WORLD JOURNAL OF PHARMACEUTICAL RESEARCH
SJIF Impact Factor 6.805
Volume 5, Issue 6, 1966-1977. Review Article ISSN 2277– 7105

A REVIEW ON SOME 2,5-DISUBSTITUTED [1,3,4] THIADIAZOLE SUBSTITUTED THIAZOLIDINONE DERIVATIVES AS A POTENT ANTIMICROBIAL AGENTS

Manisha Kaushal* **and Amandeep Kaur**

Department of Pharmaceutical Chemistry, ASBASJSM College, Bela, Ropar, India.

Article Received on
19 April 2016,

Revised on 09 May 2016,
Accepted on 29 May 2016

DOI: 10.20959/wjpr20166-6383

***Corresponding Author**
Manisha Kaushal
Department of Pharmaceutical Chemistry, ASBASJSM College, Bela, Ropar, India.

ABSTRACT

A series of [2-(substituted aryl)-3-(5-(4-chlorophenyl)-1,3,4-thiadiazol-2-yl) thiazolidin-4-one derivatives were synthesized by the reaction of the substituted Schiff-bases with thioglycolic acid in ethanol. Structure of the synthesized compounds were confirmed on the basis of physicochemical and spectral data (IR,^{1}HNMR and Mass). All the synthesized compounds were screened on gram positive, gram negative bacteria using cup-plate-agar diffusion method. These compound showed significant activity against staphylococcus aureus, pseudomonas aeruginosa and Bacillus subtilis respectively.

KEYWORDS: Antimicrobial activity, Schiff basis, 1,3,4-thiadazoles.

1. INTRODUCTION

1.1 ANTIMICROBIAL AGENTS

Treatment of infectious diseases still remains an important and challenging problem because of a combination factors including newly emerging infectious diseases and increasing number of multi-drug resistant microbial pathogens with particular relevance for Gram-positive bacteria. Antimicrobial agents are the drugs, chemicals, or other substances that kill or slow the growth of microbes. The need for new antimicrobial agents is greater than ever because of the emergence of multi drug resistance in common pathogen, the rapid emergence of new infectious, and the potential for use of multidrug-resistant agents. Antimicrobial resistant is threatening the management of infections such as pneumonia, tuberculosis, malaria, and AIDS. The drug resistance has become a growing problem in the treatment of infectious disease caused by bacteria, fungi and viruses. They lead to infections which are responsible for the death of the millions of patients worldwide. The search of new antibiotic drugs

become an urgent need. The large number of antibiotics and chemotherapeutics are available for medicinal use. During recent year remarkable progress has been made in the development of thiadiazole, many of which are known to possess interesting pharmacological properties such as anticancer, antitubercular, antibacterial, antifungal, antimicrobial, anti-inflammatory, analgesic, anticonvulsant, and antisecretory activities. An antimicrobial is any substance of natural, semisynthetic or synthetic origin that kills or inhibits the growth of microorganisms but causes little or no damage to the host. All antibiotics are antimicrobials, but not all antimicrobials are antibiotics. In recent years there is rapid increase in the emergence of microbes that are resistant to use of antibiotics that have been observed. The discovery of antimicrobials like penicillin and tetracycline paved the way for better health for millions around the world.

The 4-Thiazolidinone derivatives constitute an important class of heterocyclic compounds for which diverse biological properties such as antimicrobial, anti-inflammatory, anti-proliferative, antiviral, anticonvulsant, anti-diabetic, anti-hyperlipidemic, cardiovascular, anti-tubercular, antifungal and antibacterial. In recent years 4-thiazolidinone derivatives with antitumor activity on leukemia, melanoma, lung, colon, CNS, ovarian, renal, prostate and breast cancers cell lines have become a promising area of research. The 4-thiazolidinone moiety is very versatile and has featured in many drugs and several compounds with 4-thiazolidinone core structure were found to kill selectively drug resistant cancer cells and induce cell death. This assemblage recapitulates ongoing medicinal chemistry investigations worldwide, to explore novel chemical entities that can be useful in the treatment of many ailments.

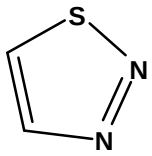
1.2 1,3,4 THIADIAZOLE

The 1,3,4- thiadiazole nucleus is one of the most important and well-known heterocyclic nuclei, which is a common and integral feature of a variety of natural products and medicinal agents. Thiadiazole nucleus is present as a core structural component in an array of drug categories such as antimicrobial, anti-inflammatory, analgesic, antiepileptic, antiviral, antineoplastic, and antitubercular agents. The broad and potent activity of thiadiazole and their derivatives has established them as pharmacologically significant scaffolds. In this study, an attempt has been made with recent research findings on this nucleus, to review the structural modifications on different thiadiazole derivatives for various pharmacological activities.

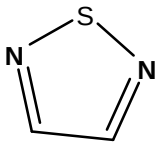
1,3,4-thiadiazole derivatives possess interesting biological activity probably conferred to them due to strong aromaticity of the ring system which leads to great *in vivo* stability and generally lack of toxicity for higher vertebrates including humans when diverse functional group that interact with biological receptor are attached to aromatic ring**.** Thiadiazoles act as bioisosteric replacement of thiazole moiety. It is also bioisosteres of oxadiazole, oxazole and benzene. Substitution of these heterocycles with a thiadiazole typically leads to analogues with improved activities because sulfur atom imparts improved liposolubility.

1.3 TYPES OF THIADIAZOLE

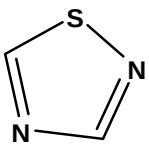
Thiadiazole is a versatile moiety that exhibits a wide variety of biological activities. Thiadiazole contains the five membered heterocyclic ring structure composed of two nitrogen atom and one sulfur atom. The sulfur atom and two-electron donor nitrogen system exhibit a wide variety of biological activity. Thiadiazole and related compounds are called 1, 3, 4-thiadiazole (two nitrogen and one other heteroatom in a five- membered ring). There are four isomeric forms. 1,2,3-thiadiazole,1,2,5-thiadiazole, 1,2,4-thiadiazole, 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, antitubercular , anticonvulsant and anti-hepatitis B viral activities.



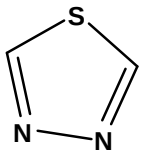
(1)



(2)



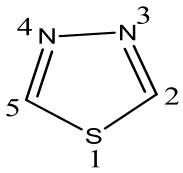
(3)



(4)

1.4 CHEMISTRY OF THIADIAZOL

Thiadiazole moiety act as a “hydrogen binding domain” and “two-electron donar system”. Thiadiazole act as a bioisosteric replacement of thiazole moiety. So, it acts as third and fourth generation cephalosporin. The numbering of monocyclic azole system begins with the heteroatom that is in the highest group in the periodic table and with the element of lowest atomic weight in that group. Hence, the numbering of 1,3,4-thiadiazole is done in the following manner. This designated that one sulphur group is present in the ring.

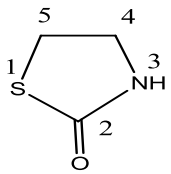


1.5 CHEMISTRY OF THIAZOLIDINONE

Thiazolidinones are a saturated form of thiazole, called thiazolidine, with a carbonyl group. 1,3-thiazolidine-4-ones are heterocycles that have an atom of sulphur at position 1, a nitrogen at position 3 and a carbonyl group at position 4. New derivatives of 4- thiazolidinones have been obtained by modifications of the parent structure in several ways.

1. Substituents in the 2,3 and 5-positions may be varied, but the greatest difference in structure and properties is exerted by the group attached to the carbon atom at the 2-position.
2. Variations in the substituents attached to the nitrogen atom and the methylene carbon atom are possible for the structures .
3. The carbonyl group of 4-thiazolidinone is highly unreactive. However, in a few cases, 4-thiazolidinone on reaction with lawesson's reagent gives corresponding 4-thione derivative.

The unsubstituted 4-thiazolidinones are usually solids, often melting with decomposition, but the attachment of an alkyl group to the nitrogen lowers the melting point. The 4-thiazolidinones not containing any aryl or higher alkyl substituents are somewhat soluble in water.

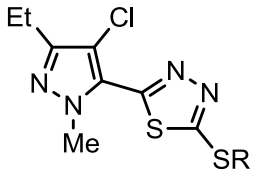


2. BIOLOGsICAL REVIEW

2.1 ANTIMICROBIAL ACTIVITY

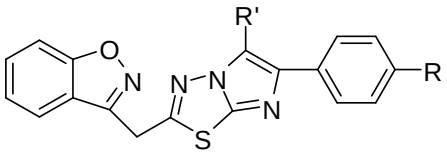
The compound were studied for their antimicrobial activity against the gram positive staphylococcus aureus and gram negative E.coli and pseudomonas aeruginosa and for their antifungal activity against candela albicans by neat sample and serial plate dilution method.

Chen, H. et al., reported the synthesis of active pyrazolyl-substituted 1,3,4-thiadiazole compounds. The synthesized compounds were screened for antifungal activity against R.Solanii. The compounds (1a), (1b), (1c), and (1d) have showed good antifungal activity.



Compounds: (1a): R= Me; (1b): R= Propyl; (1c): R= Allyl; (1d): R= Amyl.

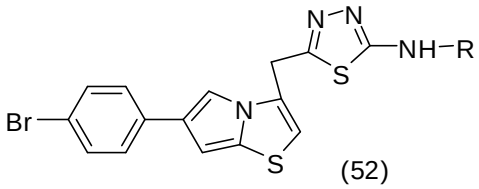
Lamani R.S. et. al.; reported the synthesis of novel methylene bridged benzisoxazolyl imidazo [2,1-b][1,3,4]thiadiazoles. The newly synthesized compounds were screened for their antibacterial and antifungal activity using Agar Diffusion method. The antibacterial activity was screened against S. aureus, B. subtilis, P. aeruginosa and E. coli. The antifungal activity was screened against C. albicans and A. fumigates. The compounds**(51a), (51b), (51c), (51d)** and **(51e)** shows moderate to good bacterial inhibition, while the compounds**(51b), (51f), (51g), (51h)** and **(51i)** showed good antifungal activity.



(51)

Compounds: 51a: R=Cl, R'=H; **51b:** R=Br, R'=H; **51c:** R=Cl, R'=Br; **51d:** R=O-Me, R'=Br; **51e:** R=Cl, R'=SCN; **51f**: R=3-coumarinyl, R'=H; **51g**: R=O-Me, R'=SCN; **51h:** R=H, R'=H; **51i:** R=3-coumarinyl, R'=SCN.

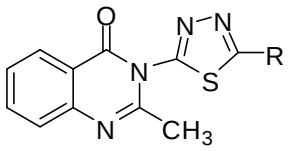
Guzeldermirci N.U. et. al.; reported the synthesis of a series of 2-alkyl/arylamino-5-((6-(4-bromophenyl)imidazo[2,1-b]thiazol-3-yl) methyl)-1,3,4thiadiazoles. The synthesized compounds were evaluated for in vitro antibacterial activity against S. aureus, P. aeruginosa and E. coli as well as for antifungal activity against C. albicans, C. parapsilosis, C. krusei, T. mentagraphytes, M. gypseum and T. tonsurans using Micro-broth dilution method. Compounds**(52a)** and**(52b)** showed the highest activity against T. tonsurans and E. coli respectively. The most active compound was**(52c)** which has phenylamino group at the 2nd position of the thiadiazole ring.



(52)

Compound: 52a: R=CH_3; **52b:** R=C_2H_5; **52c:** R=C_6H_5

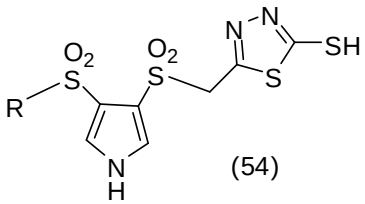
Jatav V. et. al.; reported the synthesis of a series of novel 2-methyl-3-(1,3,4-thiadiazoyl)-4-(3H)quinazolinones. The synthesized compounds were screened for antibacterial potential against S. aureus, B. subtiis and E. coli and for antifungal potential against C. albicans, A. niger and C. lanata by liquid dilution method. Compound**(53a)** emerged as potential antibacterial and antifungal. Compound**(53b)** exhibit moderate antifungal and antibacterial activity.



(53)

Compound: 53a: R=p-(cl)C_6H_5; **53b:** R=C_4H_9.

Padmavati V. et. al.; reported the synthesis of a new class of heterocyclic pyrrolyl thiadiazoles. The synthesized compounds were tested for their antibacterial activity against S. aureus, B. subtilis, E. coli and K. pneumoniae and antifungal activity against F. solani, C. lunata and A. niger by using Agar disc diffusion method. Compound**(54a)** showed excellent antibacterial activity while the compounds**(54b)** and**(54c)** exhibit good antifungal activity as compared to the standards**.**

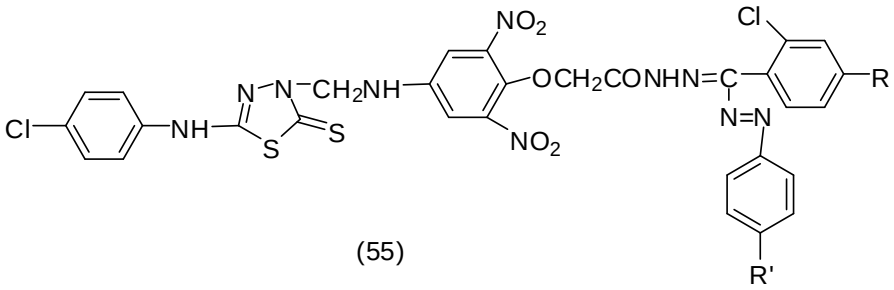


(54)

Compounds: 54a: R=C_6H_5; **54b:** R=4-(CH_3)C_6H_5; **54c:** R=4-(Cl)C_6H_5

Shah P. et. al.; reported the synthesis of formazans from mannich bases of 5-(4-chlorophenyl-amino)-2-mercapto-1,3,4-thiadiazole. Antimicrobial screening of the form

azans was done by using disc diffusion method. The synthesized compounds were screened for their in vitro antibacterial activity against E. coli and S. typhi and antifungal activity against A. niger, Penicillium species and C.albicans. Compounds**(55a)** showed maximum antibacterial activity against E. coli while**(55b)** and**(55c)** showed moderate activity. Compound**(55a)** and**(55b)** showed good antifungal activity while**(55d)** showed moderate activity.

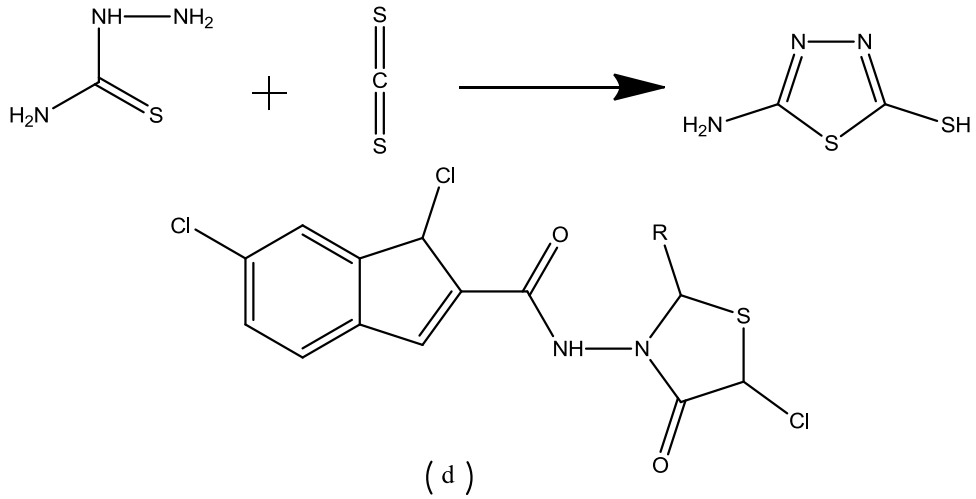


(55)

Compound: 55a: R=2-Cl, R'=4-NO_2; **55b:** R=2-Cl, R'=2-CH_3-4NO_2; **55c:** R=2-Cl, R'=SO_2OH; **55d:** R=3-OCH_3, R'=SO_2NH-pyrimidinyl.

2.2 ANTI-TUBERCULAR ACTIVITY

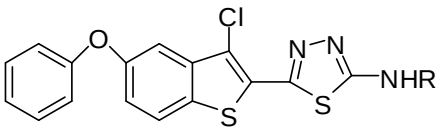
Khedekar et al. studied many substituted 1,2- dihydro compounds (c) and (d) for their antitubercular activity, which was carried out by taking into consideration various physicochemical descriptors.



(d)

Vasoya S.L. 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. Compunds**(61a), (61b),**

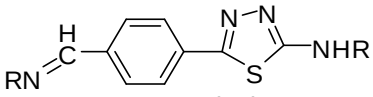
(61c), (61d) showed 29, 60, 60 and 91 percentage inhibition respectively. Compounds having 2-methyl, 2-methoxy substitutions showed higher activity than the other derivatives.



(61)

Compounds: 61a: R=4-(Cl)C_6H_4; **61b:** R=2-(CH_3)C_6H_4; **61c:** R=2-(OCH3)C_6H_4; **61d:** R=4-(OCH_3)C_6H_4.

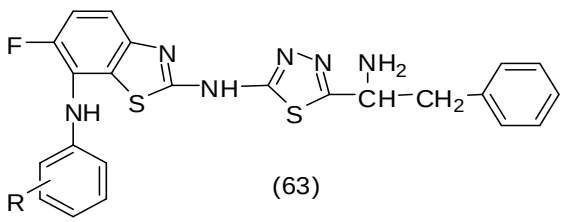
Solak N. et. al.; reported the synthesis of 2-(aryl/alkylamino)-5-(4-aminophenyl)-1,3,4 thiadiazoles. The synthesized compounds were screened for antitubercular activity against Mycobacterium tuberculosis H_{37}Rv using BACTEC 460 radiometric system. The tubercular tests indicated that the compound**(62a)** has showed highest inhibition. Compounds**(62b), (62c), (62d)** and**(62e)** has showed moderate antitubercular activity.



(62)

Compounds: 62a: R=Methyl, R'=2-hydroxyphenyl; **62b:** R=Methyl, R'=3-nitrophenyl; **62c:** R=benzyl, R'=2-hydroxyphenyl; **62d:** R=Benzyl, R'=5-nitrofurfuryl; **62e:** R=benzyl, R'=3-nitrophenyl.

Sathe S.B. et. al.; reported the synthesis of N-[5-(1-amino-2-phenylethyl)-1,3,4 thiadiazol-2-yl]-6-flouro-7-substituted1,3-benzothiazol-2-amine. The tubercular activity of synthesized compounds was assessed against Mycobacterium tuberculosis H_{37}Rv in BACTEC medium. Compounds**(63a), (63b), (63c), (63d), (63e), (63f)** and**(63g)** have shown good antitubercular activity.



(63)

Compounds: 63a: R=o-NO_2; **63b**: R=m-NO_2; **63c:** R=p-NO_2; **63d:** R=o-CH_3; **63e:** R=m-OCH_3; **63f:** R=p-OCH_3; **63g:** r=o-Cl.

3. REFERENCES

1. Roberts M.C. Synthesis, spectral studies and biological activity of some novel biphenyl Imidazo[2,1-b][1,3,4]Thiadiazole derivatives. Curr Drug Targets Infect Discord, 2004; 4: 207-215.
2. Dessen A, Di Guilmi A.M., Vernet T, Dideberg O. Synthesis, spectral studies and biological activity of some novel biphenyl Imidazo[2,1-b][1,3,4]Thiadiazole derivatives. Curr Drug Targets Infect Discord, 2001; 1: 63-77
3. Muroi H, Nihe i K, Tsujimoto K, Kubo I. Synthesis, spectral studies and biological activity of some novel biphenyl Imidazo[2,1-b][1,3,4]Thiadiazole derivatives. Bioorg. Med. Chem, 2004; 12: 583-587.
4. Chopra I, Schofield C, Everett M, O' Neill K, Miller K, Wilcox M. Synthesis, spectral studies and biological activity of some novel biphenyl Imidazo[2,1-b][1,3,4]Thiadiazole derivatives. Lancet infect Dis, 2008; 133-139.
5. Tripathi K.D. Essentials of Medicinal Pharmacology, 6th edition, Jaypee Brothers Medical Publishers, New Delhi. 2006; 667.
6. Cohen M.L. Novel Biphenyl Imidazo[2,1-b][1,3,4]-Thiadiazole-a versatile scaffold. Science, 1992; 57: 1050.
7. Hadizadeh F, Vosoogh R. Novel Biphenyl Imidazo[2,1-b][1,3,4]-Thiadiazole-a versatile scaffold. J. Heterocyclic. Chem, 2008; 45: 1-3.
8. Nath M, Sulaxna Song X, Eng G. Novel Biphenyl Imidazo[2,1-b][1,3,4]-Thiadiazole-a versatile scaffold. Spectrochemica Part A, 2006; 64: 148-155.
9. Siddiqui N, Ahuja P, Ahsan W, Pandeya S.N., Alam M.S. A review on 1,3,4-Thiadiazole Derivatives. J. Chem. Pharma. Research, 20009; 1(1): 19-30.
10. Mihai Barboiu, Marilena Cimpoesu, Comelia Guran, Claudiu Supuran. Metal based drug. 1996; 3(5): 227-232.
11. Tripathy R, Ghose A, Singh J, Bacon E.R., Angeles T.S., Yang S.X. Bioorg. Med. Chem. Letters, 2007; 17: 1793-1798.
12. Jitendra Kumar Gupta, Rakesh Kumar Yadav, Rupesh Dudhe, Pramod Kumar Sharma. Recent advancements in the synthesis and pharmacological evaluation of substituted 1,3,4 thiadiazole derivatives. Inter. J. Pharma. Tech. Research, 2010; 2(2): 1493-1507.
13. Bhuva H, Sahu D, Shah B.N., Dixit C.M., Patel M.B. Biological profile of Thiadiazole. Pharmacologyonline, 2011; 1: 528-543.
14. Al- Amiery A.A.H., Yousif M, Shakir M.A. Novel Biphenyl Imidazo[2,1-b][1,3,4]-Thiadiazole-a versatile scaffold. Eng. Tech. J, 2009; 27: 891-897.

15. Cao S.L., Feng Y.P. Bio & Med. Chem. Letters, 2005; 15(7): 1895-1899 .
16. Terzioglu N, Gursoy A. Synthesis, spectral studies and biological activity of some novel biphenyl Imidazo[2,1-b][1,3,4]Thiadiazole Derivatives. Eur. J. Med. Chem, 2003; 38: 781-786.
17. (a) Kempegowda, Kunar S, Prakash D, Mani T. Pharma Chemica, 2011; 3(2): 330- 334.
(b) Khazi I.A., Gadad A.K., Lamani R.S., Bhongade B.A. Synthesis, spectral studies and biological activity of some novel biphenyl Imidazo[2,1-b][1,3,4]Thiadiazole Derivatives. Tetrahedron, 2011; 30:1-28.
(c) Fohlisch B, Braun R, Angew W. A simple synthesis of 1,3,4-Thiadiazole. Chem. Int, 1967 ; 6: 361-362.
18. Schenetti M.L., Teddi F, Greci L, Marchetti L, Milani G, Andreeti G.D., Bocelli G., Sgarabotto. Journal of Perkin Society, Perkin transaction 2.J.C.S, 1980; 421- 426.
19. Jadhav V.B., Kulkarni M.V., Rasal V.P., Biradar S.S., Vinay M.D. Synthesis and anti-inflammatory evaluation of methylene bridged benzofuranyl Imidazo[2,1-b][1,3,4]thiadiazoles. Eur. J. Med, Chem, 2008; 43: 1721-1729.
20. Hamid M.K., Hafez A.A., Koussi N.A., Mahfouz N.M., Innocenti A, Suparan C.T. Bioorg. Med. Chem, 2007; 15: 6975-6984.
21. Poorrajeb F, Ardestani S.K., Emami S, Fardmoghadam M.B. Shafiee A, Foroumadi A. Significance of Thiadiazole derivatives as antimicrobial agents. Eur. J. Med. Chem, 2009; 44: 1758-1762.
22. Jakhar A, Makrandi J.k. A review on 1,3,4-Thiadiazole Derivatives. In. J. Chem, 2010; 49b: 1547-1551.
23. Alegaon S.G., Alagawadi K.R. A review on 1,3,4-Thiadiazole Deivatives. Eur. J. Chem, 2011; 2(1): 94-99.
24. Yadav R, Kaur A, Yadav D, Paliwal S. A review on 1,3,4-Thiadiazole Derivatives. In. J. RDPL, 2012; 2(1): 57-62.
25. Sharba A.H.K., Al-Bayati R.H., Rezki N, Aouad M.R. Synthesis of thiadiazoles and 1,2,4- triazoles derived from cy-clopropane dicarboxylic acid. Molecules, 2005; 10: 1153-1160.
26. Gadad A.K., Noolvi M.N., Karpoormath R.K. Synthesis of thiadiazoles and 1,2,4-triazoles derived from cy-clopropane dicarboxylic acid. Bioorg. Med. Chem, 2004; 12: 5651-5659.

27. Lamani R.S., Shetty N.S.; Kamble R.R., khazi I. Synthesis and antimicrobial studies of novel methylene bridged benzisoxazolyl Imidazo[2,1-b][1,3,4]thiadiazoles. Eur. J. Med. Chem, 2009; 44: 2828-2833.
28. Desai N.C., Bhavsar A.M., Shah M.D., Saxena A.K. Significance of Thiadiazole derivatives as antimicrobial agents. Ind. J. Chem, 2008; 47: 579-589.
29. Akhtar T, Hamid S, Al-Masoudi N.A., Khan K.M. A review on 1,3,4-Thiadiazole Derivatives. Heteroatom. Chem, 2007; 18: 316- 322.
30. Foroumadi A, Mansouri S, Kiani Z, Rahmani A. Significance of Thiadiazole derivatives as antimicrobial agents. Eur. J. Med. Chem, 2003; 38: 851-854.
31. Gupta N, Basappa S, Priya S, Prabhuswamy B. Synthesized some condensed heterocyclic 4,6-disubstituted-1,,4-triazolo-1,3,4-thiadiazole derivatives as antimicrobials. Eur. J. Med. Chem, 2006; 11B: 542-549.
32. Lamani R.S., Shetty N.S., Kamble R.R., Khazi I. Synthesis and antimicrobial studies novel methylated bridged benzisoxazolyl Imidazo[2,1-b][1,3,4]thidiazoles. Eur. J. Med. Chem, 2009; 44: 2828-2833.
33. Guzeldermirci N.U., Kucukbasmak O. Synthesis and antimicrobial activity evaluation of new 1,2,4-triazoles and 1,3,4-thiadiazoles bearing Imidazo[2,1-b]thiazole moiety. Eur. J. Med. Chem, 2010; 45: 63-68.
34. Jatav V, Jain S.K., Mishra P. Novel Biphenyl Imidazo[2,1-b][1,3,4]-Thiadiazole-a versatile scaffold. Ind. J. Pharma. Sci, 2006; 68(3): 360-363.
35. Padmavati V, Mohan A.V., Thriveni P., Shazia A. Recent advancements in the synthesis and pharmacological evaluation of substituted 1,3,4 thiadiazole derivatives. Eur. J. Med. Chem, 2009; 44: 2313-2321.
36. Shah P, Bidawat P, Seth M., Gharu C.P. Arb. J. Chem, 2010; 47: 663-670.
37. Gadad A.K., Mahajanshetty C.S., Nimbalkar S, Raichurkar A. Synthesis and antibacterial activity of some 5-guanylhydrazone/thiocynato-6-arylimidazo[2,1-b][1,3,4]Thiadiazole-2-sulfonamide derivatives. Eur. J. Med. Chem, 2000; 35: 853-857.
38. Abdel-Wahab, Abdel- Hamid, M.K., Abdel- Hafez, Supuran, C.T. Bioorg. Med. Chem, 2007; 15: 6975-6984.
39. Alagwadi K.R., Alegaon S.G. Synthesis, spectral studies and biological activity of some novel biphenyl Imidazo[2,1-b][1,3,4]Thiadiazole derivatives. Arb. J. Med. Chem, 2010.
40. Basappa S.J.S., Priya B.S., Prabhuswamy B, Doreswamy B.H., Prasad J.S., Rangappa K.S. Synthesized some condensed heterocyclic 4,6-disubstituted-1,,4-triazolo-1,3,4-thiadiazole derivatives as antimicrobials. Eur. J. Med. Chem, 2006; 41: 531-538.

41. Shrivastava, Makrandi J.K. Thiadiazole: A brief review. Indian. J. Chem, 2012; 51: 291-296.
42. Vasoya S.L., Paghdar D.J., Chovatia P.T., Joshi H.S. A review on 1,3,4-Thiadiazole Derivatives. J. Sci. Isl. Rep. Iran, 2005; 16(1): 33-36.
43. Solak N, Rollas S. Synthesis and antimicrobial activity evaluation of new 1,2,4-triazoles and 1,3,4-thiadiazoles bearing Imidazo[2,1-b]thiazole moiety. Arkivoc, 2006; 12: 173-181.
44. Sathe B.S., Jayachandran E, Chaugule D, Jagtap V.A. A review on 1,3,4-Thiadiazole Derivatives. J. Phar. Res, 2011; 4(4): 1031- 1032.
45. Kolavi G, Hedge V, Khazi I.A., Gadad P. Synthesis and evaluation of antitubercular activity of Imidazo[2,1-b][1,3,4]Thiadiazole derivatives. Bioorg. Med. Chem, 2006; 14: 3069-3080.
46. Terioglu N, Gursoy A. Synthesis and anticancer evaluation of some new hydrazone derivatives of 2,6-dimethylimidazo[2,1-b][1,3,4]Thiadiazole-5-carbohydrazide. Eur. J. Med. Chem, 2003; 38: 781-786.
47. Karki S.S., Panjamurthy K, Kumar S, Nambia M, Ramareddy S.A., Chiruvella K.K., Raghwan S.C. Novel Biphenyl Imidazo[2,1-b][1,3,4]Thiadiazole- A versatile scaffold. Eur. J. Med. Chem, 2011; 45: 1-8.
48. Matysiak J, Opolski A. A review on recent progress in biological activities. Biosorg. Med. Chem, 2006; 14: 4483-4489.