1,2,4-thiadiazole and 1,3,4-thiadiazole. 1, 3, 4-thiadiazole isomer of thiadiazole series and its dihydro-derivatives provide a bulk of literature on thiadiazole.

Thiadiazole

Thiadiazole is a versatile moiety that exhibits a wide variety of biological activities. It acts as “hydrogen binding domain” and “two electron donor system” with a constrained pharmacophore. Many drugs containing thiadiazole nucleus are available in the market such as acetazolamide, methazolamide, sulfamethazol, etc. Thiadiazole can act as the bio-isosteric replacement of thiazole moiety. So it act like third and fourth generation cephalosporins. Hence can be used in antibiotic preparations. Thiadiazole is 5-membered ring system containing two nitrogen and one sulphar atom. They occur in nature in four isomeric forms viz. 1, 2, 3-thiadiazole; 1, 2, 5-thiadiazole; 1, 2, 4-thiadiazole and 1, 3, 4-thiadiazole. The 1, 3, 4-thiadiazole isomer of thiadiazole series and its dihydro-derivatives provide a bulk of literature on thiadiazole.

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1,3,4–Thiadiazole

It represents an important heterocyclic system due to their pharmacological activities and are associated with diverse biocidal activities probably by virtue of toxophoric -N=C-S grouping [5]. The thiadiazoles have occupied an important place in drug industry. It has wide applications in many fields. The earliest uses were in the pharmaceutical area as in antibacterial with known sulphonamide drugs. These compounds possess such interesting biological properties that may be conferred to them by their strong aromatic ring system. As ligands they also provide many potential binding sites for complexation and have obtained a diversified biological activity [6].

Synthetic Review of Various 1,3,4-thiadiazole Derivatives

Rakesh Yadav et al has reported the reactions of reactions of biphenyl carboxylic acid with thiosemicarbazide in the presence of phosphorous oxychloride resulted in biphenyl containing 2-amino-1,3,4-thiadiazole(5) which is then further subjected to condensation with α-bromoarylketone under reflux in dry ethanol. The structures of the newly synthesised compounds were characterized by various spectral techniques [7].

![Synthetic Review of Various 1,3,4-thiadiazole Derivatives](image)

Yusuf M et al reported the synthesis of 5-amino-1,3,4-thiadiazole-2-thiol imines and thio benzyl. This route was based upon the preparation of 5-amino-1,3,4-thiadiazole-2-thiol (6) by the addition of carbon disulfide (7) to thiosemicarbazide (8) under reflux. Compound (9) was prepared in single step by addition of different chalcones to 2-amino-5-mercaptop-1,3,4-thiadiazoles under reflux for 5 to 8 hrs. Compound (9) was refluxed with ethanolic alkali to give the desired (10) and (11) [8].

![Synthetic Reaction](image)

**Reagents and conditions:** (a) reflux for 4 hrs. (b) reflux for 5-8 hrs, chalcones (c) (chloromethyl)benzene (d) 1-chloro-4-(chloromethyl)benzene

**Compound:** 10a R=H, R’=H; 10b R= Cl, R’= OCH3; 10c R=Cl, R’=Cl; 10d R=OH, R’=Cl;

11a R=H, R’=H; 11b R=Cl, R’=OCH3; 11c R=Cl, R’=Cl; 11d R=OH, R’=Cl.

Alegaon, S.G. et al reported the synthesis of imidazo[2,1-b][1,3,4]thiadiazoloderivatives. The starting material 2-amino-5-[3,4,5-trimethoxyphenyl]-1,3,4-thiadiazole (12) was obtained by direct cyclization of 3,4,5-trimethoxy benzonic acid and thiosemicarbazide in the presence of phosphorous oxychloride, the latter being refluxed with substituted α-haloaryl ketones in dry ethanol resulting in imidazothiadiazoles(13). Vilsmeir –Haach reaction of (13) in dimethyl formamide and phosphorus oxychloride provided 6-aryl-2-(3,4,5-trimethoxyphenyl)imidazo[2,1-b][1,3,4]thiadiazole-5-carbalde hyde(14) which was further subjected to Knoevenagel condensation with 2-(2,4-dioxo thiiazolidin-3-yl)acetic acid and 2-(4-oxo-2-thioxothiazolidin-3-yl)acetic acid to gave the final product (15) and (16) respectively[9].

![Synthetic Reaction](image)

**Compounds:** 15-16a, R=H; 15-16b, R= 4-CH3; 15-16c, R=4-OCH3; 15-16d, R= 4-NO2; 15-16e, R= 4-NO2; 15-16f, R= 4-Br; 15-16g, R= 2,5(OCH3).
Pattan SR et al reported synthesis and biological evaluation of some 1, 3, 4-thiadiazole derivatives. A mixture of 2-thiadiazole series of 2,5,6-derivatives (19o) was refluxed for 1 hr and poured onto crushed ice.

The solid separated out was filtered, washed with water & recrystallized from ethanol [10].

![Reaction scheme](image)

Suresh Sharabassap et al have reported the synthesis of 2-(substituted aryl)-3-[5-(substituted phenyl)-1,3,4-thiadiazole]-4-oxo-thiazolidines (19).

All the synthesized compounds were analysed by IR, NMR and Mass Spectroscopy [11].

![Reaction scheme](image)

**Reagents and conditions:** (a) POCl$_3$, reflux for 4 hrs. (b) Ar-CHO, ethanol, reflux for 5 hrs. (c) SHCH$_2$COOH, ethanol, reflux for 6 hrs.

**Compounds:**
- 19a: R=4Cl-C$_6$H$_4$, Ar = 3NO$_2$-C$_6$H$_4$; 19b: R=4Cl-C$_6$H$_4$, Ar = 2,4Cl-C$_6$H$_4$;
- 19c: R= 4OCH$_3$-C$_6$H$_4$, Ar = C$_6$H$_5$; 19d: R=4OCH$_3$-C$_6$H$_4$, Ar =4OCH$_3$-C$_6$H$_4$;
- 19e: R= 4OCH$_3$-C$_6$H$_4$, Ar = 3NO$_2$-C$_6$H$_4$; 19f:R= 4OCH$_3$-C$_6$H$_4$, 4NO$_2$-C$_6$H$_4$;
- 19g:R=4F-C$_6$H$_4$, Ar =C$_6$H$_5$; 19h: R=4F-C$_6$H$_4$, Ar = 2,4Cl-C$_6$H$_4$;
- 19i:R= 4F-C$_6$H$_4$, Ar = 2,4Cl-C$_6$H$_4$; 19j: R=C$_6$H$_5$, Ar =C$_6$H$_5$;
- 19k: R=C$_6$H$_5$, Ar = 3NO$_2$-C$_6$H$_4$; 19l: R=C$_6$H$_5$, Ar = 2,4Cl-C$_6$H$_4$;
- 19m: R=C$_6$H$_5$, Ar = 4Cl-C$_6$H$_4$; 19n: R=4NO$_2$-C$_6$H$_4$, Ar = 4OCH$_3$-C$_6$H$_4$;
- 19o: 4NO$_2$-C$_6$H$_4$, 4NO$_2$-C$_6$H$_4$,

Malleshappa N. Noolvi et al have reported the synthesis of a series of 2,5,6-trisubstituted imidazo[2,1-b][1,3,4]-thiadiazole derivatives (20a-k which were prepared by reaction of 2-amino-5-cyclopropyl-1,3,4-thiadiazole and an appropriate phenacyl bromide. Further 5-bromo (21a-k and 5-thiocyanato (22a-k derivatives were synthesized [12].

Jadav VB et al has reported the synthesis of a series of 6-substituted and 5,6-disubstituted 2-(6-methylbenzofuran-3-ylmethyl)-imidazo[2,1-b][1,3,4]thiadiazoles. In this Benzofuran-3-acetic acid (23) is made to react with Thiosemicarbazide (24) to yield 5-(6-methylbenzofuran-3-
ylmethyl)-[1,3,4]thiadiazol-2-yl-amine (25). The imidazo[2,1-b][1,3,4]thiadiazole (27) was obtained by condensation of compound (25) with various α-bromaryl ketones (26) [13].

Reagents and conditions: (a) POCl₃, reflux, 30 min, KOH; (b) Dry EtOH, reflux, 24 h, Na₂CO₃; (c) Morpholine, HCHO, AcOH, MeOH, reflux, 8 h.

Compounds:
27a: R = Cl; 27b: R = Br; 27c: R = NO₂;
28a: R = Cl; 28b: R = Br; 28c: R = NO₂.

Jakhar A et al reported the synthesis of series of 2-substituted-6-(4-methyl-6-substituted cinnoline-3-yl)imidazo[2,1-b][1,3,4]thiadiazoles. Treatment of 3-(2-bromoacetyl) 4-methyl-6-substitutedcinnoline (29) with various 2-amino-5-substituted-1,3,4 thiadiazoles (30) in absolute ethanol as solvent resulted in final product 2-substituted-6-(4-methyl-6-substituted cinnoline-3-yl) imidazo[2,1-b][1,3,4]thiadiazoles (31) [14].

Kidwai M et al reported the green synthesis of substituted imidazothiadiazoles using ionic liquid. In this procedure ionic liquid [bmim] PF₆(1-butyl-3-methylimidazolium hexafluorophosphate) was used as recyclable catalyst. A mixture of α-bromoacetophenone (37) and 5-alkyl/aryl-1,3,4-thiadiazole (38) with sodium carbonate in ionic liquid[bmim]PF₆ was stirred at 60°C for appropriate time. After completion of reaction, the mixture was extracted with diethyl ether and further concentrated in vacuum to afford imidazo[2,1-b][1,3,4]thiadiazole (39) [16].
Reagents and conditions: (a) Sodium carbonate, ionic liquid [bmim]PF6, 60°C.

Compounds: 39a: R=C6H5, R’=H; 39b: R, R’=H; 39c: R=CH3, R’=H; 39d: R= n-C3H7, R’=H; 39e: R=C6H13, R’=H; 39f: R=4-CH3O,C6H5, R’=H; 39g: R= n-C6H13, R’=4-Cl; 39h: R= n-C6H13, R’= 4-Cl.

BIOLICAL REVIEW:

1. ANTIMICROBIAL ACTIVITY

Lamani R S et al reported the synthesis of novel methylene bridged benzisoxazolylimidazo[2,1-b][1,3,4]thiadiazoles. The newly synthesized compounds were screened for their anti-bacterial and antifungal activity using Agar Diffusion method. The antibacterial activity was screened against S. aureus, B. subtilis, P. aeruginosa and E. coli. The antifungal activity was screened against C.albicans and A. fumigates. The compounds (40a), (40b), (40c), (40d) and (40e) showed moderate to good bacterial inhibition, while the compounds (40b), (40f), (40g), (40h) and (40i) had shown good antifungal activity [17].

Compounds: 40a: R=Cl, R’=H; 40b: R=Br, R’=H; 40c: R=Cl, R’=Br; 40d: R= O-Me, R’=Br; 40e: R=Cl, R’=SCN; 40f: R= 3-coumarinyl, R’=H; 40g: R=O-Me, R’=SCN; 40h: R=H, R’=H; 40i: R= 3-coumarinyl, R’=SCN.

Guzeldemirici NU et al reported the synthesis of a series of 2-alkyl/arylamino-5-((6-(4-bromophenyl) imidazo[2,1-b] thiazol-3-yl) methyl)-1,3,4thiadiazoles. The synthesized compounds were evaluated for in vitro antibacterial activity against S. aureus, P. aeruginosa and E. coli as well as for antifungal activity against C. albicans, C. parapsilosis, C. krusei, T. mentagrophytes, M. gypseum and T. tonsurans using Micro-broth dilution method. Compounds (41a) and (41b) showed the highest activity against T. tonsurans and E. coli respectively. The most active compound was (41c) which has phenylamino group at the 2nd position of the thiadiazole ring [18].

Compounds: 41a: R=CH3; 41b: R= C6H5; 41c: R= C6H5.

Jahkar A et al reported the synthesis of 2-substituted-6-(4-methyl-6-substitutedcinnoline-3-yl)imidazo[2,1-b][1,3,4]thiadiazoles (42). All the synthesized compounds were screened for their antibacterial activity against both gram negative bacteria viz. Escherichia coli, Pseudomonas aeruginosa, Klebsellapneumoniae, Salmonella typhii and one gram positive bacteria viz. Staphylococcus aureus using Muller-Hilton medium. All the tested compounds showed good activity against both gram negative bacteria viz. Escherichia coli, Pseudomonas aeruginosa, Klebsellapneumonia, while against Salmonella typhii compounds (42c-h) and (42k) showed moderate activity. Against gram positive bacteria viz. Staphylococcus aureus only compound (42a) and (42d) showed moderate activity which had aliphatic substitution on thiadiazole ring [19].

Compounds: 42a: R’=H, C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 42b: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 42c: R’=H, C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 42d: R’=H, C6H5, 2-ClC6H4, 4-ClC6H4; 42e: R’=H, C6H5, 2-ClC6H4, 4-ClC6H4; 42f: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 42g: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 42h: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 42i: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 42j: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 42k: R’=H, C6H5, C6H5, 2-ClC6H4, 4-ClC6H4.

Gadad AK et al reported the synthesis of 5-guanylhydrozone/thiocyanoato-6-aryl imidazo[2,1-b][1,3,4]thiadiazole-2-sulfonamide derivatives. Cup Plate method using Mueller Hinton agar medium was employed to study the antibacterial activity of synthesized compounds against E. coli, S. aureus, P. aeruginosa, S. typhi and pneumo- cocci. Compounds (43a), (43b), (43c), (43d) and (43e) has showed good antibacterial activity. The presence of a 5-guanylhydrozone and 5-thiocyanato groups on the com- pounds resulted in producing good antibacterial activity [20].

Compounds: 43a: R’=H, C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 43b: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 43c: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 43d: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4; 43e: R’=C6H5, C6H5, 2-ClC6H4, 4-ClC6H4.
Compounds: 43a: 

\[ R=\text{p-(Cl)} C_6 H_4 , R'==2- \text{methyl} \text{ene} \text{hydrazine} \text{carboximidamide}, \]

\[ R''=\text{SO}_2 \text{NCHN(C}_3 H_2 \text{)}_2 \text{43b:} R=\text{p-(Br)} C_6 H_4 , R'==2- \text{methylene} \text{hydrazine} \text{carboxim} \text{idamide}, \]

\[ R''=\text{SO}_2 \text{NCHN(C}_3 H_2 \text{)}_2 \text{43c:} R=\text{p-(Cl)} C_6 H_4 , R'=\text{SCN}, R''=\text{SO}_2 \text{NH}_2 \text{43d:} R=\text{p-(Br)} C_6 H_4 , R'=\text{SCN}, R''=\text{SO}_2 \text{NH}_2 \text{43e:} R=\text{p-(NO}_2 \text{)} C_6 H_4 , R'=\text{SCN}, R''=\text{SO}_2 \text{NH}_2 . \]

2. ANTI-TUBERCULAR ACTIVITY

Sathe SB et al reported the synthesis of N-[5-(1-amino-2-phenylethyl)-1,3,4-thia diazole zol-2-yl]-6-fluoro-7-substituted1,3-benzothiazol-2-amine. The antitubercular activity of synthesized compounds was assessed against Mycobacterium tuberculosis H$_3$7Rv in BACTEC medium. Compounds (54a), (54b), (54c), (54d), (54e), (54f) and (54g) have shown good antitubercular activity [21].

Compounds: 54a: 

\[ R=\text{o-NO}_2 ; \]

\[ 54b: R=\text{m-NO}_2 ; \]

\[ 54c: R=\text{p-NO}_2 ; \]

\[ 54d: R=\text{O-CH}_3 ; \]

\[ 54e: R=\text{m-OCH}_3 ; \]

\[ 54f: R=\text{p-OCH}_3 ; \]

\[ 54g: R=\text{o-Cl}. \]

Kolavi, G. et al. reported the synthesis of a series of 2,6-disubstituted and 2,5,6-trisubstitutedimidazo[2,1-b][1,3,4]thiadiazole. The structure of the compounds were elucidated and screened for antitubercular activity against Mycobacterium tuberculosis H$_3$7Rv using the BACTEC 460 radiometric system and broth dilution assays. Compound (55c) and (55d) has shown the highest (100%) inhibitory activity. The in vitro anti-tubercular activity reports of compounds (55a), (55b), (55e), and (55f) against M. tuberculosis strain H$_3$7Rv showed moderate activity at MIC of $\geq 6.25 \mu g/ml$ [22].

Compounds: 55a: 

\[ R=\text{Cyclohexyl}, R'=\text{H}, R''=\text{CHO}; \]

\[ 55b: R=\text{Cyclohexyl}, R'=\text{Br}, R''=\text{CHO}; \]

\[ 55c: R=\text{2-Furyl}, R'=\text{H}, R''=\text{CHO}; \]

\[ 55d: R=\text{Cyclohexyl}, R'=\text{H}, R''=\text{CH}_3 \text{OH}; \]

\[ 55e: R=\text{2-Furyl}, R'=\text{H}, R''=\text{CH}_3 \text{OH}; \]

\[ 55f: R=\text{Cyclohexyl}, R'=\text{H}, R''=\text{CH}=\text{NOH}. \]

Vasoya SL et al reported the synthesis of 2-(3’-chloro-5’-phenoxybenzo [b] thiophen-2’-yl)-5-arylamino-1,3,4-thiadiazole. Antitubercular activity of synthesized compounds was evaluated at 6.25µg/ml concentration against Mycobacterium tuberculosis H$_3$7Rv in BACTEC 12B medium using the ALAMAR radiometric system. Compounds (56a), (56b), (56c), (56d) showed 29, 60, 60 and 91 percentage inhibition respectively. Compounds having 2- methyl, 2- methoxy substitutions showed higher activity than the other derivatives [23].

Compounds: 56a: 

\[ R=\text{4-(Cl)} C_6 H_4 ; \]

\[ 56b: R=\text{2-(CH}_3 \text{)} C_6 H_4 ; \]

\[ 56c: R=\text{2-(OCH}_3 \text{)} C_6 H_4 ; \]

\[ 56d: R=\text{4-(OCH}_3 \text{)} C_6 H_4 . \]

3. ANTI-CANCER ACTIVITY

Terzioglu N et al reported the synthesis of novel 2,6-dimethyl-N-substituted phenyl methylene-imidazo[2,1-b][1,3,4]thiadiazole-5-carboxhydrazides 58(a-h). The newly synthesized compounds were evaluated in the National Cancer Institute’s 3-cell line, one dose in vitro primary cytotoxicity assay. Compounds (58c) and (58h) passed the criteria for activity in this assay (20-29% growth percentage) and 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 [24].

Compounds: 58a: 

\[ \text{Ar}=\text{C}_6 \text{H}_4 ; \]

\[ 58b: \text{Ar}=\text{4-(CH}_3 \text{)} C_6 \text{H}_4 ; \]

\[ 58c: \text{Ar}=\text{2-(OH)} C_6 \text{H}_4 ; \]

\[ 58d: \text{Ar}=\text{4-CH}_3 \text{OC}_6 \text{H}_4 ; \]

\[ 58e: \text{Ar}=\text{4-(Br)} C_6 \text{H}_4 ; \]

\[ 58f: \text{Ar}=\text{4-(Cl)} C_6 \text{H}_4 ; \]

\[ 58h: \text{Ar}=\text{4-(NO}_2 \text{)} C_6 \text{H}_4 . \]

Karki, S.S. et al., reported the synthesis of novel 2-aralkyl-5-substituted-6-(4’-fluro phenyl)-imidazo[2,1-b][1,3,4]thiadiazole. The newly synthesized compounds 59(a-n) were screened for anticancer activity on human T-cell leukemia cell line, CEM. CEM cells were treated with increasing concentration of compounds (10, 50,100 and 250 µM) and cell viability was determined by Trypan blue assay. Compound (59b),(59j) and (59m) induced maximum toxicity on leukemia cells while the effect was moderate with (59a),(59c), (59h), (59j) and (59m) and the compounds (59b),(59d), (59f) and (59g) were least...
sensitive. The cell proliferation effect of synthesized compounds was further tested using MIT assay and results showed that the compound (59j) has maximum cytotoxicity with an IC_{50} value of ~ 8µM[25].

**Compounds:** 59a: R= H, R’=SCN; 59b: R= Cl, R’= SCN; 59c: R= F, R’= SCN; 59d: R= Br, R’=SCN; 59e: R= CH₃, R’=SCN; 59f: R= R= H, R’=H; 59g: R= Cl, R’=H; 59h: R= F, R’= H; 59i: R= CH₃, R’= H; 59j: R= H, R’=Br; 59k: R= Cl, R’= Br; 59l: R= H, R’= CHO; 59m: R= Cl, R’=CHO; 59n: R= CH₃,R’= CHO.

Matysiak J et al reported a series of 5-substituted 2-(2,4-dihydroxyphenyl)-1,3,4-thia diazole and evaluated for their antiproliferative activity. The panel substitution included alkyl, alkoxy, aryl and heteroaryl derivatives. The highest activity was found with ID_{50} values comparable HCV39T and SW707 or significantly lower T47D than for cisplatin. Compounds (60a) and (60b) proved to be more active. The presence of another atom of high electronegativity in the vicinity of C-5 ring causes formation of a strong electron gap at this atom of carbon which may be essential in ligand–receptor inter actions[26].

**Compounds:** 60a: R= 4-(CH₃)₂C-C₆H₄; 60b: R= 4-OCH₃-C₆H₄-C₆H₄O.

**4. ANTI-INFLAMMATORY ACTIVITY**

Jadhav VB et al reported the synthesis of a series of 6-substituted and 5, 6-disubstituted 2-(6-methylbenzofuran-3-ylmethyl)-imidazo[2,1-b][1,3,4] thiadiazoles. The new compounds have been tested for their in vitro anti-inflammatory activity. Compound (62a) and (62b) showed good inhibition while the compound (62c) showed significant inhibition [27].

**Compounds:** 62a: R=Br, R’=H; 62b: R=NO₂, R’= H; 62c: R= Cl, R’= CN.

Gilani SJ et al reported the synthesis of a series of 6-substituted 1,2,4-triazolo-[3,4-b][1,3,4] thiadiazoles. The synthesized compounds were evaluated for their antiinflammatory activity using Ibuprofen as a reference compound. The compound (63a) showed the maximum inhibition while the compounds (63b) and (63c) showed decreased inhibition as compared to (63a)[28].

**Compounds:** 63a: R= 4(NO₂)C₆H₄; 63b: 2-(Cl)C₆H₄; 63c: R= 2-(OCOCH₃)C₆H₄.

Schenone S et al reported the synthesis of two series of N-[5-oxo-4-(arylsulfonyl)-4,5-dihydro-1,3,4-thiadiazol-2-yl]amides. The new compounds were tested in vivo for their anti-inflammatory activity in the carrageenan rat paw edema test, using Indomethacin as reference compound. Compound (64a) and (64b) were the most active while the compound (64c) and (64d) showed moderate activity[29].

**Compounds:** 64a: R=4-fluorophenyl; 64b: R=4-trifluorophenyl; 64c: R=4-methoxyphenyl; 64d: R= 2-furoyl.

**5. ANTI-HIV ACTIVITY**

Akhtar T et al reported the synthesis and anti-HIV activity of 2-substituted 5-(4 chlorophenylamino)-1,3,4-thia diazoles. The synthesized compounds were assayed against HIV-1 and HIV-2 strains in human T-lymphocytes MT-4 cells. The compound (65) was the most potent compound [30].
6. **Carbonic Anhydrase Inhibitor Activity**

Kasimogullari R et al reported the synthesis anti glaucoma activity of the novel pyrazole derivatives of 5-amino-1,3,4-thiadiazole-2-sulfonamide. The inhibitory effects of the synthesized compounds on hydratase and esterase activities of carbonic anhydrase isoenzymes (hCA-1 and hCA-11) have been studied in vitro. Compounds (66a), (66b) and (66c) had more inhibitory effect than the standard compound [31].

![Chemical Structure](66)

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**REFERENCES**