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Pharmacological Activities Of 1, 3, 4-Oxadiazole Derivatives: A Review.

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ABSTRACT

Oxadiazole moiety and its different derivatives concentrated much of the time in the previous couple of decades and discovered intense in different pharmacological and pathological conditions. Oxadiazole is a versatile ring. There are four possible isomers of oxadiazole. Among these, 1, 3, 4-oxadiazole is widely used as medicinal agents. This compound is found to have different biological activities, for example, antibacterial, antifungal, antiviral, antimicrobial, anticancer,anti-inflammatory,anti-oxidant,anticonvulsant,anti-HIV,anti-amoebic,anti-obesity,etc. This manuscript is to collect the literature work reported by researchers on oxadiazole derivatives for their various pharmacological activities.

Keywords: Oxadiazole, anti-inflammatory, antimicrobial, antioxidant

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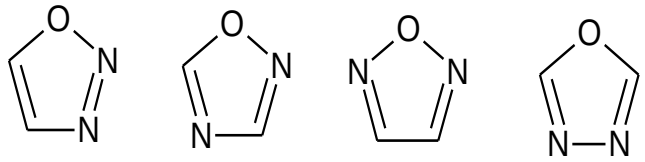
INTRODUCTION

The most important heterocyclic systems are those having five and six membered rings having hetero atoms such as N, O, S, P, Si, and B etc… [1, 2] Heterocyclic compounds are most imperative because of their diverse biological activities. [3, 4] One such imperative heterocyclic nucleus of medicinal use is oxadiazole. Oxadiazole are five membered heterocyclic compounds with two nitrogen atoms and one oxygen atom having general formula $C_2H_2ON_2$. It is obtained from furan by substitution of two Methylene groups (=CH) with two pyridine type nitrogen's (-N=). Depending on the position of nitrogen atom in the ring there are four possible isomers of oxadiazole they are 1, 2,3 oxadiazole, 1,2,4 oxadiazole, 1,2,5 oxadiazole and 1,3,4 oxadiazole.[5] Among these, 1,2,4 oxadiazole, 1,2,5 oxadiazole, and 1,3,4 oxadiazole are stable, but the 1,2,3 is unstable. Activities such as Anti-inflammatory, Analgesic, Antimicrobial, Antineoplastic, Anthelmintic, Anti-tubercular and hypoglycemic etc are mostly observed on compounds containing oxadiazole ring.



1, 2, 3 1, 2, 4 1, 2, 5 1, 3, 4

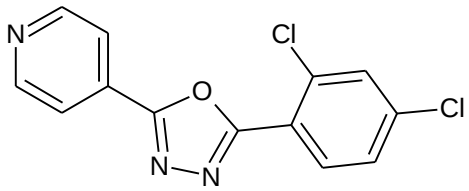
PHARMACOLOGICAL ACTIVITIES

Even though the oxadiazole derivatives possess a broad-spectrum of pharmacological activities, in this review we are mainly focusing on the following activities which includes anti-inflammatory, antioxidant, antibacterial, antimicrobial, antiviral, anticonvulsant, and anti-HIV, antifungal.

ANTIINFLAMMATORY ACTIVITY

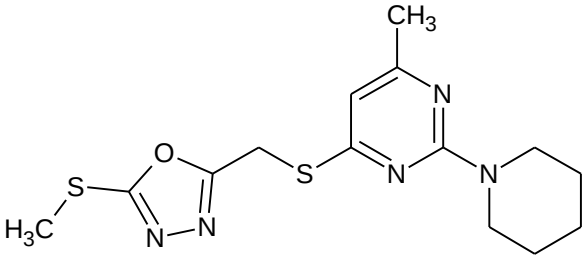
Anti-inflammatory activity is defined as the property of a substance to reduce inflammation. The response of a tissue to injury is termed as inflammation. Derivatives of arachidonic acid a 20-carbon unsaturated fatty acid produced from membrane phospholipids are the potent mediators of inflammation. The 5-lipoxygenase pathway, which produces a collection of leukotriene's and the cyclooxygenase (COX) pathway, which produces prostaglandin are the principal pathways of arachidonic acid metabolism. Pharmacological inhibition of COX can relief the symptoms of inflammation and pain, this is the method of action of non-steroidal anti-inflammatory. [6]

A series of 4-[5- (2, 4-dichlorophenyl)-1, 3, 4-oxadiazol-2- yl] pyridine derivatives was synthesized by Gilani *et al* and screened them for their anti-inflammatory, activities. [7]



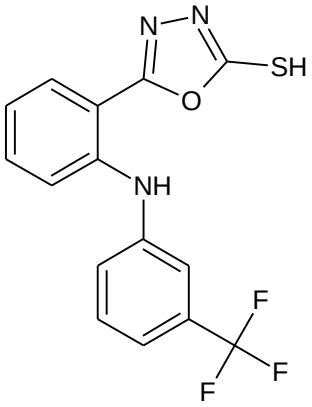
4-[5-(2,4-dichlorophenyl)-1,3,4-oxadiazol-2-yl]pyridine

A series of 5- [(2-disubstitutedamino-6-methyl-pyrimidin-4-yl)-sulfanylmethyl]-3*H*-1,3,4- oxadiazole-2-thione derivatives was synthesized by Burbuliene *et al* and subjected them for their *in-vivo* anti-inflammatory activity by carrageenan induced paw oedema method. [8]



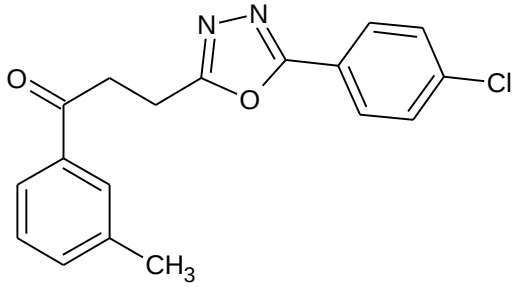
4-methyl-6-({[5-(methylsulfanyl)-1,3,4-oxadiazol-2-yl]methyl}sulfanyl)-2-(piperidin-1-yl)pyrimidine

A novel series of 1, 3, 4-oxadiazole derivatives was synthesized by Boschelli *et al* and evaluated for their anti-inflammatory activity by inhibition of cyclooxygenase and 5-lipoxygenase enzymes. [9]



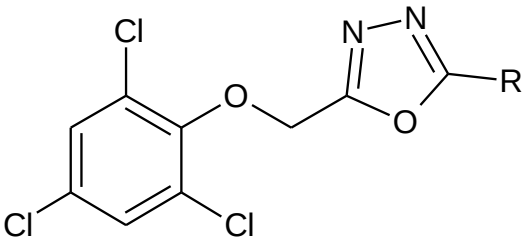
5-(2-{[3-(trifluoromethyl)phenyl]amino}phenyl)-1,3,4-oxadiazole-2-thiol

A series of 2, 5- disubstituted-1, 3, 4-oxadiazoles based on aryl propionic acid moiety was synthesized by Akhter *et al* and screened them for anti-inflammatory and lipid peroxidation activities. Some compounds showed better anti-inflammatory activity comparable to standard drug Ibuprofen. [10]



3-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-1-(3-methylphenyl)propan-1-one

Some new 2-substituted aryl -5- (2, 4, 6-trichloro phenoxy methyl)- 1,3,4-oxadiazole derivatives was synthesized by Amir M *et al* and pharmacologically evaluated for their in vitro anti-inflammatory activity by using carrageenan induced rat paw edema method. [11]



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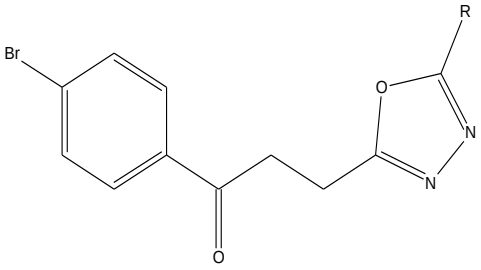
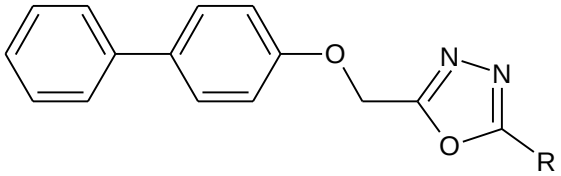
A novel series of 2-[3-(4-bromophenyl) propan-3-one]-5-(substituted phenyl)-1, 3, 4-oxadiazole was synthesized by AsifHussain *et al* and were evaluated for anti-inflammatory activity on wistar rats. Indomethacin used as reference drug for comparison. [12]



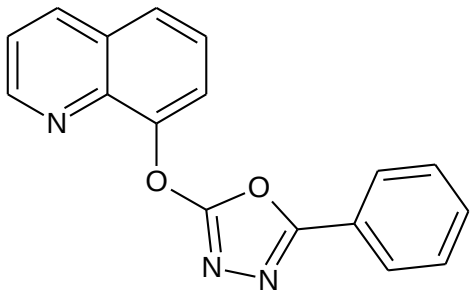
Kumar Harish *et al* synthesized a series of 1, 3, 4-oxadiazole derivatives of biphenyl-4-yloxy acetic acid and were evaluated for their potent anti-inflammatory activity by using carrageenan induced rat paw edema. The synthesized compound showed more anti-inflammatory activity (81.81%) than the reference drug flurbiprofen (79.54%). [13]



ANTIMICROBIAL ACTIVITY

Microbes are mainly of two types prokaryotic and eukaryotic. Prokaryotic organisms are lacking membrane bound organelles and include eubacteria and archaebacteria while Eukaryotic microorganisms possess membrane-bound cell organelles and include fungi and protists.[14] Bacteria are grouped as 'Gram positive' and 'Gram negative' based on the results of Gram staining method. Peptidoglycans are the major constituents of the cell walls of Gram-positive bacteria (almost 95%) for example *Staphylococcus epidermidis, S. aureus, S. pyogenes, Clostridium tetani* while Gram-negative bacteria possess an additional layer of phospholipids and lipopolysaccharides for example *Escherichia coli, Bordetella pertussis, Salmonella typhi, Vibrio cholera*. Majority of the bacterial species are pathogenic and cause infectious diseases. Bacterial infections can become severe as they can cause organ damage and severe complications including cholera, syphilis, anthrax, leprosy, and bubonic plague. [15, 16]

A novel 5-aryl-(8- quinolinoxymethyl)-1, 3, 4-oxadiazole derivatives was synthesized by Mohammed *et al* and were screened for antibacterial and antifungal activity in-*vitro* by using cup-plate method. The activities of the compounds were tested at a concentration range of 5-100 µg/ml. Ampicillin and Clotrimazole were used as standard drugs against bacteria and fungi respectively at concentration of 25µg/ml. The results of antibacterial and antifungal effect of the newly synthesized compounds were reported as MIC against bacterial strains such as *Staphylococcus aureus, Bacillus subtilis, Escherichia coli, Salmonella typhi* and fungal stains like *Candida albicans and Aspergillus niger*. [17]



8-[(5-phenyl-1,3,4-oxadiazol-2-yl)oxy]quinoline

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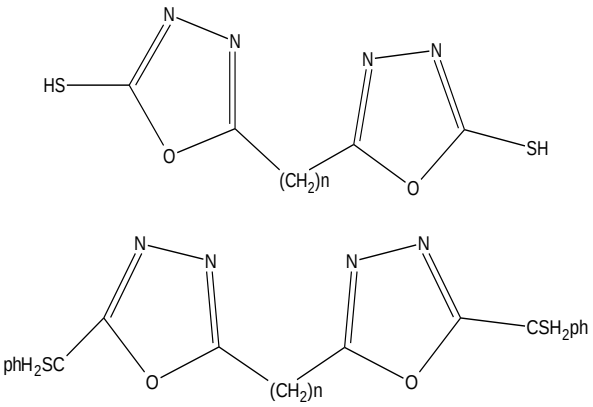
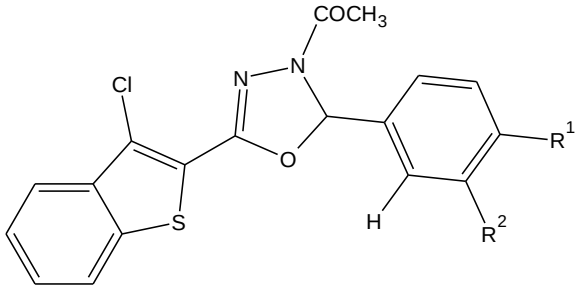
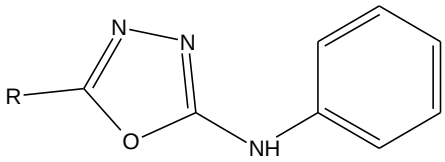
A series of 5,5'-dimercapto-bis-[1,3,4-oxadiazol-2-yl]propane,5,5'-dimercapto-bis-[1,3,4-oxadiazol-2-yl]butane,5,5'-dimercapto-bis-[1,3,4-oxadiazol-2-yl]octane and 5,5'-dibenzylthio-bis-[1,3,4-oxadiazol-2-yl butane was synthesized by Ahmed O. Maslat *et al* and for their antibacterial, antifungal activities against *S.aureuss* and *B.subtilis*.[18]



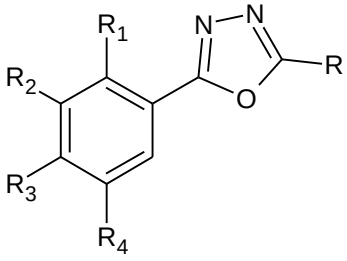
A new series of 3-acetyl-5-(3-chloro-1benzo[b]thiophen-2-yl)-2-substituted phenyl-2, 3-dihydro-1, 3, 4-oxadiazoles and 2-(3-chloro-1-benzo[b]thiophen-2-yl)-5-substituted phenyl-1, 3, 4-oxadiazoles was synthesized by Rakesh Chawla *et al* and screened them for anti-microbial activity. [19]



A series of 5-alkenyl/hydroxyl alkenyl-2-phenylamine-1, 3, 4-oxadiazoles was synthesized by Farshori *et al* and by disc diffusion method the compounds were evaluated for invitro antimicrobial activities. The compounds were found to be active against fungal strain i.e.; *penicillium marneffei* and the standard drug used was greseofulvin. [20]



A series of new 1, 3, 4-oxadiazole with 2-fluoro-4-methoxy moiety was synthesized by B.chandrakantha *et al* and screened for antimicrobial activity. All compounds showed significant anti-fungal activity against *C.Albicans* and anti-bacterial activity against *Pseudomonas aeruginosa* and *Escherichia coli*. [21]



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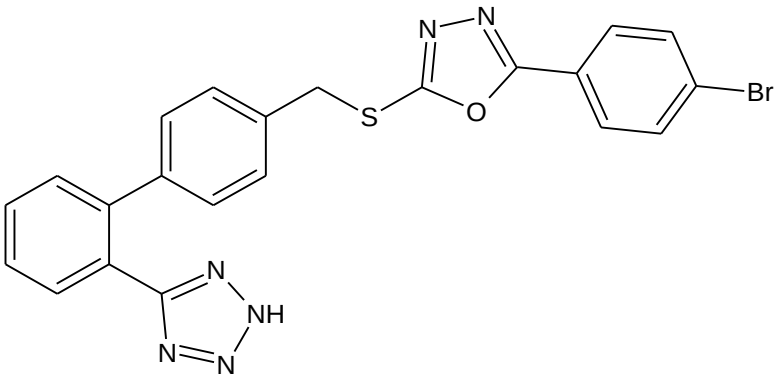
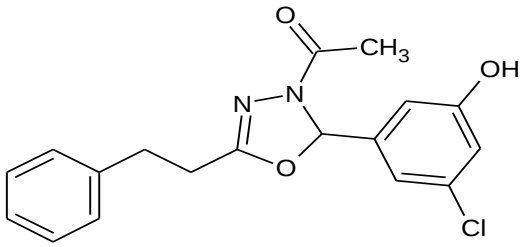
Jun-Shu et al synthesized a series of several new 5-[4'-(5-phenyl-1, 3, 4-oxadiazole-2-yl-sulfonylmethyl)-biphenyl-2-yl] - tetrazole derivatives and these compounds were evaluated for their antimicrobial activity against *B. subtilis* and *E. coli* at the concentration of 100µg/ml in nutrient agar media. These compounds showed significant antimicrobial activities as compared with standard drug. [22]



5-[4'-({[5-(4-bromophenyl)-1,3,4-oxadiazol-2-yl]sulfanyl}methyl)biphenyl-2-yl]-2*H*-tetrazole

New series of 1-(2-aryl-5-phenethyl-1, 3, 4-oxadiazole-3(2*H*)-yl)-ethanones were synthesized by Fuloria *et al* and screened for their antimicrobial activities. These newly synthesized compounds demonstrated good antibacterial activity against the stains of micro-organisms like *S.aureus, P. aeruginosa* as compared with standard drug. [23]

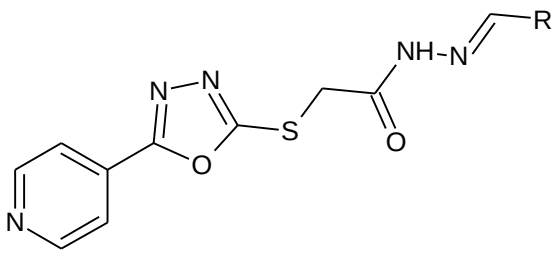


1-[2-(3-chloro-5-hydroxyphenyl)-5-(2-phenylethyl)-1,3,4-oxadiazol-3(2*H*)-yl]ethanone

ANTICANCER ACTIVITY

Cancer is a genetic disease resulting from faulty DNA. Mutations can occur in genes, causing normal cell to become cancerous. More specifically, a defective gene can lead to increased cellular proliferation in one cell and it can be passed down to a daughter cell. The accumulation of mutations in subsequent generations of daughter cells can cause cells to proliferate even more rapidly and eventually undergo structural changes to become malignant. Cancer cells are believed to be result from at least two genetic mutations to a normal cell. These mutations cause the cells to divide uncontrollably.

A series of new 1,3,4-oxadiazole derivatives containing pyridine and acylhydrazone moieties as potential telomerase inhibitors was synthesized by Zhang, F. *et al* . The compounds exhibited significant broad-spectrum anticancer activity against the four cancer cell lines (HEPG2, MCF7, SW1116 and BGC823). [24]



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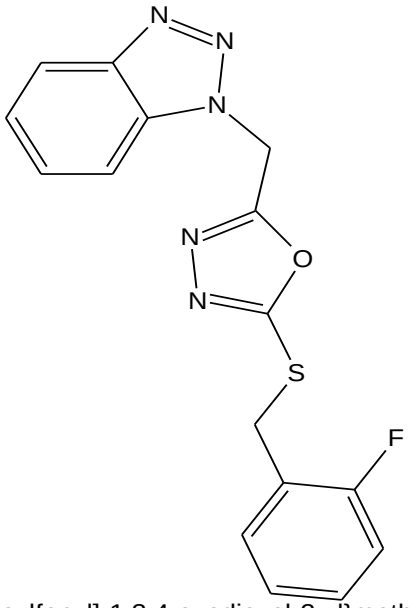
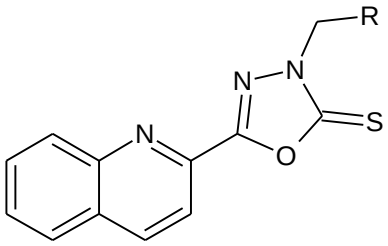
A series of new 1, 3, 4- oxadiazole derivatives containing benzotriazole moiety as potential Focal Adhesion Kinase (FAK) inhibitors was synthesized by Zhang, S. *et al*. Some compounds showed the most potent inhibitory activity against MCF-7 and HT29 cell lines. Apoptosis was carried out by flow cytometry, showed that compound below induced apoptosis against MCF-7 cells and may be a potential anticancer agent against MCF-7 cancer cell. [25]

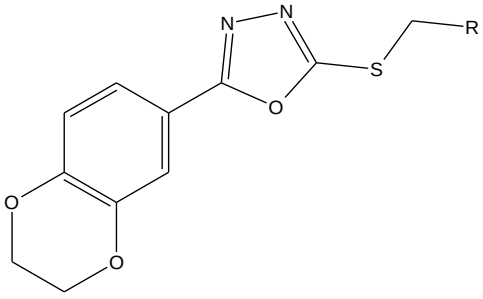


1-({5-[(2-fluorobenzyl)sulfanyl]-1,3,4-oxadiazol-2-yl}methyl)-1*H*-benzotriazole

A series of quinoline derivatives was synthesized and their biological activities were also evaluated as potential telomerase inhibitors by Sun, J. *et al*. The compounds exhibited substantial broad-spectrum antitumor activity against the three cancer cell lines (HepG2, SGC-7901 and MCF-7). [26]



A series of new 1, 3, 4- oxadiazole derivatives containing 1, 4-benzodioxan moiety as potential telomerase inhibitors was synthesized by Zhang, X. M. *et al*. The bioassay tests showed that some of the compounds exhibited broad-spectrum antitumor activity with IC50 concentration range from 7.21 lM to 25.87 lM against the four cancer cell lines, HEPG2, HELA, SW1116 and BGC823. [27]



Some novel 2-substituted-1, 3, 4-oxadiazole-5-yl bearing β-carboline derivatives for their antitumor activity was synthesized and evaluated by *in-vitro* process by Formagio, A. S. N. *et al*. The compounds showed

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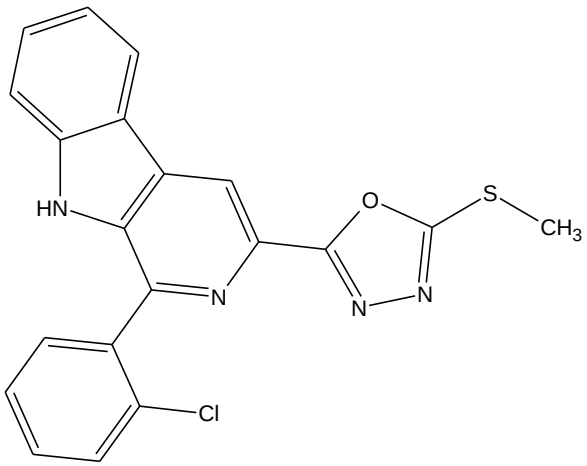
high selectivity and potent anticancer activity against human tumor lines melanoma, breast, lung, leukaemia, ovarian, prostate, colon and renal. Two compounds showed significant anticancer activity on comparison with standard anticancer drug. [28]

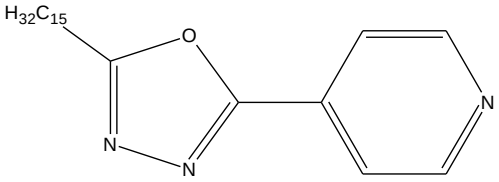


1-(2-chlorophenyl)-3-[5-(methylsulfanyl)-1,3,4-oxadiazol-2-yl]-9*H*-β-carboline

ANTITUBERCULAR ACTIVITY

Tuberculosis, MTB, or TB is a common lethal infectious disease caused by various strains of mycobacteria usually *Mycobacterium tuberculosis*. [29] TB usually targets the lungs but can also attack other body parts. It is transmitted through the air when people have an active MTB infection cough, sneeze, or otherwise transmit their saliva through the air. [30]The major symptoms are a chronic cough with blood-tinged sputum, fever, night sweat and weight loss. Diagnosis relies on radiology (chest X-rays), a tuberculin skin tests, blood tests as well as microscopic culture of bodily fluids. Treatment is different and requires long courses of multiple antibiotics. Antibiotic resistance is a growing problem in multi-drug resistant tuberculosis.
Treatment of TB uses antibiotics to kill bacteria.

Novel 4-(5-substituted-1, 3, 4-oxadiazole- 2-yl) pyridine derivatives was synthesized and evaluated them for anti-tubercular activity by Vazquez, G. N. *et al*. at concentration of 62.5µg/ml. One compound synthesized was more potent and active than standard drugs like Isoniazid, Streptomycin and Ethambutol against *Mycobacterium tuberculosis*. [31]



A novel series of 5-aryl-2-thio-1, 3, 4-oxadiazoles was designed and synthesized by Macaev, F. *et al*. and tested for their invitro antimycobacterial activity against *Mycobacterium tuberculosis* using the alamar blue assay method. [32]

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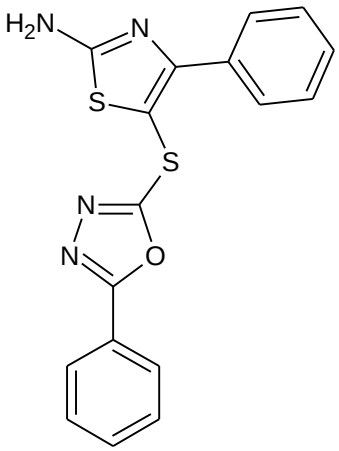
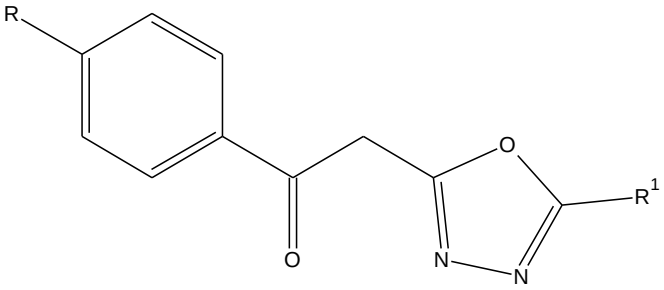
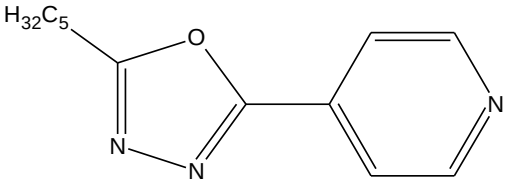


4-phenyl-5-[(5-phenyl-1,3,4-oxadiazol-2-yl)sulfanyl]-1,3-thiazol-2-amine

A novel series of 4-pyrrol-1-yl-benzoic acid hydrazide analogs derived 5 substituted-2 thiol-1,3,4 oxadiazole was synthesized by S.D Joshi *et al* . He evaluated the compound for anti-tubercular activity against *Mycobacterium tuberculosis* H37Rv strain by broth dilution assay method. The compound show better activity against *M.tuberculosis* H37Rv. [33]



Vazquez et al. synthesized 4-(5-substituted-1,3,4-oxadiazole-2-yl)pyridine derivatives and evaluated for antimycobacterial activity at concentration of 62.5µg/ml. Compound was found to be more potent and active than standard drugs like Isoniazid, Streptomycin and Ethambutol against *Mycobacterium tuberculosis*.[34]



A novel series of 5-aryl-2-thio-1, 3, 4- oxadiazoles was designed and synthesized by Macaev *et al*. Compound was tested for their *in-vitro* antimycobacterial activity against *Mycobacterium tuberculosis* using the alamar blue assay method. One compound showed potent anti-tubercular activity when compared with standard drug. [35]

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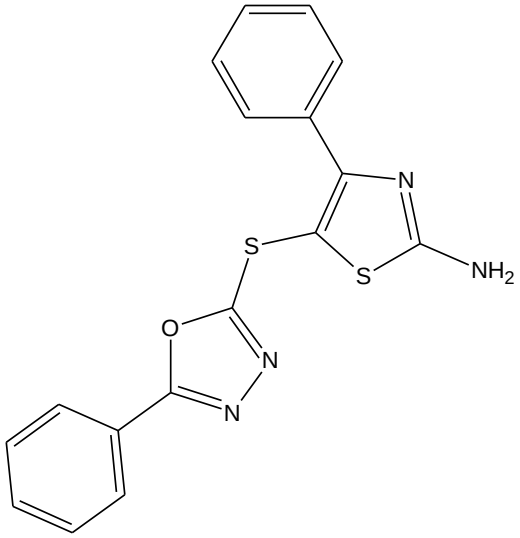
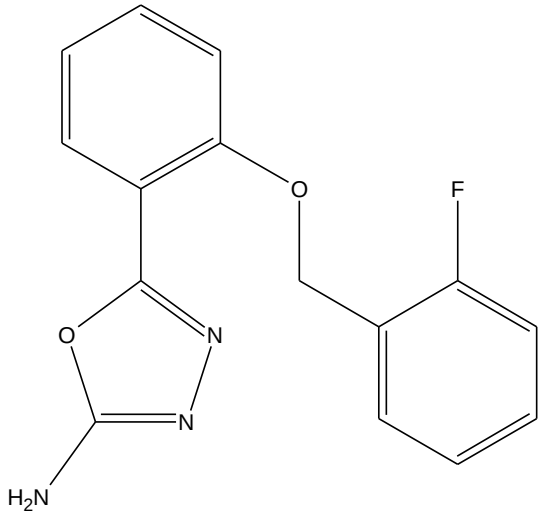


4-phenyl-5-[(5-phenyl-1,3,4-oxadiazol-2-yl)sulfanyl]-1,3-thiazol-2-amine

ANTICONVULSANT ACTIVITY

Convulsion or epilepsy is defined as the repetitive attack of seizure .Seizure means the high frequency abnormal discharge from aggregate of neurons in the cerebral cortex. Benzodiazepine receptors are responsible for the anticonvulsant effect. Benzodiazepine agonists are widely used in the treatment of CNS disorders like convulsion. Benzodiazepines exert their effect by specific binding to GABA $_A$ receptors known as benzodiazepine receptors. They increase the frequency of Cl^- channel opening in response to GABA action and thus producing anticonvulsant effect.

A novel group 2- substituted -5- [2-(2-halobenzyloxy) phenyl]-1, 3, 4-oxadiazoles was synthesized by Zarghi *et al* and studied for their anticonvulsant activities. One compound with fluoro substitution at ortho position of benzyloxy moiety had the best anticonvulsant activity as compared with the standard drug. [36]



5-{2-[(2-fluorobenzyl)oxy]phenyl}-1,3,4-oxadiazol-2-amine

New derivatives of 2-(4-chlorophenyl)-amino-5-(4-pyridyl)-1, 3, 4 oxadiazole was synthesized and screened by Y. Mohammad et al for their anticonvulsant activity. The range of all compounds showed activity in 33-100%. [37]

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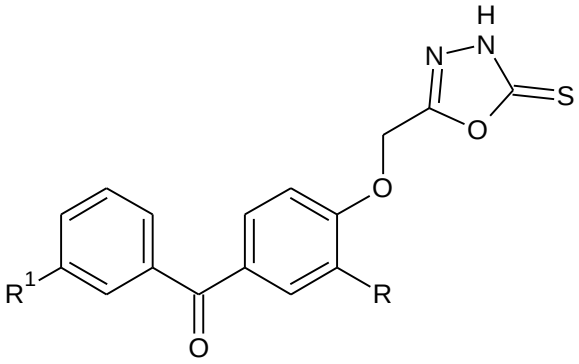


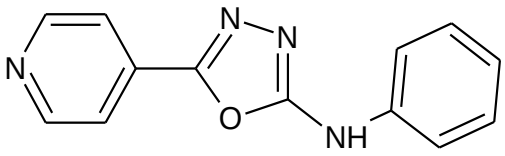
a :R, R1 =H

b :R =CH3 ,R1 =H

c:R =H, R1=Cl

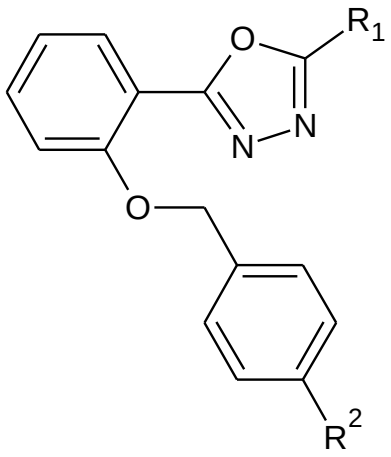
d :R=CH3 ,R1=Cl

5- (4-Aroyl) -aryloxy methyl-2-thio-1, 3, 4-oxadiazole was synthesized by B.S.Sudha *et al* by the intramolecular cyclization of thiosemicarbazides generated by the action of hydrazides on carbon disulphide in the presence of potassium hydroxide. These compounds were screened for anticonvulsant activity against standard phenytoin. [38]



N-phenyl-5-(pyridin-4-yl)-1,3,4-oxadiazol-2-amine

A series of new 2-substituted-5-(2-benzyl -oxyphenyl)-1, 3, 4-oxadiazoles was synthesized and evaluated by S. J. Gilani *et al* for their anticonvulsant action. Compound shows considerable anticonvulsant activity both in PTZ and MES models. Benzodiazepine receptors are responsible for this mechanism. [39]



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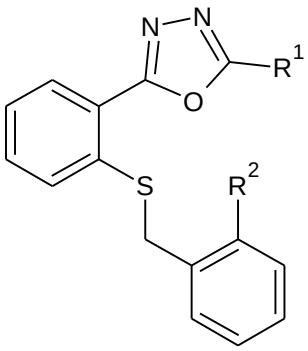
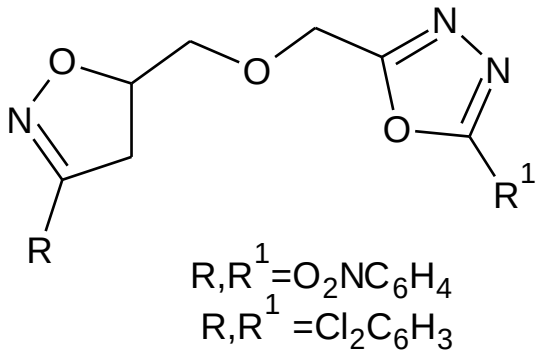
New series of 2-substituted-5-{2-[(2-halobenzyl) thio) phenyl}-1, 3, 4-oxadiazoles were designed and synthesized by Zarghi Afshin et al.The synthesized compound were screened for their anticonvulsant activity in MES method. The compounds contain main essentials pharmacophore for binding to the benzodiazepine receptor. [40]



ANALGESIC ACTIVITY

Analgesics are the drug that relieves pain selectively without blocking the conduction of nerve impulses, markedly altering sensory perception, or affecting consciousness.

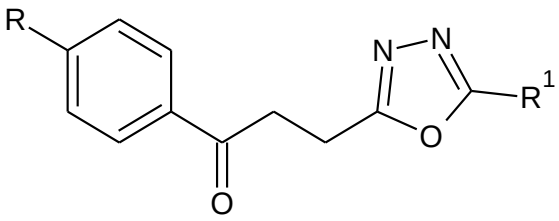
B. Jayashankar *et al* synthesized two 1, 3, 4 oxadiazole derivatives. The synthesized compounds were screened for analgesic activities. [41]



$R,R^1=O_2NC_6H_4$

$R,R^1=Cl_2C_6H_3$

Azad bismillah *et al* synthesized aroylpropionic acid based 2, 5-di-substituted-1, 3, 4-oxadiazoles were and tested for their strong analgesic activity. [42]



Some 2-[3-(4-bromophenyl) propane-3-ones]-5-(substituted phenyl)-1, 3, 4-oxadiazoles were synthesized by Asif Husain *et al* with the aim to get a better analgesic activity. The analgesic activity was screened by acetic acid induced writhing method. [43]

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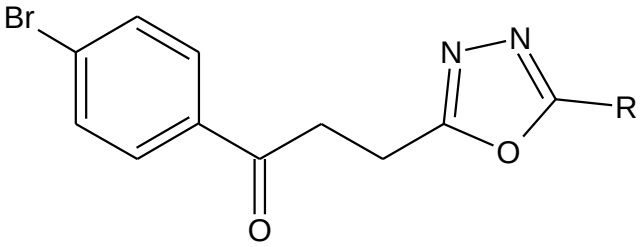
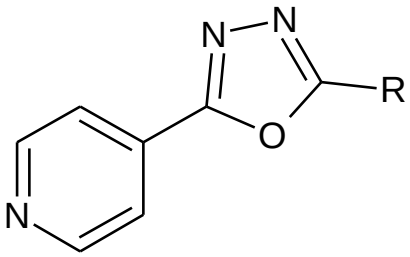
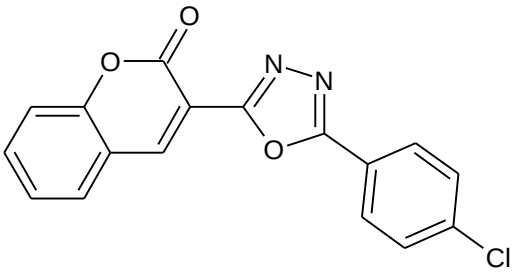


Some novel 2, 5 di-substituted-1, 3, 4-oxadiazole & their synthetic analogs were synthesized by Dewangan Dhansay. These compounds have been found to possess analgesic activity by using acetic acid induced writhing method as compare to the standard drug diclofenac. [44]

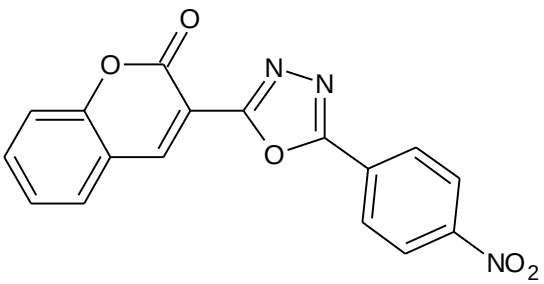


Seigmund. E and Cadmus. R synthesized 6 compounds and the activity was carried out on wistar mice weighing between 20-30 gm using tail flick method. The test compounds and standard drug (pentazocine 5mg/kg) were administered orally. Compounds 1,2,3,4 showed good analgesic activity (88.85, 76.32, 80.5 & 86.11 respectively) while compounds 5 and 6 showed moderate activity (55.5, 68.25 respectively) in compare to the standard drug pentazocine. [45]



3-[5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl]-2*H*-chromen-2-one

1



3-[5-(4-nitrophenyl)-1,3,4-oxadiazol-2-yl]-2*H*-chromen-2-one

2

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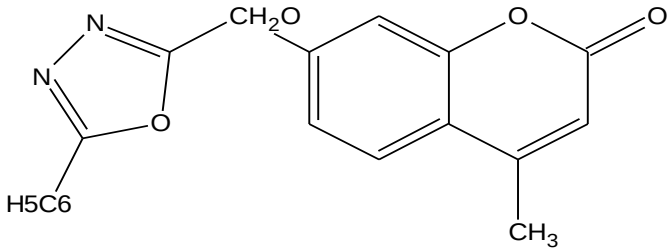

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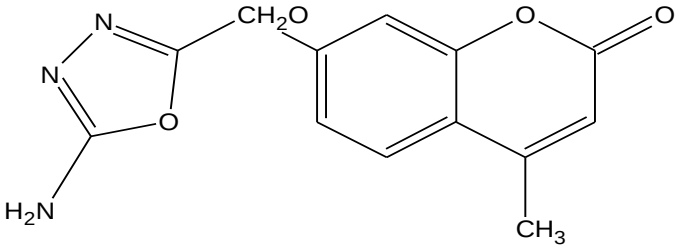

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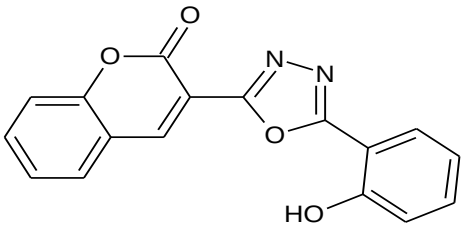
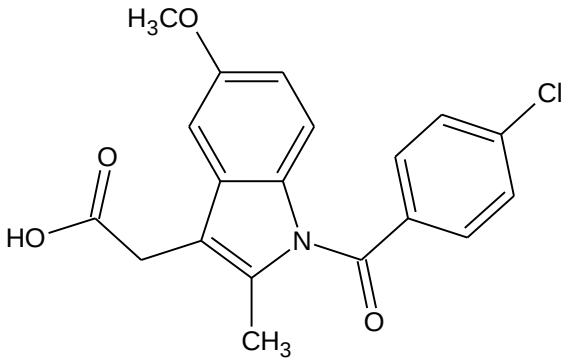


3-[5-(2-hydroxyphenyl)-1,3,4-oxadiazol-2-yl]-2*H*-chromen-2-one

5



[1-(4-chlorobenzoyl)-5-methoxy-2-methyl-1*H*-indol-3-yl]acetic acid

6

ANTI-ALZHEIMER'S ACTIVITY

Alzheimer's is a neurodegenerative disorder of CNS. Alzheimer's disease is characterized by the loss of cholinergic neurons in the nucleus basalis of Maynert, whereas Parkinson's disease is associated with a loss of dopaminergic neurons in the substantia nigra. Dementia of the Alzheimer's type has three distinguishing features:

1) Accumulation of senile plaques (Î²-amyloid accumulations),
2) Formation of numerous neurofibrillary tangles, and
3) Loss of cortical neurons particularly cholinergic neurons.

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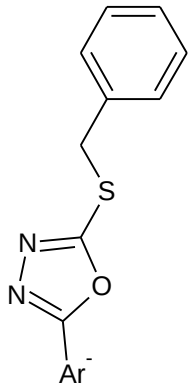
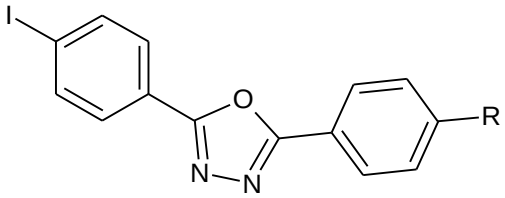
Glycogen syntheses kinase-3b (GSK-3b) which is a protein produced during abnormal hyper phosphorylation of tau protein and its inhibitors are considered to be best therapeutic agents for the treatment of Alzheimer's disease.

Afshin Zarghi and his co-workers designed and synthesized a variety of oxadiazole derivatives as GSK-3b inhibitors. Among these compounds, one compound showed highly selective and potent GSK-3b inhibitory activity in vitro and its binding mode was determined by obtaining the X-ray co-crystal structure of 20x and GSK-3b. [46]



A novel series of 2, 5-diphenyl-1, 3, 4-oxadiazole derivatives were synthesized by Morihisa Saitoh *et al* for detecting b-amyloid plaques in Alzheimer's brains. The affinity for amyloidal plaques was assessed by an in vitro binding assay using preformed synthetic Ab42 aggregates. 2, 5-diphenyl-1, 3, 4-oxadiazole derivatives were compared with 3, 5-diphenyl-1, 2, 4-oxadiazole (1, 2, 4- DPOD) derivatives, The former displayed good penetration of and fast wash out from the brain in bio distribution experiments.[47]



ANTIOXIDANT ACTIVITY

An antioxidant is a molecule that inhibits the oxidation of other molecules. Oxidation is a chemical reaction involving the loss of electrons or an increase in oxidation state. Oxidation reactions can produce free radicals. In turn, these radicals can start chain reactions. When the chain reaction occurs in a cell, it can cause damage or death to the cell. Antioxidants terminate these chain reactions by removing free radical intermediates, and inhibit other oxidation reactions.

A new series of Mannich base of 1, 3, 4-oxadiazole derivatives possessing 1, 4-benzodioxan were synthesized by Ma *et al.* In vitro activity of these compounds were screened by employing 2, 2'-diphenyl-1-picrylhydrazyl radical (DPPH), 2, 2'-azinobis (3-ethylbenzothiazoline-6-sulfonate) cationic radical and ferric reducing anti-oxidant power scavenging assays. The compounds exhibited good anti-oxidant activities due to the combination of 1, 4-benzodioxan, 1, 3, 4-oxadiazoles and substituted phenyl ring. Particularly, compounds 3-([(2, 6-Difluorophenyl)amino]methyl)- 5-(2,3-dihydrobenzo[b][1,4]dioxin-6-yl)-1, 3, 4-oxadiazole-2(3H)-thione and 5-(2,3-Dihydrobenzo[b][1,4]dioxin-6-yl)-3-([(3,4,5- trifluorophenyl)amino]methyl)-1, 3,4-oxadiazole-2(3H)-thione showed significant radical scavenging ability comparable to the commonly used anti-oxidants, butylated hydroxytoluene (BHT) and Trolox. As compared to standard oxidizing agents such as Trolox and BHT, the oxadiazole derivatives which are substituted with phenyl exhibited better anti-oxidant activity. [48]

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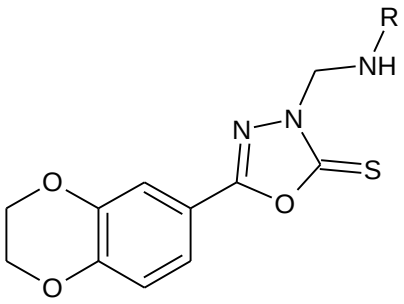
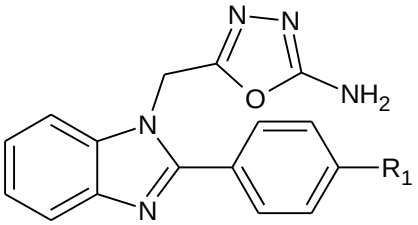


Kerimov *et al.* Synthesized and evaluated the anti-oxidant properties of two new series of 2-amino-1, 3, 4-oxadiazoles and 5-aryl-1, 3, 4-oxadiazoles carrying benzimidazole moiety. The anti-oxidant properties of these compounds were screened *in vitro* by the determination of the microsomal NADPH-dependent inhibition of lipid peroxidation levels, the microsomal ethoxyresorufin O-deethylase activity, and DPPH radical scavenger effects. Among the tested compounds, 2-([2-(4-chlorophenyl)-1H-benzo (d) imidazole-1-yl] methyl)-5-(4-fluorophenyl)-1, 3, 4-oxadiazole was found to be the most active compound in all three *in vitro* systems. [49]



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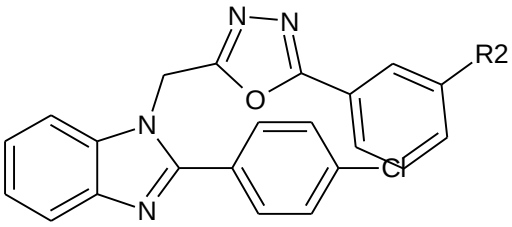

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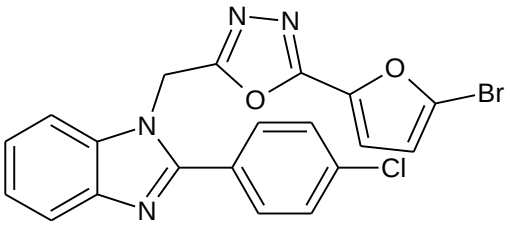

3

ANTIDIABETIC ACTIVITY

Diabetes is defined as a group of metabolic diseases in which there is high blood glucose (blood sugar), either

- Type 1 Diabetes - the body does not produce insulin. Approximately 10% of all diabetes cases are type 1.
- Type 2 Diabetes - the body does not produce enough insulin for proper function. Approximately 90% of all cases of diabetes worldwide are of this type.

Shingalapur et *al* synthesized & tested a group of 1, 3, 4-oxadiazole containing 2-mercepto benzimidazole moieties were for anti-diabetic activity using oral glucose tolerance test (OGTT). [50]

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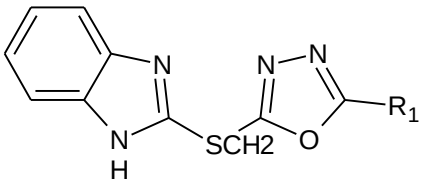
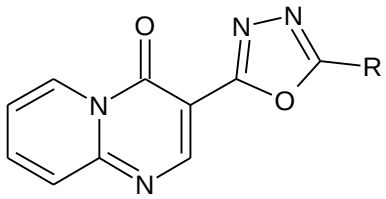


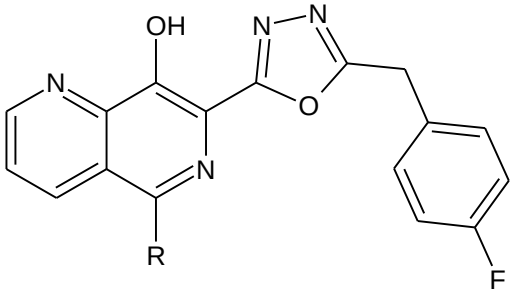
ANTI- HIV ACTIVITY

The human immunodeficiency virus (HIV) is a lentivirus (a subgroup of retrovirus) that causes the acquired immunodeficiency syndrome(AIDS), a condition in humans in which progressive failure of the immune system allows life-threatening opportunistic infections and cancers to thrive. HIV infects vital cells in the human immune system such as helper T cells (specifically $CD4^+$ T cells), macrophages, and dendritic cells.

Hajimahdi *et al.* designed and synthesized a new series of 4-oxo- 4H-pyrido (1, 2-a) pyrimidine derivatives containing 1, 3, 4-oxadiazole derivatives. These compounds were evaluated for their *in vitro* anti-HIV-1 activity. Most of the compounds exhibited moderate inhibitory properties against HIV-1 virus (NL4-3) in Hela cell cultures. The substitution of phenyl ring at c-5 position that is in para position of the 1, 3, 4-oxadiazole ring led to increased anti-HIV activity. [51]



Ravichandran V *et al* synthesized and conducted QSAR study of substituted 1, 3, 4-oxadiazole naphthyridines and the compounds were found as HIV-1 integrase inhibitors. [52]



ANTHELMINTIC ACTIVITY

The parasitic disease constitutes a major health hazard world over. Anthelmintic are drugs that either kill (vermicide) or expel (vermifuge) infesting helminthes & treat parasitic infection due to flat worm & round worm.

Patel *et al* Synthesized 3-amino-1-(2, 4-dinitro phenyl)-5-[(5-substituted-1, 3, 4-oxadiazole-2 yl) amino]-1-Hpyrazole-4-carboxamide and screened for their anthelmintic activity and the compound is compared to the reference drug Albendazole of 0.075%, 0.150%. The synthesized compounds have been shown a better activity against pherituma posthuma. [53]

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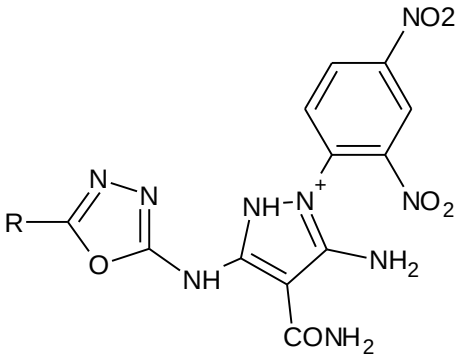
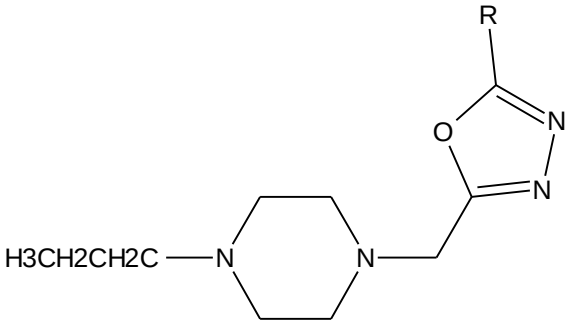


Srinivas *et al* synthesized new compounds of 1-[(5-substituted-1, 3, 4-oxadiazole-2-yl) methyl]-4-propylpiperazines derivatives and screened for their anthelmintic activity. [54]



CONCLUSION

This manuscript has summarized information about the pharmacological aspects of 1, 3, 4- oxadiazole scaffold and its derivatives based on the literature survey. It has been found that oxadiazole derivatives show their promising medicinal importance as antimicrobial, antiepileptic, anticancer, anti-inflammatory, anti-diabetic, anti-tubercular, and antiviral agents. Therefore it can be concluded that oxadiazole derivatives may be exploited further in the drug design and development of novel drugs to provide better treatment for various fatal diseases like microbial, epilepsy, inflammatory, viral, diabetes, and cancer diseases.

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