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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.

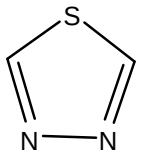
Keywords: Thiadiazole, Biological activities, Heterocyclic compounds.

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). 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 are important because of their versatile biological actions. In particular, compounds bearing the 1, 3, 4-thiadiazole nucleus is known to have unique antibacterial and anti-inflammatory activities. Differently substituted thiadiazole moieties have also been found to have other interesting activities such as analgesic, antimicrobial, anti-tubercular, anticonvulsant and anti-hepatitis B viral activities. In this review article different compounds having heterocyclic nucleus have been shown to possess different activity [1].

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, sulfamethazole, etc. Thiadiazole can act as the bio-isosteric replacement of thiazole moiety. So it act like third and fourth generationcephaelosporins. 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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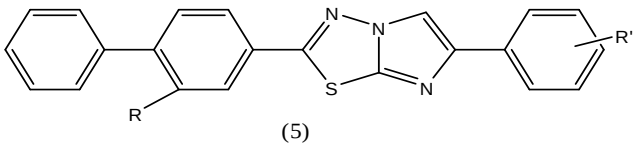
1,3,4 –Thiadiazole

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

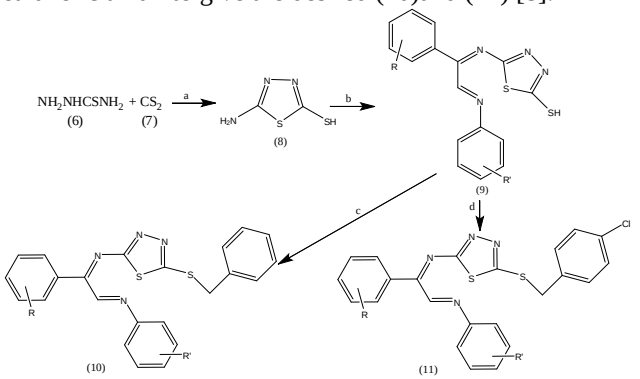
Rakesh Yadav et al has reported the reactions of reactions of biphenyl carboxylic acid with thiosemicarbazide in the presence of phosphorous oxychloride resulted in biphenyl containing 2-amino-1,3,4-thiadiazole**(5)** which is then further subjected to condensation with α-bromoarylketone under reflux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



(5)

R= H or F
R'=a:H; b:4'Cl; c:4'F; d: 2',4' diCl; e: 4'NH_2;
f: 2'4' diOH; g: 4'Br; h: 2'OH.

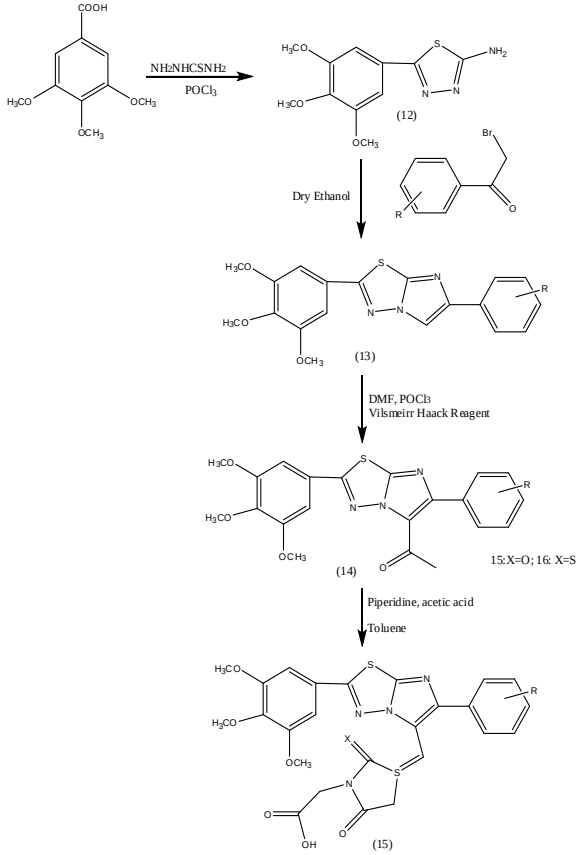
Yusuf M et al reported the synthesis of 5-amino-1,3,4-thiadiazole-2-thiol imines and thiobenzyl. This route was based upon the preparation of 5-amino-1,3,4-thiadiazole-2-thiol (6) by the addition of carbon disulfide (7) to thiosemicarbazide (8) under reflux. Compound (9) wasprepared in single step by addition of different chalcones to 2-amino-5-mercapto-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].



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

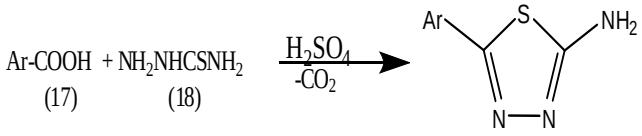
Compound:10a R=H, R'=H; 10b R= Cl, R'= OCH3; 10c R=Cl, R'=Cl; 10d R=OH. R'=Cl;
11a R=H, R'=H; 11b R=Cl, R'=OCH3; 11c R=Cl, R'= Cl; 11d R=OH,R'=Cl.

Alegaon, S.G. et al reported the synthesis of imidazo[2,1-b][1,3,4] thiadiazolederi- vatives.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 benzoic acid and thiosemi- carbazide in the presence of phosphorus 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 thiazolidin-3-yl)acetic acid and 2-(4-oxo-2-thioxothiazolidin-3-yl)acetic acid to gave the final product (15) and (16)respectively[9].

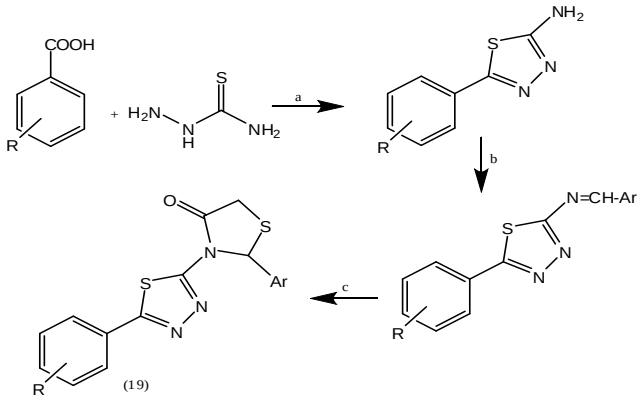


Compounds:15-16a,R=H; 15-16b, R= 4-CH_3; 15-16c, R=4-OCH_3; 15-16d, R= 4-NO_2; 15-16e, R= 4-NO_2; 15-16f, R= 4-Br; 15-16g, R= 2,5(OCH_3).

Pattan SR et al reported synthesis and biological evaluation of some 1, 3, 4 -thiadiazolederivatives .A mixture ofthiosemicarbazide (17), aryl carboxylic acid (18), in the presence of sulphuric acid was refluxed for 1 hr and poured onto crushed ice.
The solid separated out was filtered, washed with water & recrystallized from ethanol [10].



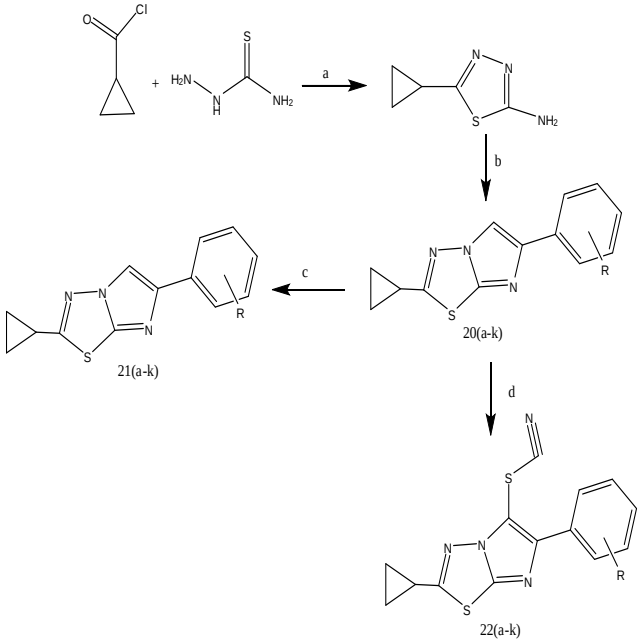
Suresh Sharabassapa et al has reprted the synthesis of Synthesis of [2-(substituted aryl)-3-{ 5- (substituted phenyl)- 1,3,4- thiadiazole }-4-oxo-thiadiazolidines] (19). All the synthesized compounds were analysed by IR, NMR and Mass Spectroscopy [11].



Reagents and conditions: (a) $POCl_3$, reflux for 4 hrs. (b) Ar-CHO, ethanol, reflux for 5 hrs. (c) $SHCH_2COOH$, ethanol, reflux for 6 hrs.

Compounds:
19a: R=4Cl-C_6H_4, Ar = 3NO_2-C_6H_4; **19b:** R=4Cl-C_6H_4, Ar = 2,4Cl-C_6H_4;
19c: R= 4OCH3-C6H4, Ar = C6H5; **19d:** R=4OCH3-C6H4, Ar =4OCH_3-C_6H_4;
19e: R= 4OCH_3-C_6H_4, Ar = 3NO_2-C_6H_4; **19f:**R= 4OCH_3-C_6H_4, 4NO_2-C_6H_4,
19g:R= 4F-C_6H_4, Ar =C_6H_5; **19h:** R=4F-C_6H_4, Ar = 2,4Cl-C_6H_4;
19i:R= 4F-C_6H_4, Ar = 2,4Cl-C_6H_4; **19j:** R=C_6H_5, Ar =C_6H_5;
19k: R=C_6H_5, Ar = 3NO_2-C_6H_4; **19l:** R=C_6H_5, Ar = 2,4Cl-C_6H_4;
19m: R=C_6H_5, Ar = 4Cl-C_6H_4; **19n:** R=4NO_2-C_6H_4, Ar = 4OCH_3-C_6H_4;
19o: 4NO_2-C_6H_4, 4NO_2-C_6H_4,

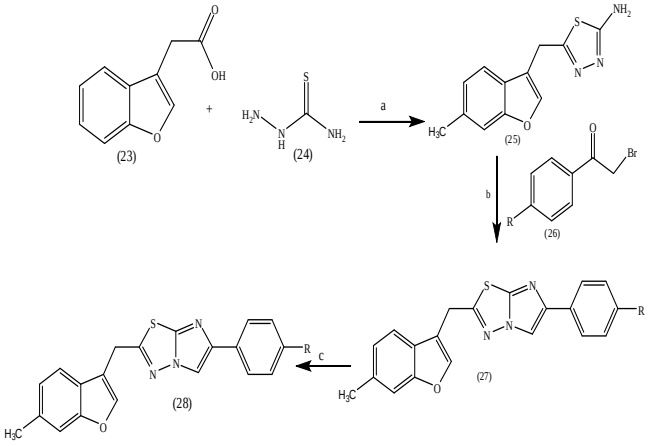
Malleshappa N. Noolviet al has reported the synthesis of a series of 2,5,6-trisubstituted imidazo[2,1-b][1,3,4]-thiadiazole derivatives (20)a-k which were prepared by reaction of 2-amino-5-cyclopropyl-1,3,4-thiadiazole and an appropriate phenacyl bromide. Further 5-bromo (21)a-k and 5-thiocyanato (22)a-k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



Reagents and conditions: (a)$POCl_3$, reflux (b) substituted phenacyl bromides, alcohol, reflux (c) Br_2, GAA (d) KSCN, Br_2, GAA
Compounds:
20a, R = H21a, R = H 22a, R = H
20b, R = 4-Cl 21b, R = 4-Cl 22b, R = 4-Cl
20c, R = 4-Br 21c, R = 4-Br 22c, R = 4-Br
20d, R = 4-F 21d, R = 4-F 22d, R = 4-F
20e, R = 2,4-di-Cl 21e, R = 2,4-di-Cl 22e, R= 2,4-di-Cl
20f, R = 2,4-di-OH 21f, R = 2,4-di-OH 22f, R = 2,4-di-OH
20g, R = 3-NH_2 21g, R = 3-NH_2 22g, R = 3-NH_2
20h, R = 4-NH_2 21h, R = 4-NH_2 22h, R = 4-NH_2
20i, R = 3-NO_2 21i, R = 3-NO_2 22i, R = 3-NO_2
20 j, R = 4-NO_2 21j, R = 4-$NO_2$22j, R = 4-NO_2
20k, R = 2-OH 21k, R = 2-OH 22k, R = 2-OH

Jadhav VB et al has reported the synthesis of a series of 6-substituted and 5,6-disubstituted 2-(6-methyl-benzofuran-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].



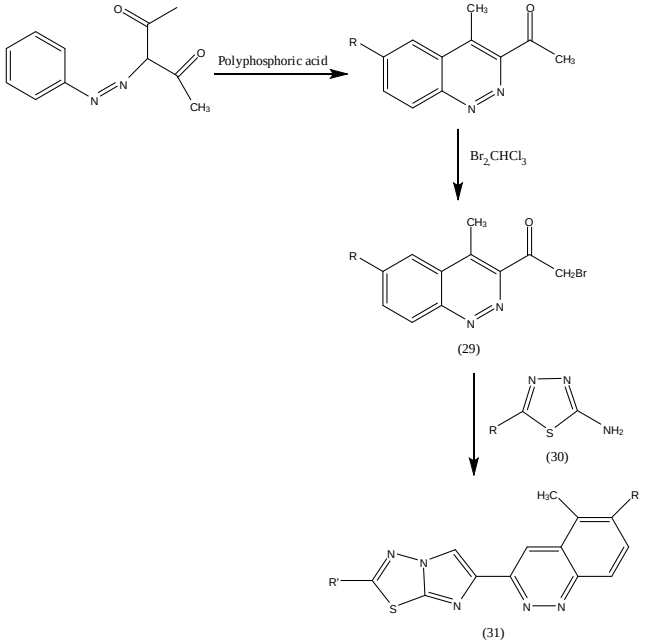
Reagents and conditions: (a) $POCl_3$, reflux, 30 min, KOH.; (b) Dry EtOH, reflux, 24 h, Na_2CO_3; (c) Morpholine,HCHO, AcOH, MeOH, reflux, 8 h.

Compounds:

27a: R = Cl; **27b:** R = Br; 27c: R = NO_2.

28a: R = Cl; **28b:** R = Br; 28c: R = NO_2.

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 thiadi azoles (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].



Compounds:

31a: R=H, R'=H; **31b:** R=H, R'=C_2H_5; **31c:** R=H, R'= 2Cl-C_6H_4;

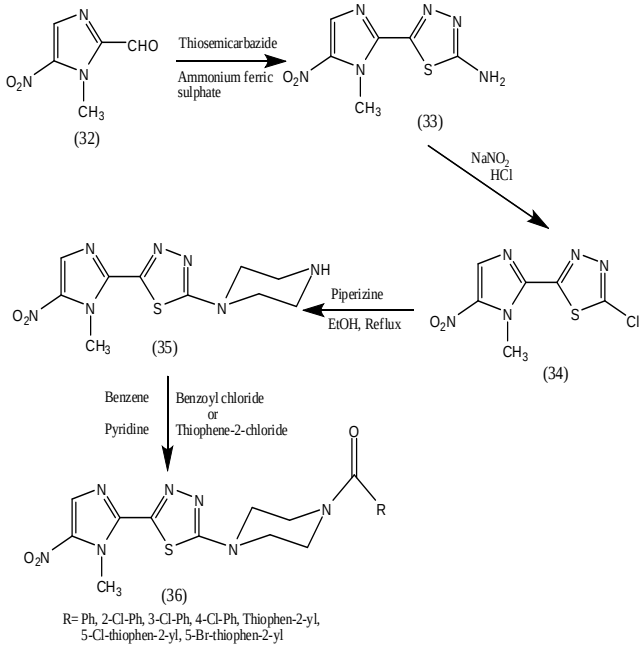
31d: R=H, R'=C_6H_5; **31e:** R=H, R'=4Cl-C_6H_4; **31f:** R=Cl, R'= 2Cl-C_6H_4;

31g: R=C_6H_5, R'=2Cl-C_6H_4; **31h:** R=Cl, R'=4Cl-C_6H_4;

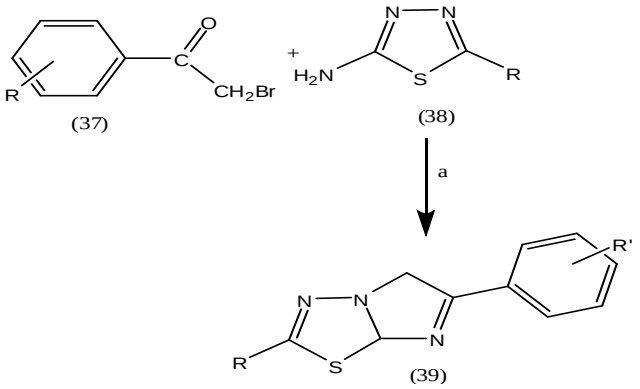
31i: R=CH_3, R'= 2Cl-C6H4; **31j:** R=C_6H_5, R'=Cl;

31k: R=CH_3, R'=4Cl-C_6H_4;

Poorrajab F et al reported the synthesis of some nitroimidazoyl-1,3,4 thiadiazoles. Treatment of 1-methyl-5-nitroimidazole-5-carboxaldehyde (32) with thiosemicarbazide in the presence of HCl results in corresponding thiosemicarbazone which upon cyc- lization with ammonium ferric sulphate gave 2-amino-1,3,4-thiadiazole (33).Diazotization of (33) amine in HCl solution, in the presence of copper powder, gave 2-chloro-1,3,4-thiadiazole (34). Further treatment of (34) with piperizine in refluxing ethanol gave N-piperazinyl compound (35). N-aroylation of (35) with appropriate benzoyl chloride or thiopin-2-carbonyl chloride gave the final compound (36) [15].



Kidwai M et al reported the green synthesis of substituted imidazothiadiazoles using ionic liquid. In this procedure ionic liquid [bmim] PF_6(1-butyl-3-methylimidazolinum hexaflourophosphate) was used as an recyclable catalyst. A mixture of α- bromoacetophenone (37) and 5-alkyl/aryl-1,3,4-thiadiazole (38) with sodium carbonate in ionic liquid[bmim]PF_6 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, 60ºC.

Compounds: 39a: R=C_6H_5, R'=H; **39b:** R, R'=H; **39c:** R=CH_3, R'=H;

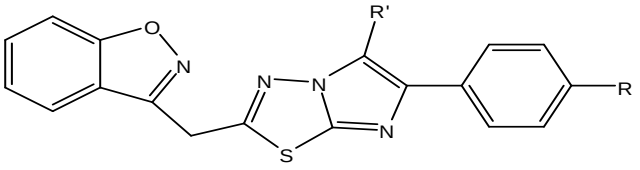
39d: R= n-C_7H_{15}, R'=H; **39e:** R=C_6H_{13},R'=H; **39f:**R=4-CH_3O-C_6H_4, R'=H;

39g: R= n-C_7H_{15},R'=4-Cl; **39h:** R= n-C_6H_{13}, R'= 4-Cl.

BIOLOGICAL 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].



(40)

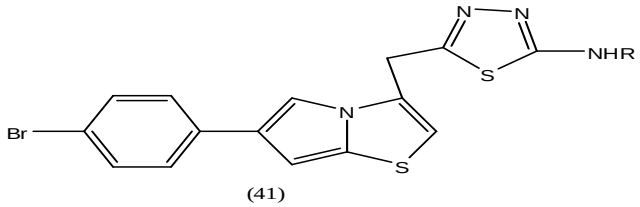
Compounds: 40a: R=Cl, R'=H; **40b:** R=Br, R'=H; **40c:** R=Cl, R'=Br;

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.

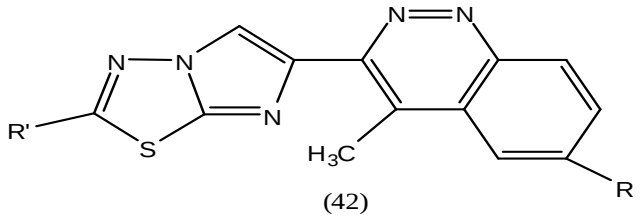
Guzeldermirci NU et al reported the synthesis of a series of 2-alkyl/arylamino-5-((6-(4-bromophenyl) imidazo[2,1-b] thiazol-3-yl) methyl)-1,3,4thiadiazoles. The synthesized compounds were evaluated for in vitro antibacterial activity against *S. aureus*, *P. aeruginosa* and *E. coli* as well as for antifungal activity against *C. albicans*, *C. para-psilosis*, *C. krusei*, *T. mentagraphytes*, *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].



(41)

Compounds: 41a: R=CH_3**;** 41b: R= C_2H_5; 41c: R= C_6H_5.

Jakhar 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 compounda (42a) and (42d) showed moderate activity which had aliphatic substitution on thiadiazole ring [19].

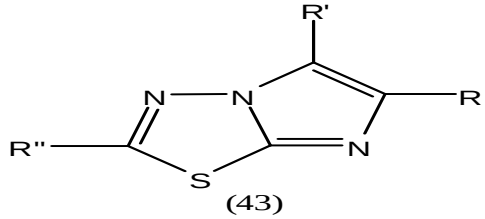


(42)

R'=H, C_2H_5, C_6H_5, 2-ClC_6H_4. 4-ClC_6H_4

R=H, CH_3, Cl.

Gadad AK et al reported the synthesis of 5-guanylhydrazone/thiocyanato-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-guanylhydrazone and 5-thiocyanato groups on the com- pounds resulted in producing good antibacterial activity [20].

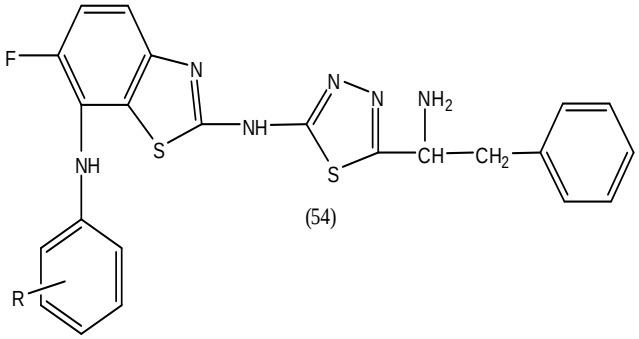


(43)

Compounds:43a:R=p-(Cl)C_6H_4,R'=2-methylenehydrazinecarboximidamide, R"=$SO_2NCHN(CH_3)_2$;43b: R= p-(Br)C_6H_4, R'=2-methylenehydrazinecarboximidamide, R"= $SO_2NCHN(CH_3)_2$;43c: R= p-(Cl)C_6H_4, R'=SCN, R"= SO_2NH_2;43d: R= p-(Br)C_6H_4, R'= SCN, R"= SO_2NH_2;43e: R= p-(NO_2)C_6H_4, R'=SCN, R"= SO_2NH_2.

2. ANTI-TUBERCULAR ACTIVITY

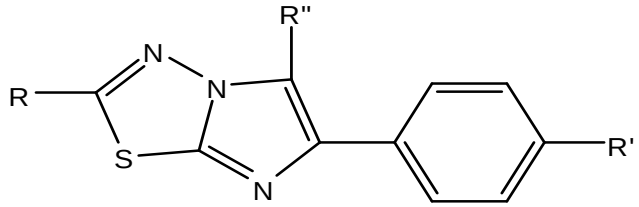
Sathe SB et al reported the synthesis of N-[5-(1-amino-2-phenylethyl)-1,3,4thiadia zol-2-yl]-6-fluoro-7-substituted1,3-benzothiazol-2- amine.The antitubercular activity of synthesized compounds was assessed against Mycobacterium tuberculosis $H_{37}Rv$ in BACTEC medium. Compounds (54a), (54b), (54c), (54d), (54e), (54f) and (54g) have shown good antitubercular activity [21].



(54)

Compounds: 54a: R=o-NO_2; **54b:** R= m-NO_2; **54c:** R= p-NO_2; **54d:** R=o- OCH_3;
54e: R= m-OCH_3; **54f:** R= p-OCH_3; **54g:** R= o-Cl.

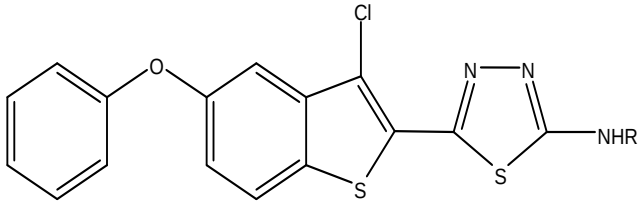
Kolavi, G. *et al.*,reported the synthesis of a series of 2,6-disubstituted and 2,5,6-trisub- stitutedimidazo[2,1-b][1,3,4] thiadiazoles. The structure of the compounds were eluci dated and screened for antitubercular activity against Mycobacterium tuberculosis $H_{37}Rv$ using the BACTEC 460 radiometric system and broth dilution assays. Compound (55c) and (55d) had shown the highest (100%) inhibitory activity. The in vitro anti-tubercular activity reports of compounds (55a), (55b), (55e), and (55f) against M. tuber- culosis strain $H_{37}Rv$ showed moderate activity at MIC of ≥6.25µg/ml[22].



(55)

Compounds: 55a: R= Cyclohexyl, R'= H, R''= CHO;
55b: R= Cyclohexyl, R'= Br, R"= CHO;
55c: R= 2- Furyl, R'= H, R"= CHO;
55d: R= Cyclohexyl, R'= H, R"= CH_2OH;
55e: R= 2- Furyl, R'= H, R"= CH_2OH;
55f: R= Cyclohexyl, R'= H, R"= CH=NOH.

Vasoya SL et al reported the synthesis of 2-(3´-chloro-5´-phenoxy-benzo [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 $H_{37}Rv$ 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].

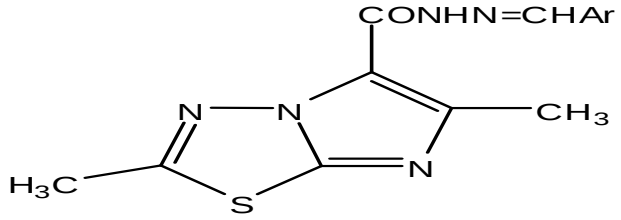


(56)

Compounds:56a: R= 4-(Cl)C_6H_4; **56b:** R= 2-(CH_3)C_6H_4; **56c:** R=2-(OCH_3)C_6H_4; **56d:** R= 4-(OCH_3) C_6H_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-carbohydrazides **58(a-h)**. The newly synt- hesized 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].

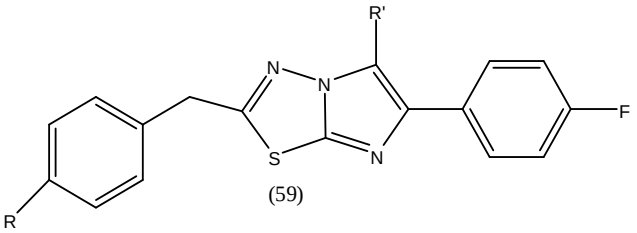


(58)

Compounds: 58a: Ar= C_6H_5; **58b:** Ar= 4-(CH_3)C_6H_4; **58c:** Ar= 2-(OH)C_6H_4; **58d:** Ar= 4-$CH_3OC_6H_4$; **58e:** Ar= 4-(Br)C_6H_4; **58f:**Ar= 4-(Cl)C_6H_4; **58h:**Ar= 4-(NO_2)C_6H_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 (59i),(59l) and (59n) 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

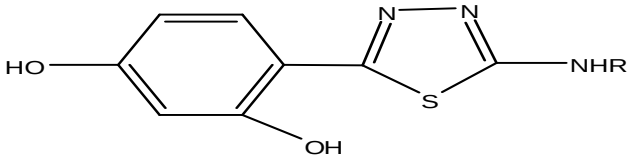
sensitive. The cell proliferation effect of synthesized compounds was further tested using MIT assay and results showed that the compound **(59l)** has maximum cytotoxicity with an IC_{50} value of ~ 8µM[25].



(59)

Compounds: 59a: R= H, R'=SCN; **59b:** R= Cl, R'= SCN; **59c:** R= F, R'= SCN;
59d: R= Br, R'=SCN; **59e:** R= CH_3, R'=SCN; **59f:** R= H. R'=H;
59g: R= Cl, R'=H; **59h:** R= F, R'= H; **59i:** R= CH_3, R'= H;
59j: R= H, R'=Br; **59k:** R= Cl, R'= Br; **59l:** R= H, R'= CHO;
59m: R= Cl, R'=CHO; **59n:** R= CH_3,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 hetroaryl 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].

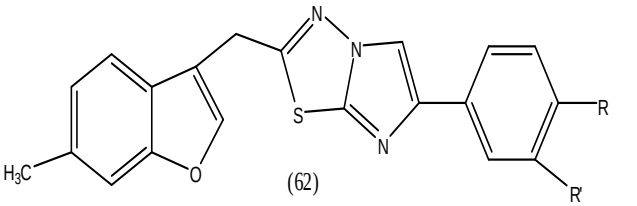


(60)

Compounds: 60a: R= 4-$(CH_3)_3C$-C_6H_4; **60b:** R= 4-OCH_3-C_6H_4-CH_2O.

4. ANTI-INFLAMMATORY ACTIVITY

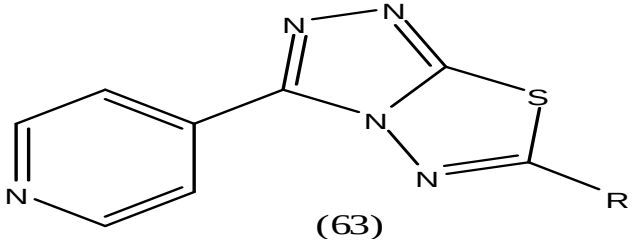
Jadhav VB et al reported the synthesis of a series of 6-substituted and 5, 6-disubsti- tuted 2-(6-methyl-benzofuran-3-ylmethyl)-imidazo[2,1-b][1,3,4] thiadiazoles. The new compounds have been tested for their in vitro anti-inflammatory activity. Compound (62a) and (62b) showed good inhibition while the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



(62)

Compounds: 62a: R=Br, R'=H; **62b:** R=NO_2, R'= H; **62c:** R= Cl, R'= CN.

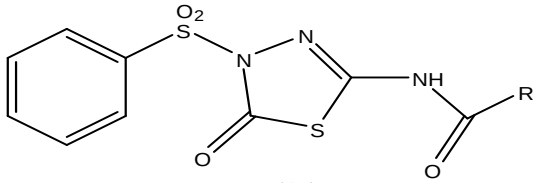
Gilani SJ et al reported the synthesis of a series of 6-substituted1,2,4-triazolo-[3,4-b][1,3,4] thiadiazoles. The synthesized compounds were evaluated for their antiinflam- matory activity using Ibuprofen as a reference compound. The compound (63a) showed the maximum inhibition while the compounds (63b) and (63c) showed decreased inhibition as compared to (63a)[28].



(63)

Compounds: 63a: R= 4-$(NO_2)C_6H_4$; **63b:** 2-$(Cl)C_6H_4$; **63c:** R= 2-$(OCOCH_3)C_6H_4$.

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].

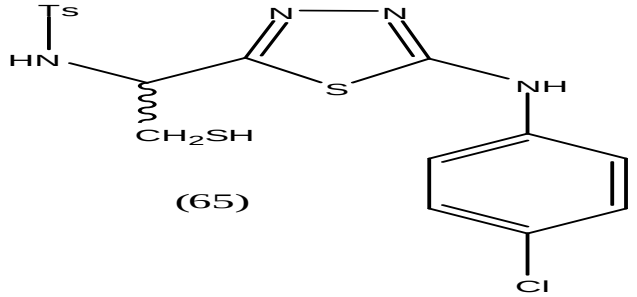


(64)

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

5. ANTI-HIV ACTIVITY

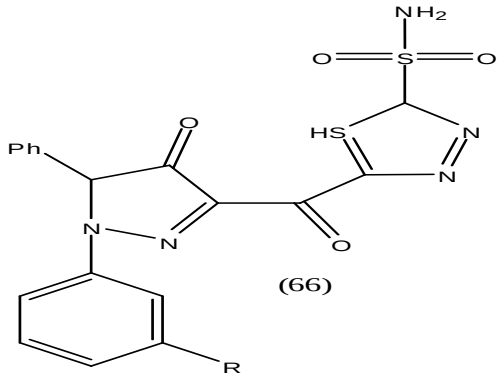
Akhtar T et al reported the synthesis and anti- HIV activity of 2-substituted 5-(4 chlorophenylamino)-1,3,4-thiadiazoles.The synthesized compounds were assayed against HIV-1 and HIV-2 strains in human T-lymphocytes MT-4 cells. The compound (65) was the most potent compound [30].



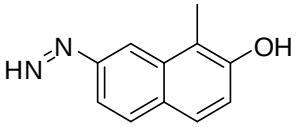
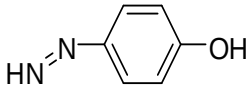
(65)

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].



(66)

Compound	R
66a	
66b	
66c	I

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