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REVIEW ON PHARMACOLOGICAL ASPECT OF THIADIAZOLE

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ABSTRACT

Thiadiazole is an indegenous heterocyclic moiety having 5-member ring with a sulphur atom and a two- electron nitrogen carrier arrangement with two double bonds having wide array of biological activity. Thiadazoles have become an important category of heterocycles and a passionate concern in studies owing to their different kinds of biological activities. The thiadiazole nucleus is acknowledged as a main structural unit in various drugs available in the market. Thiadiazole has a wide spectrum of biological activities. In a majority of drugs, thiadiazole moiety is present such as antimicrobials, antiepileptics, antituberculants, anti-inflammatory, antivirals, antineoplastics, analgesics, antioxidants, antidiabetics and antihypertensives.

KEYWORDS: Thiadiazole, Heterocycles, Biological activity.

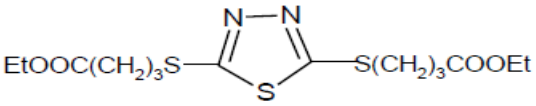
INTRODUCTION

Antibiotic resistance is one of the major health challenge in the present time. The need to design a new compounds to deal with this resistance has become one of the most important areas of research today. 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. Many drugs containing thiadiazole nucleus are available in the market such as acetazolamide, methazolamide, sulfamethazole etc. The nitrogen atom at various positions as (1,3,4), (1,2,3), (1,2,4) and (1,2,5) forms respective isomeric thiadiazole derivatives. The various isomeric forms of thiadiazoles are 1,3,4- thiadiazole; 1,2,3-thiadiazole; 1,2,4-thiadiazole and 1,2,5- thiadiazole.

BIOLOGICAL ACTIVITY

Antimicrobial activity

Nadjet R. et al synthesized Novel thiadiazole derivatives diethyl4,4′- [(1,3,4-thiadiazol- 2,5 diyl)bis (sulfa nediyl)]dibutanoate (1) and 4,4 - (1,3,4- thiadiazole-2, 5-diyl)bis (sulfa nediyl) dibutanehydrazide (2). Two compounds (1) and (2) showed maximum antibacterial activities against Gram-positive bacteria, Gram- negative bacteria and fungi.[1]



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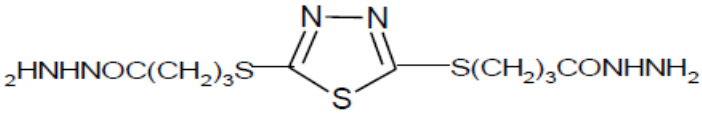

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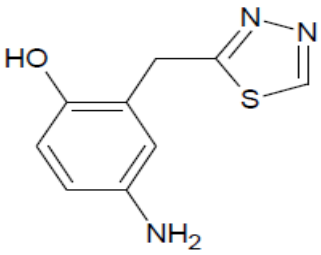
Husain et al derived a series of novel 4-amino-2-{5-[(4-substituted phenyl)amino]-1,3,4-thiadiazole-2-yl} phenol (3). Antibacterial and antifungal activity was evaluated for the synthesized compound. The synthesized compounds showed high degree of antibacterial and antifungal activity against S. aureus (gram- positive) and E.coli (gram-negative) bacteria and antifungal activityagainst A. niger fungi.[2]



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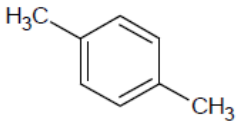

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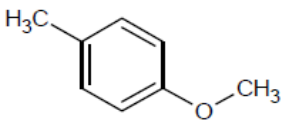

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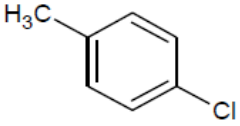

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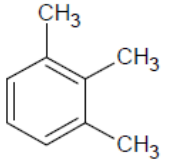

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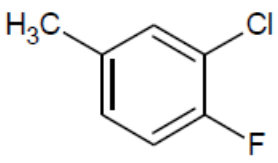

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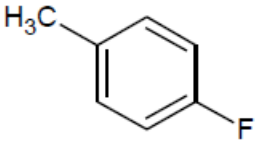

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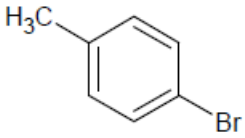
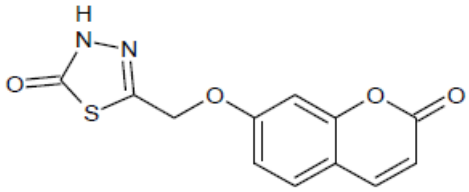


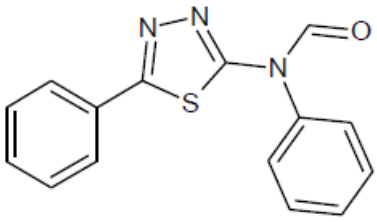
10

Novel thiadiazoles substituted with coumarin moiety (11) were produced by Al-Amiery et al. In vitro anti- bacterial and anti-fungal activities were evaluated against Staphylococcus aureus, Escherichia coli, Klebsiella pneumoniae, Proteus vulgaris, Pseudomonas aeruginosa and Aspergillus niger, Candida albicans respectively.[3]



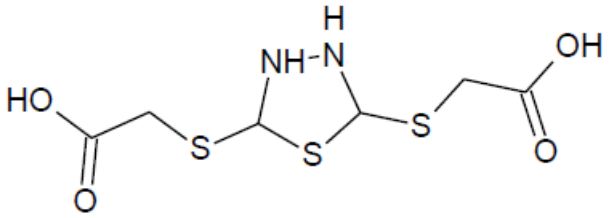
11

A series of 2-benzoylamino-5-(dihydroxyphenyl)-1,3,4-thiadiazoles derivatives (12) were prepared by Quandil et al. Antimicrobial activity was evaluated for all the synthesized compounds. These compounds have showntheselective activityagainst gram-positive S.aureus.[4]



12

A sequence of novel 2,5-(dithioacetic acid)-1,3,4-thidiazole (13) and 2,5-di-[5-amino-1,3,4thiadiazole-2- thiomethyl]-1,3,4-thiadiazole (14) derivatives were prepared by Salimon et al. The produced derivatives were examined for antibacterial activitiy against the Gram-positive (S. aureus, S. cerevisiae and C. diphtheriae) and the Gram-negative bacteria(E.coli and P. aeruginosa).[5]



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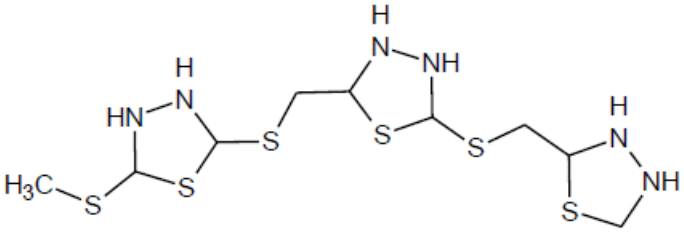
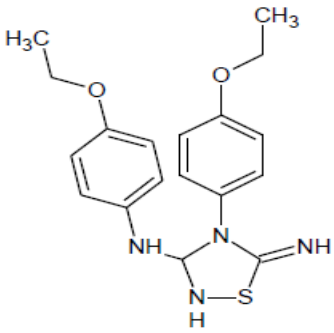


14

Anticonvulsant activity

Gupta et al synthesized a series of 3-aryl amino/amino-4-aryl-5-imino-D2-1,2,4-thiadiazoline (15-16). The anticonvulsant activity of all the synthesized compounds was evaluated against maximal electroshock induced seizures MES) and subcutaneous pentylenetetrazole (ScPTZ) induced seizure models inmice.[6]



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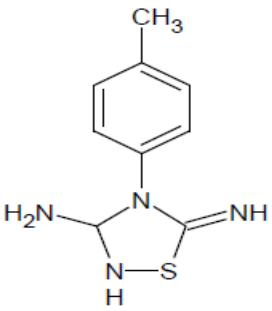
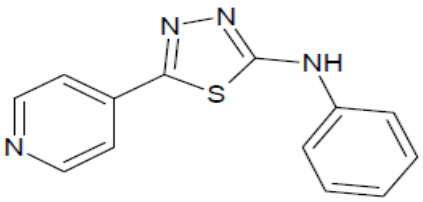


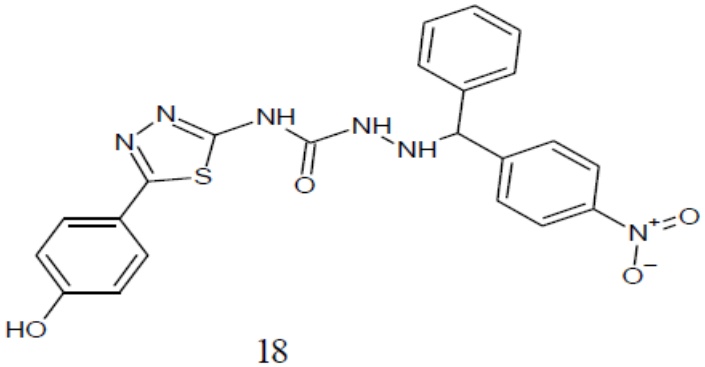
16

Shahar Yar et al synthesized 2-Phenylamino-5-(4-pyridyl)-1,3,4-thiadiazole derivatives (17). All the newly synthesized compounds were evaluated for their anticonvulsant activity by MES method. Synthesized compounds showed good anticonvulsant activity.[7]



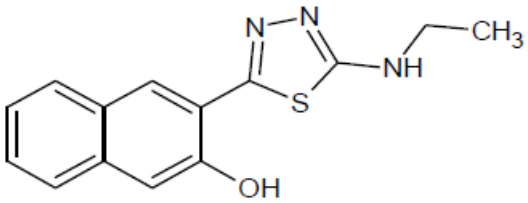
17

Rajak et al. carried out the synthesis of some 2,5-Disubstituted 1,3,4-Thiadiazoles and evaluated their potential anticonvulsant activity. The results showed that the compound with 4-nitrophenyl-substituted semicarbazone (18) was themost active compound comparable with carbamzepine.[8]



18

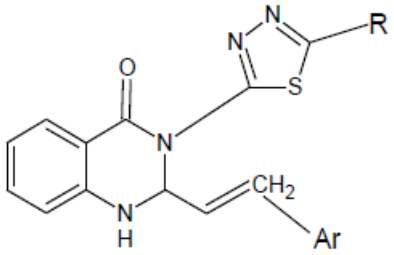
Dogan et al synthesized a series of 2-(N-alkyl/aryl-Nacetylamino)-5-(3acetyloxy-2-naphthyl)-1,3,4- thiadiazole derivatives (19). Compound 2-ethylamino-5-(3-hydroxy-2-naphthyl)-1,3,4-thiadiazole showed 90% protection against pentylenetetrazole-induced generalized convulsions.[9]



19

Jatav et al produced a series of new 3-[5-substituted phenyl-1,3,4-thiadiazol-2-yl]-2-styryl quinazoline4(3H)- ones (20) and evaluated for anticonvulsant activity. Compounds were examined for the maximal electroshock (MES) induced seizures and subcutaneous

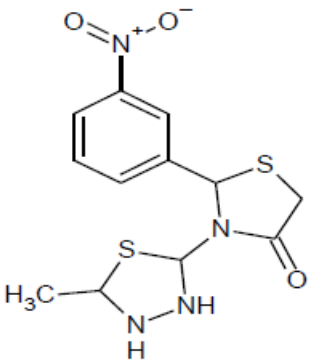
pentylenetetrazole (scPTZ)-induced seizure models. Few compounds showed good anticonvulsant activityin the test models.[10]



20

Anticancer activity

Novel thiadiazoles substituted with thiazolidin-4-ones moieties were obtained by Joseph A. et al. Synthesized compounds were evaluated for anticancer activity on human breast adenocarcinoma cells (MCF-7) by MTT assay. 3-(5-methyl-1,3,4-thiadiazol-2-yl)-2-(2-nitrophenyl)4-oxothiazolidin (21) 2-(3-fluorophenyl)-3-(5- methyl-1,3,4-thiadiazol2-yl)-4-oxothiazolidin (22) and 2-(4-chlorophenyl)-3-(5-methyl-1,3,4thiadiazol-2-yl)- 4-oxothiazolidin showed good activityamong all the compounds.[11]



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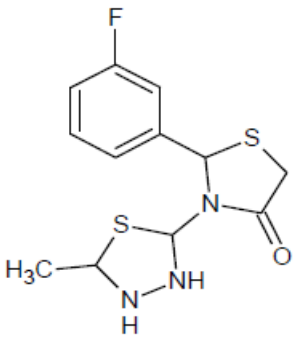
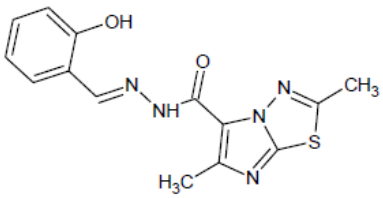


22

A series of novel 4-thiadiazole substituted with carbohydrazides were prepatred by Terzioglu N. et al. (E)- N'-(2-hydroxybenzylidene)-2,6-dimethylimidazo[2,1b][1,3,4]thiadiazole-5-carbohydrazide (23) and (E)-2,6- dimethyl-N'-(4nitrobenzylidene)imidazo[2,1-b][1,3,4]thiadiazole-5-carbohydrazide (24) showed maximum activity.[12]



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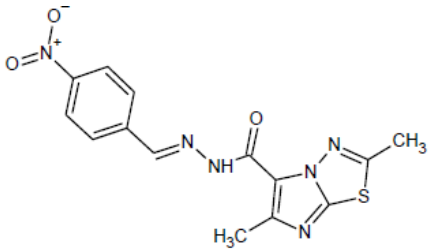
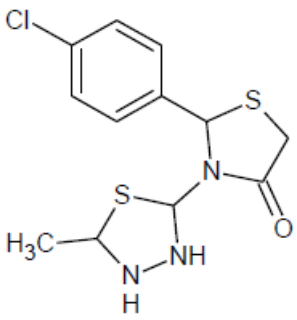


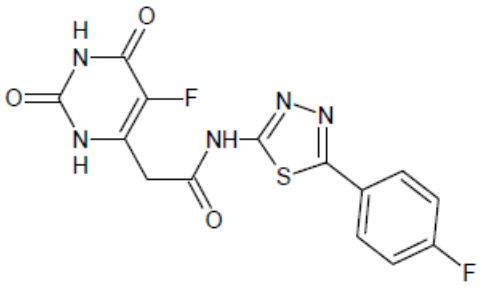
24

Novel 5-(3-indolyl)1,3,4-thiadiazole derivatives (25) were obatained by Kumar et al. The reported compounds were evaluated for anticancer activity.[13]



25

A sequence of N1-acetylamino-(5-alkyl/aryl-1,3,4-thiadiazole-2-yl)-5-fluorouracil derivatives (26-27) were produced by Zheng et al. Obtained compounds were evaluated for their anticancer activity on A-549 (human lung cancer cell), Bcap-37 (human breast cancer cell) byMTT assay.[14]



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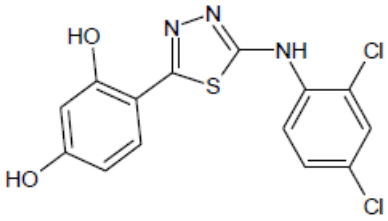
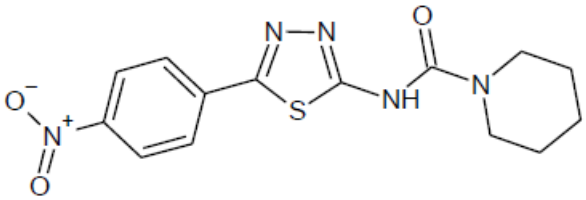


27

Antidiabetic activity

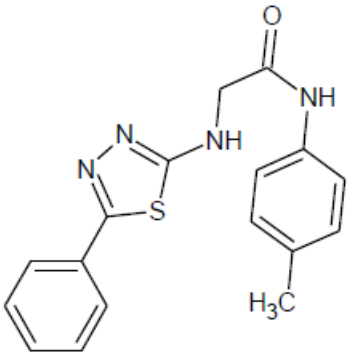
A series of novel thiadiazole derivatives (28) were introduced by Pattan et al. The

synthesized compounds were evaluated for antidiabetic activity.[15]



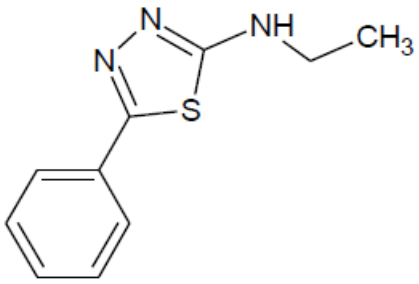
28

Thiadiazole compounds were designed and prepared by Prasanna A Datar et al as an antidiabetic agent using docking studies. Among the synthesized compound 2-(5-phenyl-1,3,4- thiadiazol-2-ylamino)-N- ptolylacetamide (29) showed the significant antidiabetic activity. Antidiabetic ativity of synthesized compounds was evaluated byalloxan induced diabetes in rat model.[16]



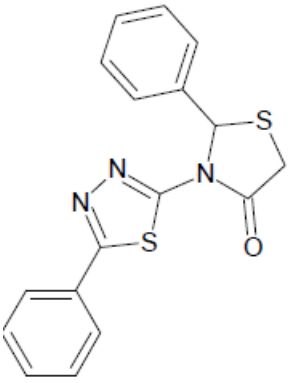
29

Mhasalkar MY et al. produced N-Ethyl-5 Phenyl-1, 3, 4 thiadiazol-2amine (30) and examined for antidiabetic activity. In the study it was found that the substitution of phenyl ring at fifth position and substitution of amine group at second position enhances the activity.[17]



30

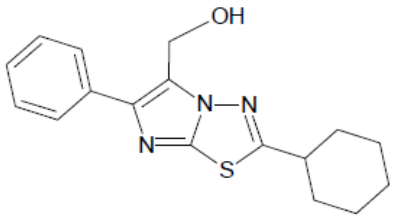
Various derivatives of 2-phenyl-3-(5-phenyl-1, 3, 4-thiadiazol-2-yl)-1, 3thiazolidin-4-one (31) were obtained and screened for antidiabetic by M. SaiHarika et al. The produced compounds were screened for an antidiabetic activity by alloxan induced diabetic Wister albino rat. Among all the synthesized compounds, substituted 1, 3, 4 thiadiazole benzaldehyde derivatives possesses promising antidiabetic activity.[18]



31

Antituberculer activity

Imidazole substituted thiadiazoles (32-33) were produced by Kolavi G. et al. The synthesized compounds were screened for their anti-tubercular activities against Mycobacterium tuberculosis H37Rv utilizing the BACTEC 460 radiometric system. Among all, two comnpounds were found to have promising antituberculer activity.[19]



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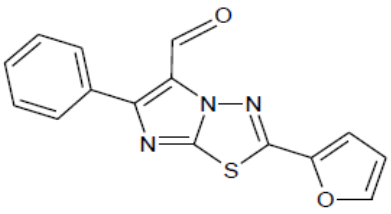
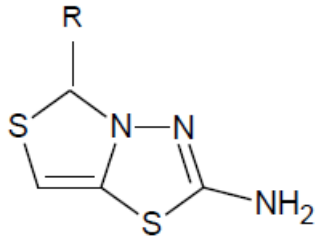


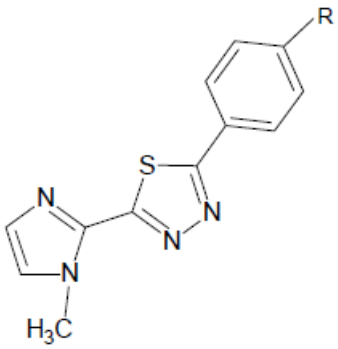
33

A sequence of thiadiazole derivatives (34)were produced by Karigar Asif A et al by using equimolar mixture of aromatic aldehydes thioglycolic acid and thiosemicarbazide in H2SO4. The synthesized compounds were examined for anti-tuberculer activity.[20]



34

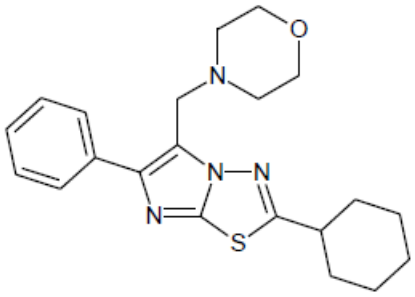
Novel imidazo [2, 1-b][1, 3, 4] thiadiazole derivatives (35) were obatained by Patel H M, Noolvi M N, Sethi N S, Gadad A K, Cameotra S S et al and the synthtesized compounds were evaluated for their antitubercular activity.[21]



35

Various novel thiadiazole derivatvies were produced by Onkol T et al. The synthesized derivatives were 4- ((2-cyclohexyl-6-phenylimidazo[2,1-b] [1,3,4] thiadiazol-5-

yl)methyl)morpholine (36), 4-((6-(4- bromophenyl)2-cyclohexylimidazo [2,1-b][1,3,4] thiadiazol-5yl) methyl)morpholine (37), 4-((2-(furan-2yl)- 6-phenylimidazo[2,1-b][1,3,4]thiadiazol-5-yl) methyl)morpholine (38) and 4-((6-(4-bromophenyl)-2-(furan- 2-yl) imidazo[2,1-b][1,3,4]thiadiazol-5-yl)methyl)morpholine (39). The synthesised compounds possess good activitivyagainst Mycobacterium tuberculosis.[22]



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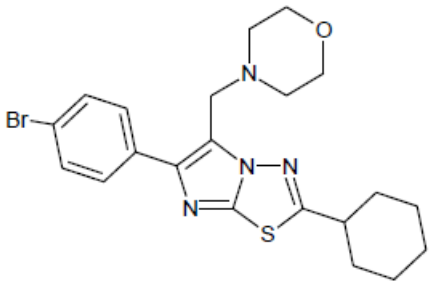

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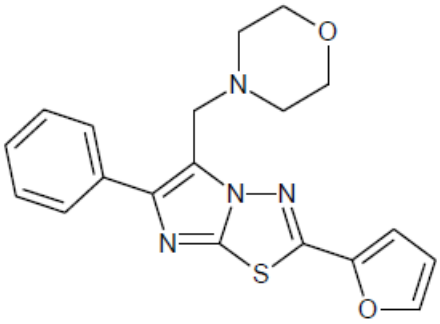

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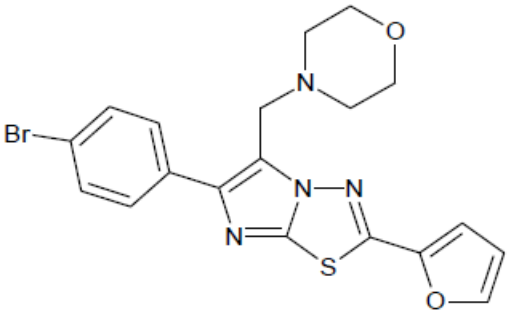
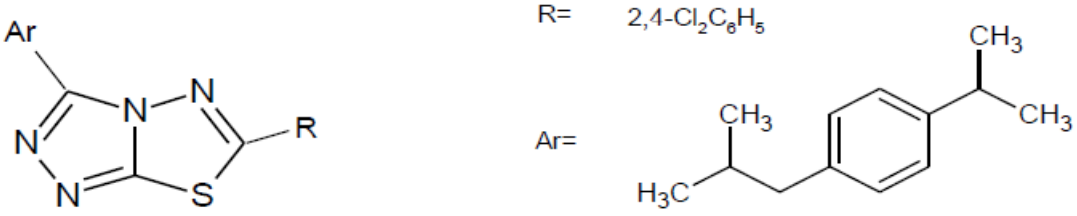


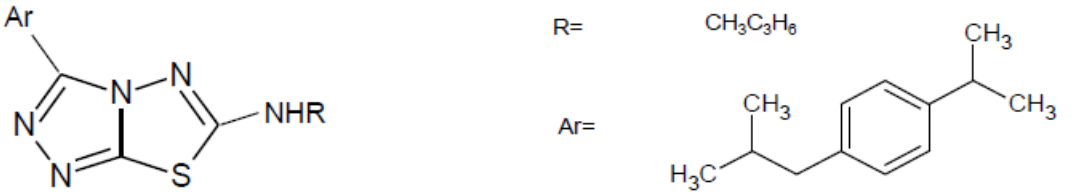
39

Anti-inflammatory

Amir et al produced a sequence of aromatic acids and aryl/ alkyl isothiocyanates substituted-1,2,4- triazolo[3,4-b]-1,3,4-thiadiazole derivatives. Synthesized compounds were screened for anti-inflammatory activity. Among all the obtained compounds, compound (40) has showed high degree of anti inflammatoryactivity.[23]

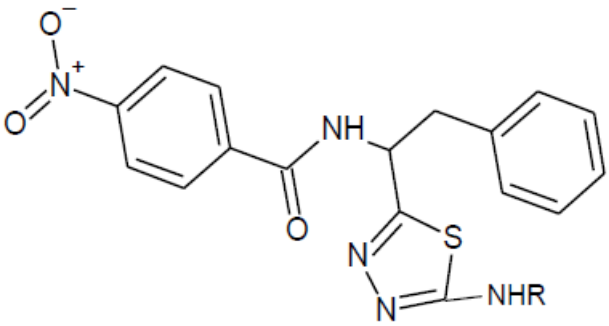


40



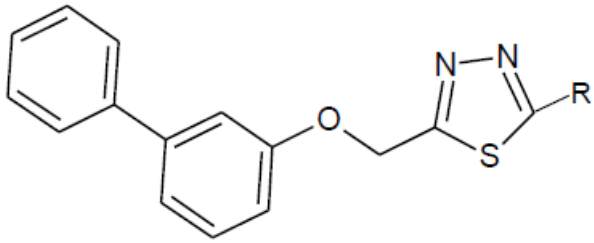
41

Novel 1,3,4-thiadiazole containing phenylalnine moiety were obtained by intramolecular cyclization of 1,4- thiosmicrbazides (42), in acid and alkaline media by Moise et al. Anti-inflammatory activity of obtained compounds was evaluated.[24]



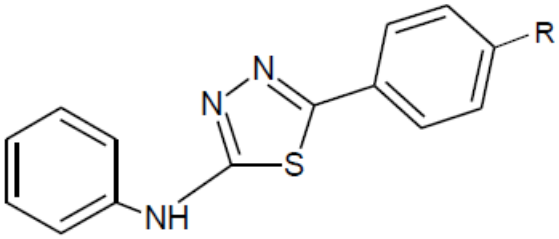
42

Novel 1,3,4-thiadiazole and their derivatives of biphenyl-4-yloxy acetic acid (43) were synthesized by Harish et al. Theobtained compounds were evaluated for anti-infalmmatoryactivityand analgesic activity.[25]



43

Kumari R, Sharma B B, Dubey V et al synthesized 1, 3,4-thiadiazole derivatives (44) and evaluated for its anti-inflammatoryactivity.[26]



44

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