Review Article

A REVIEW ON OXADIAZOLES AS A PHARMACOLOGICALLY ACTIVE NUCLEUS

ABSTRACT

The structure of the Oxadiazole skeleton is a biologically/biochemically active nucleus which have multiple number of biological activities. Oxadiazole structure is a five-membered aromatic ring and has been used in multiple number of studies and molecules prepared synthetically in laboratories. The principle structure of Oxadiazole ring with a pair of Pyridine-type of nitrogen atoms has been confirmed to be valuable for Oxadiazole analogues for having efficacious protein interaction with multiple number of enzyme protein and receptor protein present in the organ system of the human body through/via different types of interactions, like Vander walls interaction, thereby producing a huge variety of biological activities or pharmacological properties. Due to the variety in the pharmacological activity of Oxadiazole and their derivatives/analogues, they has are termed as one of the important pharmacological aspects to study. Multiple number of Oxadiazole related synthetic compounds possessing high potent action and therapeutic activity are being widely incorporated for treatment and management of multiple number of diseases and disorders, giving immeasurable progression and establishment value. Oxadiazole derivatives expresses multiple number of pharmacological activities like antimicrobial, anti-inflammatory, analgesic, antifungal, antipyretic, antidepressant, antitubercular, anticonvulsant, anticholinesterase, antihypertensive, antidiabetic, antitumor/ anticancer, anti-HIV, antioxidant, etc. The history of 1,3,4-Oxadiazole is also very interesting. It shows that it attracted many chemists/researchers/scientists to explore the Oxadiazole nucleus as a biologically active molecule having promising potency. This review article mainly focuses on the pharmacological profile of 1,3,4- Oxadiazole with various activities and examples (in form of figures/structures). Expectations are like this article will be like a path showing torch to help and serve as a guidance for new innovations/ideas along the progression of research for the evolution of more n more active/potent and less poisonous/toxic Oxadiazole based derivatives.

KEYWORDS

Oxadiazole, Antifungal, Pharmacological activity, Antimicrobial, Antitumor, Antitubercular.

INTRODUCTION

Compounds having different heterocyclic moieties have earned special interest in drug discovery. Among all the heterocyclic compounds, oxadiazoles have influenced remarkable engrossment in medicinal and pharmaceutical chemistry and exhibited a huge scope of biological and pharmacological properties/actions. 1,3,4-oxadiazole derivatives represents an array of synthetic compounds with significant medicinal importance. Oxadiazole analogues are an interesting moiety which has continuously been the principle focus for multiple number of modern studies/researches. This present article narrates

some of the numerous biological and pharmacological activities incorporated with Oxadiazole structural system.

The molecular skeleton of Oxadiazole ring is consisting of 5 atom structure with couple of pyridine-type Nitrogen (N) with single Oxygen (O) atom. Regarding isomerism, four different types of structures for Oxadiazoles are available; such as: 1,3,4-oxadiazoles, 1,2,3-oxadiazoles, 1,2,5-oxadiazoles and 1,2,4-oxadiazoles. The 1,3,4-oxadiazoles variant and 1,2,4-oxadiazoles variant have been more focused and prominently studied due to possessing influential chemical, biological and pharmacological properties. The 1,2,5-oxadiazoles (furazan) is also studied to some extent and it have been found to display some biological activities. The 1,2,3-oxadiazoles (3) are not practically isolated in laboratories because they isomerize simultaneously to α-diazo ketones (Figure 1).

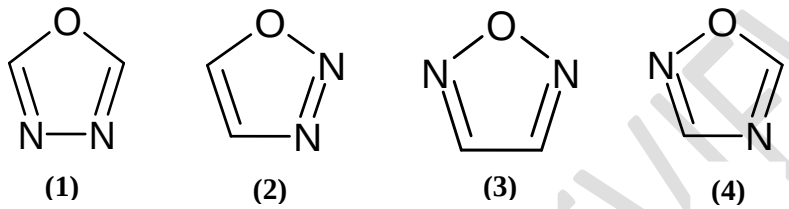


Figure 1. Structures of the regioisomeric oxadiazole rings

Oxadiazole is a very weakly basic in nature owing to the (+/-) I effect (inductive effect) shown by the additional heteroatom. When a couple of – CH moiety from the structure of furan structure are exchanged by a couple of pyridine variety of Nitrogen atom (–N), the Aromaticity property of the emerging Oxadiazole ring reduces by a significant value hence the resulting oxadiazole moiety shows/displays the characteristics/properties of conjugated diene. Because of the presence of comparatively less e^-(negative charge) cloud over the available Carbon atoms (at different positions for different isomers), the Oxadiazole ring is exceptionally non-favourable for electrophilic substitutions at the two carbon atom present; although the attack of electrophile or electrophilic groups occurs to the pyridine variety of Nitrogen atoms, when Oxadiazole moiety hydrogens are swapped with EDGs like ($-CH_3$). Nucleophile based attack is exceptionally impossible in Oxadiazoles moiety due to presence of two pyridine type Nitrogen atoms with lone pairs of electrons; however, the Oxadiazole rings with halogen groups as side chains can react in nucleophilic substitution reactions.

Oxadiazole moiety is a very resourceful and has continuously been an area of large scale and vast study in the recent years. Compounds possessing Oxadiazoles skeleton in their structures are extensively studied for biological and pharmacological activities such as antiviral, antifungal, antimicrobial, antidiabetic, anticancer, antihypertensive activity, antioxidant, neuroprotective activity, hypolipidemic activities, anticholinesterase activity, inhibition of tyrosinase and anticonvulsant activity. They have also made a valuable contribution for intermediates in organic manufacturing of various compounds and largely used as transporting agents for electrons.

In this present review, emphasis is on the diverse pharmacological properties which are associated and contributed with substituted/derivatized Oxadiazoles in the past two and a half decades (1995- 2020).

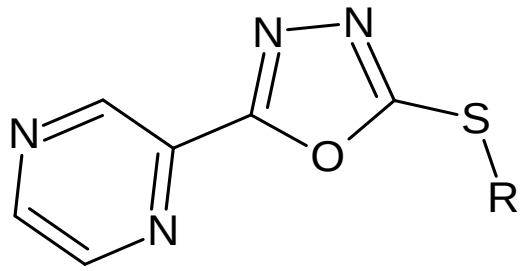
Pharmacological scaffolds of Oxadiazoles

Oxadiazoles have been included into a domain of well- known biologically and pharmacologically active compounds, like, either as a side chain group or in the form of a modification of another heterocyclic ring. There are multiple number of reports in the literatures available describing the oxadiazole derivatives

regarding a multitude of pharmacological and biological effects and few of them are covered in this review.

1. Antifungal activity

Pattan S.R. et al synthesized 2-[5-(arylthio)-oxadiazole pyrazine analogues. Compounds displayed moderate to good Antifungal activity against *Aspergillus niger* at 200mcg/ml. Griseofulvin was used as standard drug for comparison [1a-1c].



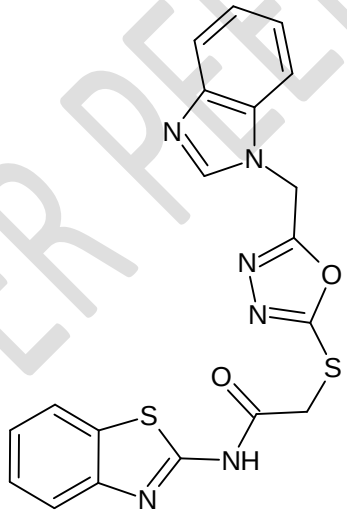
a, **R**= pyridine-2-yl

b, **R**= *o*-hydroxyphenyl

c, **R**= phenyl

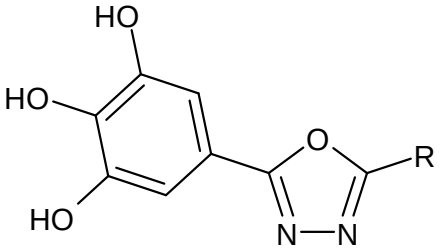
1a-1c

Rahul VP et al innovated the benzimidazole oxadiazole thio-N-phenyl benzothiazole acetamides analogues. Two compounds showed better activity against *Aspergillus niger* at 12.5µg/ml of minimum inhibitory concentration (MIC) [2].



(2)

K. Ilango et al proposed novel set of 2- trihydroxy phenyl)-5-substituted oxadiazoles analogues. Each of the proposed analogues were screened for antibacterial as well as antifungal activity. Few of the synthesized compounds displayed moderate antifungal action at an MIC value of 100µg/ml against *Aspergillus niger* while Ketoconazole was used as a standard/reference drug [3a-3c].



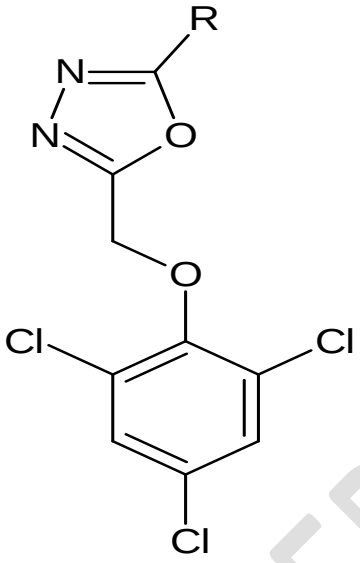
a, R= 2-hydroxy phenyl

b, R= 3-amino phenyl

c, R= 3- methoxy phenyl

3a-3c

Nadagouda S.G. et al synthesized 2-substitute-5-[(2,4,6-trochlorophenoxy) methyl]- 1,3,4-oxadiazoles derivatives. Some derivatives displayed promising fungicidal as well as fungistatic actions for *Aspergillus niger* while some showed moderate to weak activity compared with the standards of fluconazole and griseofulvin [4a-4d].



a, **R**= -S-$CH_2COOC_2H_5$

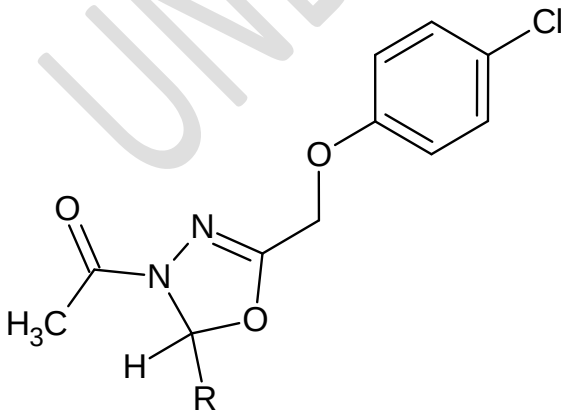
b, **R**= -S-CH_2COOH

c, **R**= -C_6H_5

d, **R**= 4-$NH_2C_6H_4$

4a-4b

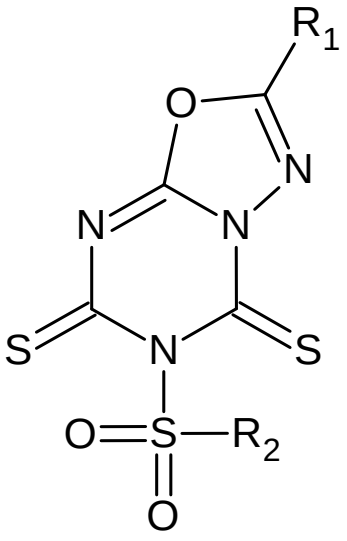
S.D. Joshi et al synthesized 2-aryl-3-acetyl-5-[4-chlorophenoxmethyl-2,3-*H*-oxadiazoles analogues. One compound showed better antifungal activity against *Aspergillus niger* [5a].



R= C_6H_5

5a

Dayashankar tripathi et al synthesized 2-arylsulphonyl-oxadiazole-triazine-5,7-dithione derivatives. Three compounds exhibited the antifungal activity nearly parallel to that of Dithane M-45 (standard) at 100ppm conc. against *Aspergillus niger* [7a-7c].



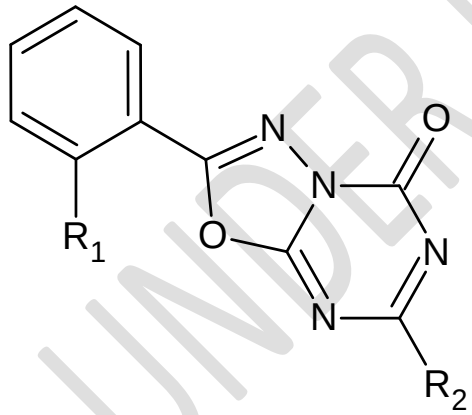
7a-7c

a, $\mathbf{R_1}$= 4-ClC_6H_4 ; $\mathbf{R_2}$= $4CH_3OC_6H_4$

b, $\mathbf{R_1}$=4-ClC_6H_4 ; $\mathbf{R_2}$=2-ClC_6H_4

c, $\mathbf{R_1}$= 4-ClC_6H_4 ; $\mathbf{R_2}$= 2-BrC_6H_4

D.V.Singh et al synthesized 2-Aryl-7-alkyl or aryl-1,3,4-oxadiazole-triazine-5-thione derivatives. Few compounds had similar activity to Mancozeb at 1000ppm and showed 53-49% growth inhibition against *Aspergillus niger* [8a-8c].



8a-8c

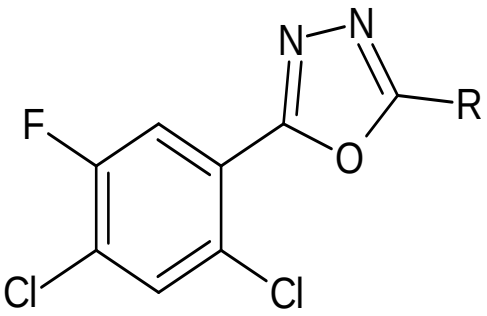
a, $\mathbf{R_1}$= Cl ; $\mathbf{R_2}$= methyl

b, $\mathbf{R_1}$= Cl ; $\mathbf{R_2}$= ethyl

c, $\mathbf{R_1}$= Cl ; $\mathbf{R_2}$= phenyl

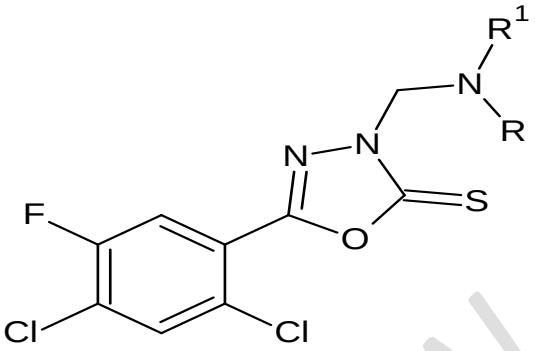
2. Anticancer activity

K. Subrahmanya bhat et al synthesized 3-(methylamino substituted)-5-(2,4-diCl-5-fluorobenzene)-oxadiazolo derivatives. Two compounds emerged active in the primary anticancer assay against breast cancer MCF-7 cell line [9a-9b].



R= 5-(3-Cl-4-F-C_6H_3)-2-furanyl-

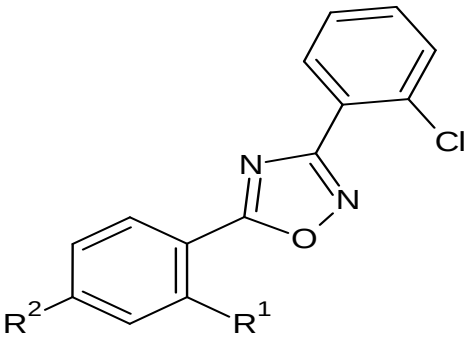
9a



NRR`= Methylpiperazino

9b

Mrityunjoy kundu et al synthesized 3-(2-Chlorophenyl)-5-substituted-1,2,4- Oxadiazole analogues. Two analogues showed potent anticancer property on Swiss albino mice [10a-10b].

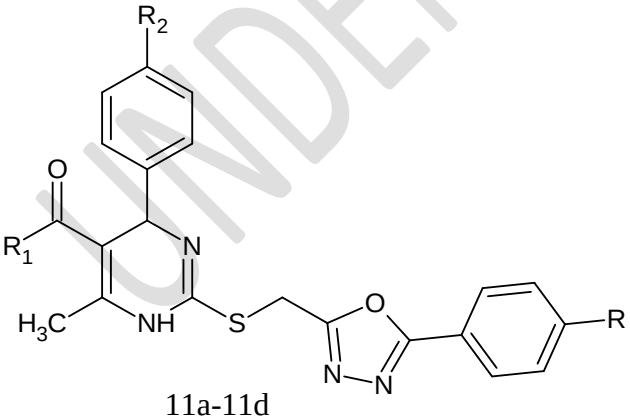


10a-10b

a, **R^1**= H ; **R^2**= Cl

b, **R^1**= Cl ; **R^2**= Cl

Fatma A.F. Ragab et al synthesized Dihydropyrimidine analogues having oxadiazole ring as monastrol derivatives. Some derivatives displayed action to combat various cancer cell lines [11a-11d].



11a-11d

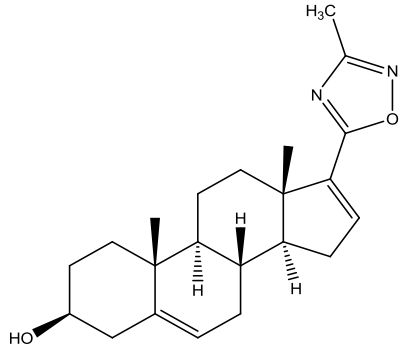
a, **R**= Cl; **R_1**= OC_2H_5 ; **R_2**= 4-Cl

a, **R**= Cl; **R_1**= OC_2H_5; **R_2**= 4-Br

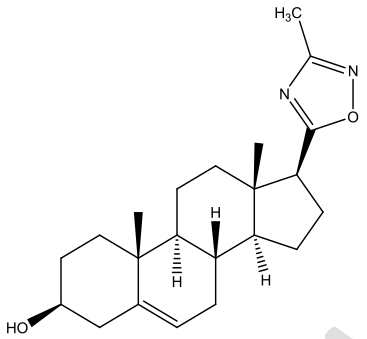
a, **R**= Cl; **R_1**= OC_2H_5 ; **R_2**= 3-Cl

a, **R**= Cl; **R_1**= OC_2H_5; **R_2**= 2,4-diCl

Dora kovacs et al synthesized novel series of Oxadiazole ring in the steroidal structure. Two compounds found to be having antiproliferative activity against 4 cell lines (HeLa, MCF7, A2780 and A431) and inhibition action over rat testicular $C_{17,20}$-lyase [12a-12b].

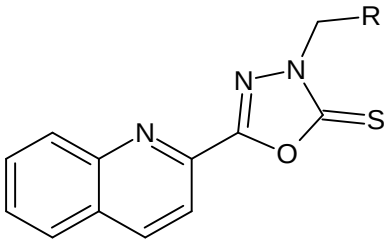


12a



12b

J. sun et al synthesized 2-aminomethyl-5-quinoline-oxadiazole-thione quinolone analogues. Two of these innovated compounds showed promising antiangiogenic activity against various cell lines like HepG2, SGC-7901 and MCF-7 [13a-13b].

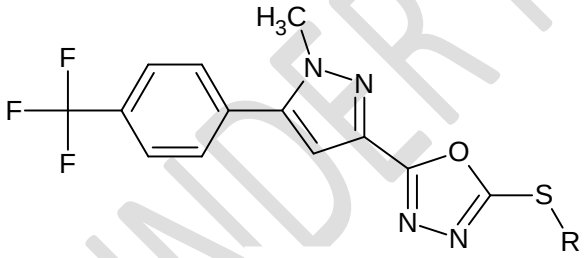


a, R= -NH-C_6H_4(2-F)

b, R= -NH-C_6H_4(4-Cl)

13a-13b

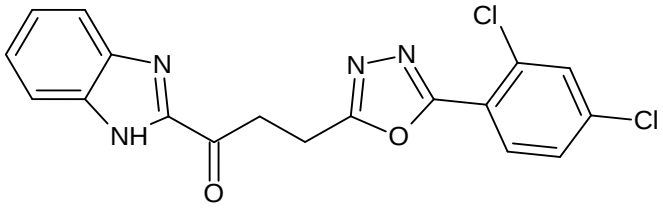
Pushpan P. et al synthesized a series of oxadiazolo having N-methyl-4-(CF_3) phenyl pyrazole group. One compound showed most potent cytotoxic activity with MIC values 15.54 mM in MCF-7 cells [14].



R= 4-CF_2-C_6H_4-CH_2-

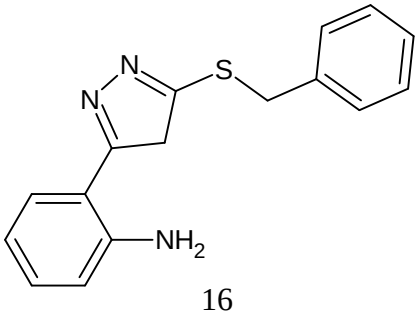
14

Mohd. Rashid et al synthesized novel series of 1-(1*H*-benzoimidazole)-3-(5-(aryl)-oxadiazole-propanone derivatives. One of the derivative exhibited maximum growth inhibition and was screened at 5 different dose concentrations (0.01, 0.1, 1, 10 and 100 mM) [15].



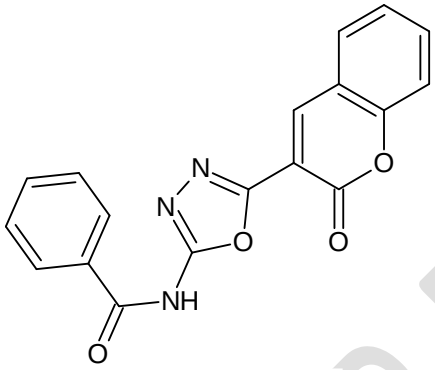
15

Kia liu et al innovated a novel set of 2-(benzylthio)-5-aryloxadiazoles. One derivative was found to have most anti-tumor activity while the evaluation on cell lines like MCF-7 and A549, B16-F10. For reference, Gefitinib was used as standard drug [16].

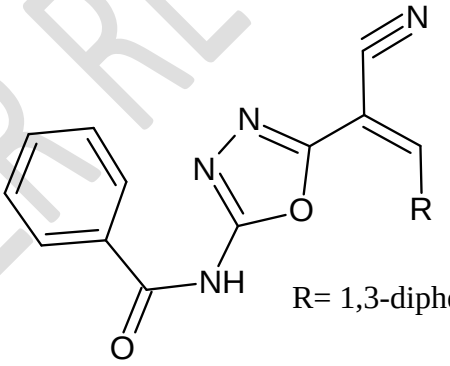


16

Samir bondock et al put forward few oxadiazoles related heterocyclic moiety. Five compounds exhibited prominent potency against HepG2, WI 38, MCF-7, & VERO at different MIC concentrations ranging from 10 to 1000µg/ml [17a-17b].



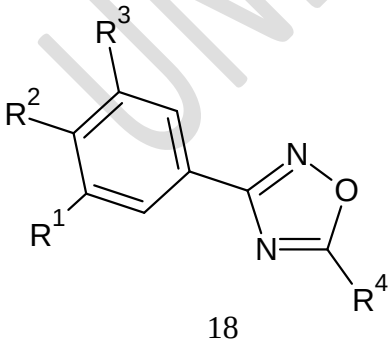
17a



R= 1,3-diphenylpyrazol-4-yl

17b

Dalip kumar et al innovated a series of 1,2,4-oxadiazolo analogues. The trichloromethyl analogues which were proved to have best activityamong the derivatives of the set with significant potent action to combat PC3, DU145, LnCaP, MCF7 MDA-MB-231, PaCa2 and DUP145 with IC_{50} 9.2 µM [18].



18

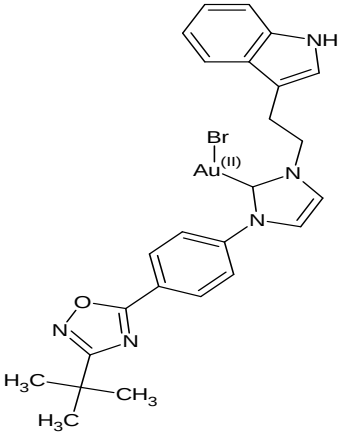
R^{1}= OC_5H_9

R^{2}= OCH_3

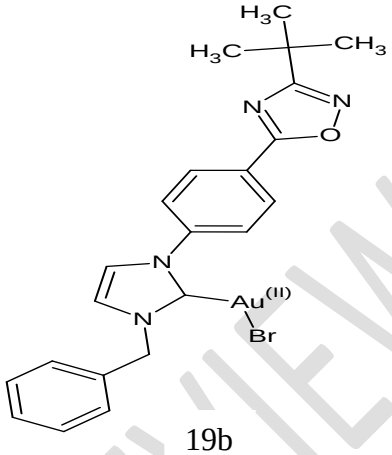
R^{3}= H

R^{4}= CCl_3

Catalin V. Maftei et al synthesized novel set of gold related nitrogen containing heterocycle carbene (NHC) combined with oxadiazole analogues through related imidazolium salts. Few compounds revealed impressive potency and tumor selectivity with IC_{50}<0.1μM against a 12 cancer cell lines [19a -19b].

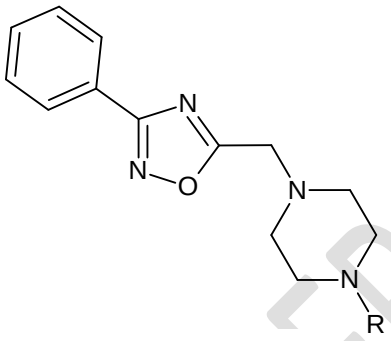


19a



19b

Wiliam caneschi et al innovated a series of 1,2,4 and 1,3,4-oxadiazoles consisting of a lipophilic moiety. Two compounds of 1,2,4- oxadiazole derivative was selectively most potent against 4T1 cell line. Few compounds of 1,3,4-oxadiazoleanalogues with aryl substitutes associated showed quite potent in anticancer assays [20a-20b].

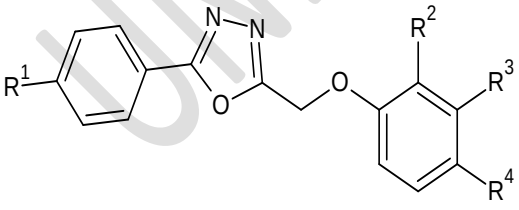


a, **R**= -$(CH_2)_9CH_3$

b, **R**= -$(CH_2)_{11}CH_3$

20a-20b

K. Lakshmithendral et al innovated 2-(phenoxymethyl)-5- phenyl-1,3,4-oxadiazoles. Two analogues showed good to moderate anti- breast cancer action in MDA-MB-453 and MCF-7 cell lines [21a-21b].

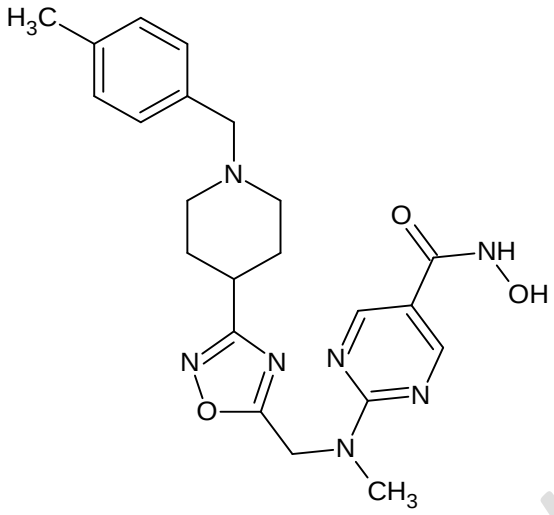


a, **R^1**= OCH_3 ; **R^2**= OCH_3 ; **R^3**= H ; **R^4**= CN

b, **R^1**= F ; **R^2**= OCH_3 ; **R^3**= H ; **R^4**= CN

21a-21b

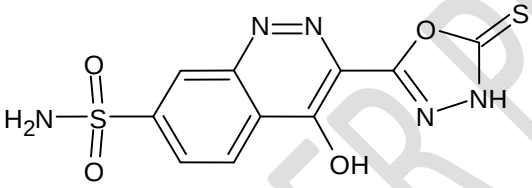
Zhuang yang et al synthesized 1,2,4-oxadiazoles comprising of hydroxamic acid analogues regarding a histone deacetylase inhibitor. The most active derivative exhibited optimum HDAC inhibition action, mostly towards HDAC with MIC values ranging 1.8 to 3.0nM, with the antiangiogenic MIC values range 9.8-44.9 nM to combat 12 different cancer cell lines [22].



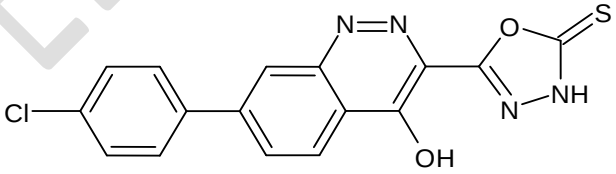
22

3. Anti-tubercular activity

Hurmath unnissa S et al proposed novel set of 3-(5-aryl-1,3,4-oxadiazole)-6-substituted cinnolin-4-ol and 5-(4-OH-6- substituted cinnoline)-1,3,4-oxadiazole-2(3)-thione analogues. Few compounds showed Anti- mycobacterial activity when tested against *M. tuberculosois* through MABA using Isoniazid as standard [23a-23b].

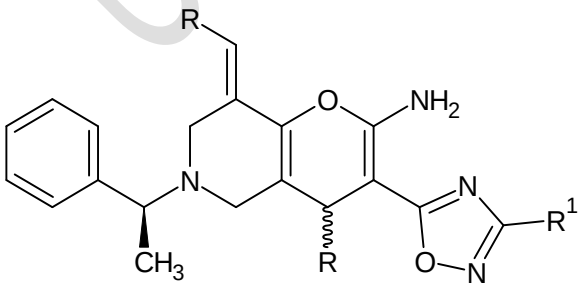


23a



23b

Abdulrahman I. Almansour et al synthesized enantiomerically pure 1,2,4- oxadiazoles through a solvent independent, synthesis based on 4 components and 1,3-dipolar cycloaddition of 4(H)- pyrans having R-CNO. Few compounds showed promising Anti- mycobacterial activity and others showed moderate activity using Isoniazid as standard [24].

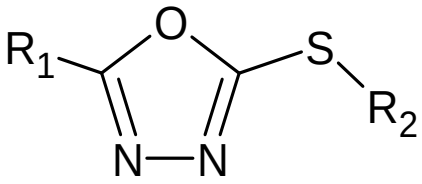


24

R= o,p-$Cl_2C_6H_3$

R^1= p-$Cl_2C_6H_4$

Ravi LB et al innovated 2-(alkyl-thio)-5-(substituted aryl-methyl)-1,3,4-oxadiazole analogues. One of the proposed compound showed almost equipotent anti-mycobacterial activity as that of Isoniazid against nine multidrug- resistant (MDR) & two poly-drug resistant MTB strains [25].

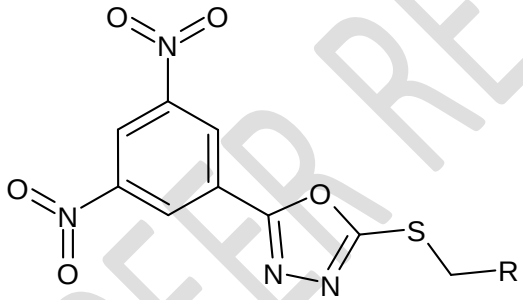


25

R_1= -CH_2-(2,4-Cl_2-C_6H_3)

R_2= - $(CH_2)_2Cl$

Galina karabanovich et al synthesized S-aryl-3,5-dinitrobenzene 1,3,4-oxadiazolo-thiols. Few compounds displayed tremendous anti-tubercular activity with minimum inhibitory concentration values 0.03- 0.06µM and cross resistance was not observed with any of the anti-tubercular drugs [26a-26f].



26a-26f

a, **R**=-(4-OCH_3)C_6H_4

b, **R**=-(2-Cl) C_6H_4

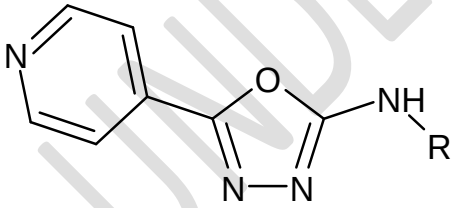
c, **R**=-(3-Cl) C_6H_4

d, **R**=-(4-Cl) C_6H_4

e, **R**=-(3,4-diCl) C_6H_4

f, **R**=-(4-Br) C_6H_4

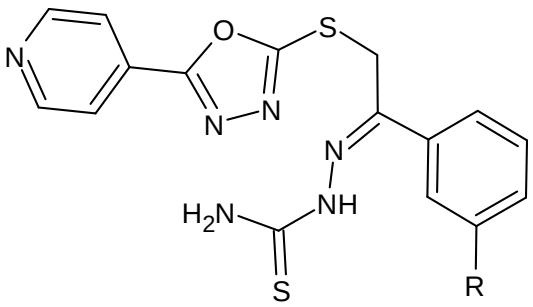
Rudolf vosatka et al innovated 1,3,4- oxadiazole analogues of Isoniazid analogues. Results of pharmacological activities were not that promising. The oxadiazole analogues showed very moderate anti-TB activity [27].



27

R= butyl, hexyl, heptyl, tridecyl, pentadecyl, hexadecyl, octadecyl

Ajay N. Ambhore et al synthesized pyridine-oxadiazole-thio-ethylidene-hydrazinecarbothioamide analogues. Few compounds showed potent growth inhibition and anti-mycobacterium activity and the others showed moderate activities as compared to the drugs Rifampicin and Isoniazid as standard [28a-28c].



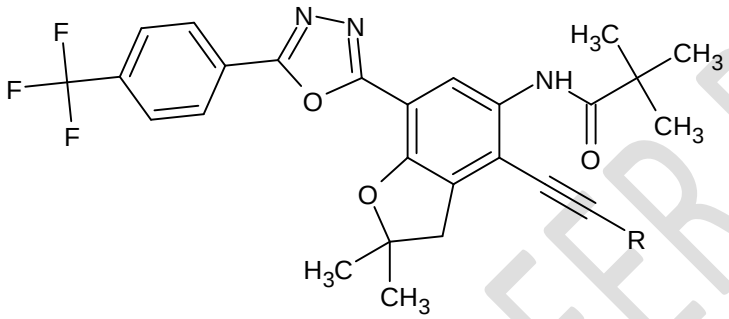
a, **R**= Br

b, **R**= NO_2

c, **R**= CH_3

28a-28c

Somnath gholap et al synthesized 2,2-diCH_3-2,3-dihydrobenzofurane linked oxadiazolo analogues. Few of the proposed derivatives exhibited significant potent activity against non-replicating with comparison to that of to combat replicating broth of *M. tuberculosis* H37Ra ex vivo as well as in vitro at MIC values ranging 2.31 to 23.91µg/ml using the cell lines THP-1, A549 and PANC-1 [29a-29e].



a, **R**= -C_6H_5

b, **R**= -cyclopentyl

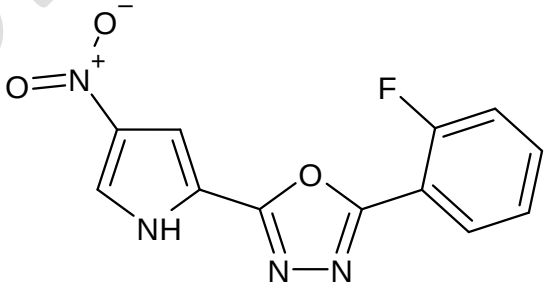
c, **R**= -cyclopropyl

d, **R**= -(4-CF_3) C_6H_4

e, **R**= -CH_2OH

29a-29e

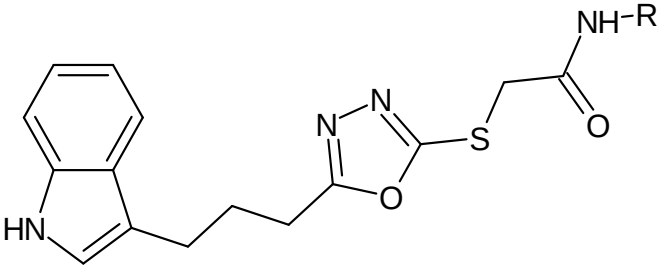
Rajesh A. Rane et al synthesized 4-nitropyrole-based 1,3,4-oxadiazole (2-(4-NO_2-pyrrol-2-yl)-5-substituted-1,3,4-oxadiazolo) analogues. One of the synthesized compounds showed anti-mycobacterial activity (0.46µg/ml) equivalent to that of reference Isoniazid (0.40µg/ml) against VERO cell line and was proved non harmful [30].



30

4. Anti-diabetic activity

Majid nazir et al synthesized 5-[3-(1*H*-indol-3-yl) propyl]-1,3,4-oxadiazolo-2-thiols analogues. Two of the synthesized compounds were most potent with MIC values ranging 9.46 ± 0.03 µM to 9.37 ± 0.03 µM. Remaining derivatives displayed nonsignificant inhibitory property. The MIC values were from 12.68 ± 0.04 to 37.82 ± 0.07, whereas the reference acarbose (MIC = 37.38 ± 0.12 µM) [31a-31b].

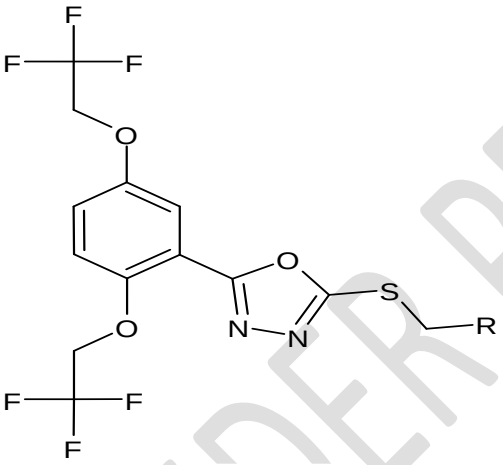


a, **R**= 2,3-dimethylphenyl

b, **R**= 5-methylpyridine-2-yl

31a-31b

Ramesh S. Gani et al synthesized new set of 5-(2,5-bis(2,2,2-trifluoroethoxy) phenyl)-1,3,4-oxadiazolo-2-thiols analogues. Two of the synthesized derivatives showed better activity both in vitro as well as in vivo at MIC=40.00- 80.00µg/ml as compared to the reference acarbose (MIC=34.72µg/ml) [32a-32b].



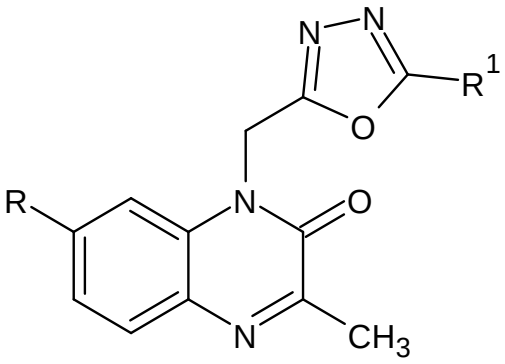
a, **R**= -C_6H_5

b, **R**= -(4-NO_2)C_6H_5

32a-32b

5. Anti-inflammatory activity

Shivananda wagle et al synthesized 2-(3-methyl-7-aryl-2-oxoquinoxalinyl)-5-(substituted)-1,3,4-oxadiazoles analogues. Few compound exhibited good anti-inflammatory action at 50mg/kg dose using carrageenan-induced paw edema method. Indomethacin was taken for reference [33a-33d].



33a-33d

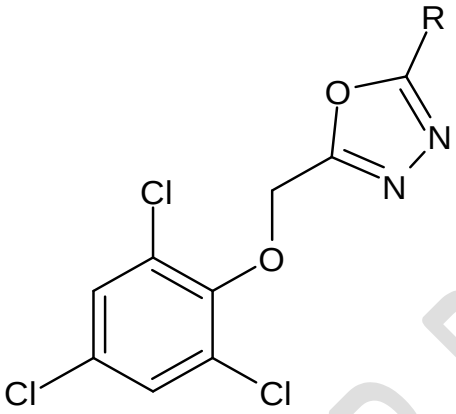
a, **R**= CH_3, Cl, H ; $\mathbf{R^1}$=4(OCH_3)C_6H_4

b, **R**= CH_3, Cl, H ; $\mathbf{R^1}$=3,4,5(OCH_3)C_6H_2

c, **R**= CH_3, Cl, H ; $\mathbf{R^1}$=-S-CH_3

d, **R**= CH_3, Cl, H ; $\mathbf{R^1}$=-S-C_2H_5

Mohd Amir et al synthesized 2-Substitutedaryl-5-(2,4,6-trichlorophenoxy methyl)-1,3,4-oxadiazolo analogues. Two of the proposed derivatives displayed maximum anti-inflammatory action while being checked by carrageenan-induced rat paw edema method with NSAIDs for reference [34a-34b].

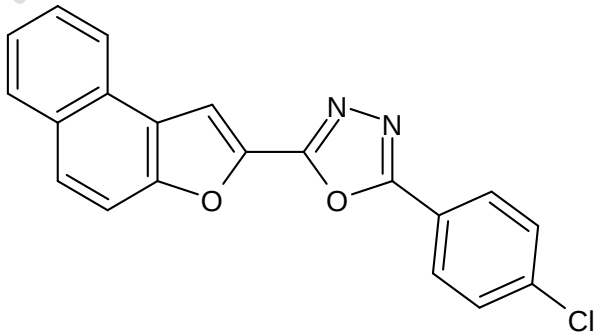


34a-34b

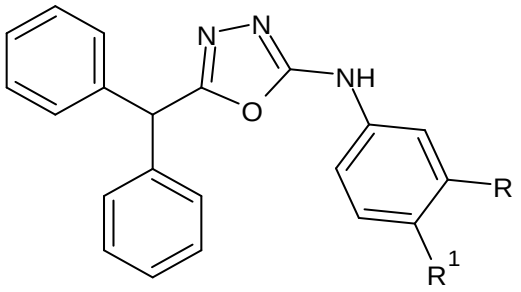
a, **R**= 2,4-Diclorophenyl

b, **R**= 1-(4-isobutylphenyl) ethyl

Ravindra KC et al innovated 2-Naphtho [2,1-b]furan-2-yl-5-substituted-1,3,4-oxadiazole derivatives. One of the synthesized compunds was displaying higher anti-inflammatory potency while compared with the reference drug using Ibuprofen for reference by carrageenan-induced rat paw edema [35].



Mohd Amir et al synthesized 5-(diphenylmethyl)-2-(4-halogenated phenyl) amino-1,3,4-oxadiazolo analogues. Two of the proposed derivatives emerged as most potent compounds (70mg/kg body weight) of the synthesis and were moderate potent, while compared with the reference Ibuprofen, using the carrageenan-induced rat paw edema method in albino rats [36a-36b].

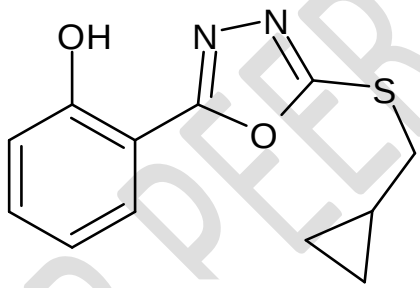


a, **R**= H ; **R**^{1}= F

a, **R=** Cl; **R**^{1}= F

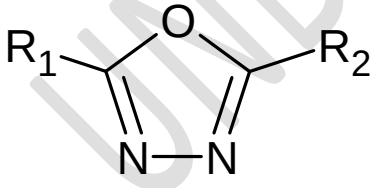
36a-36b

Kittur B.S. et al innovated 2-mercapto-1,3,4-oxadiazole analogues. Out of three proposed derivatives, only one of them was showing promising anti-inflammatory activity while the others were exhibiting moderate activity [37].



37

R.R. Somani et al proposed 2,5-Disubstitutedaryl-1,3,4-oxadiazole scaffolds. All the synthesized derivative was showing inhibitory effects towards the induced inflammation. Few of the synthesized compounds were exhibiting great percentages of inhibition [38a-38b].

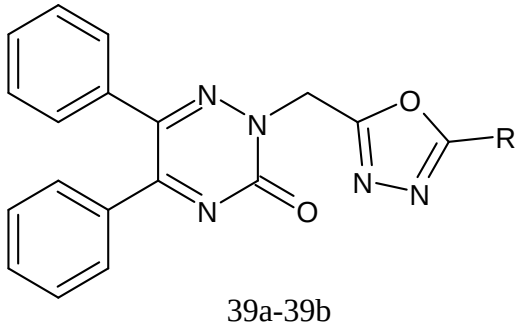


a, **R$_1$**=-[2-(2,6-Dichloroanilino) Benzyl] ; **R$_2$**= -4-methyl phenyl

b, **R$_1$**= -[2-(2,6-Dichloroanilino) phenyl; **R$_2$**= -(pyridine-4-yl)

38a-38b

Anupam G. Banerjee et al synthesized 5, 6–diphenyl–1,2,4–triazin–3(2H)–one analogues having 5–aryl Oxadiazole analogues. Few of the proposed analogues were showing decent inhibition percentage of the denaturation (80.81-76.70%) of the Bovine serum albumin (BSA) compared to the standard Indomethacin (84.88%) [39a-39e].



39a-39b

a, **R**=*o,p*-dihydroxyphenyl

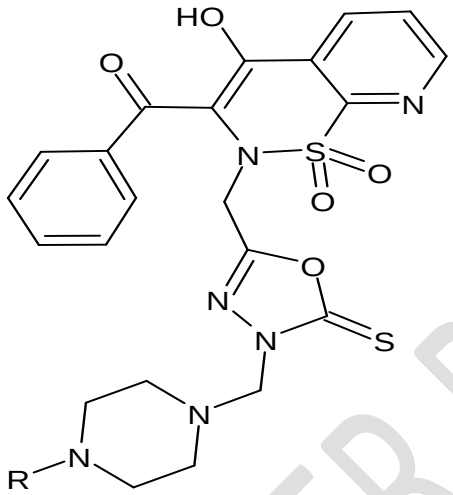
b, **R**=*p*-aminophenyl

c, **R**=*p*-chlorophenyl

d, **R**=*p*-methoxyphenyl

e, **R**=*p*-nitrophenyl

Teresa glomb et al innovated new oxadiazole analogues of pyridothiazine-1,1-dioxide. Few of the synthesized compounds exhibited COX inhibition at a minimum inhibitory concentration of 100µM (either COX-1 or COX-2) while others displayed no inhibitory activity compared to the reference Meloxicam [40a-40f].



40a-40f

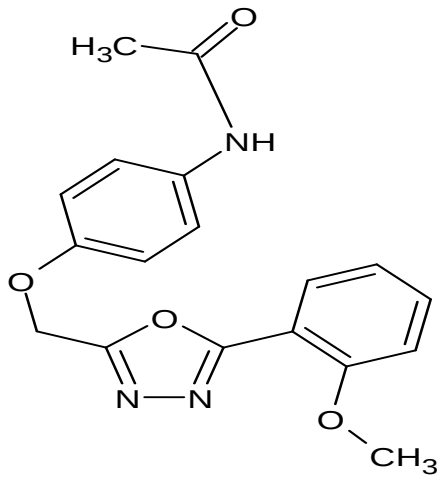
a, **R**=-3-trifluoromethylphenyl

b, **R**=-*o,p*-difluorophenyl

c, **R**=-*o*-cyanophenyl

d, **R**=-*p*-nitrophenyl

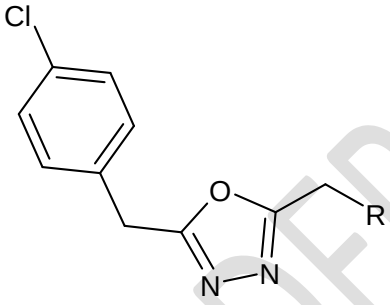
K. Ilango et al synthesized 2- (4-Acetamido phenoxy methyl) - 5-substituted- oxadiazolo analogues. One of the synthesized compounds displayed the highest anti-inflammatory activity while few of the derivatives exhibited moderate activities against carrageenan induced paw edema in rats at the concentration of 50mg/ml using Diclofenac sodium as standard drug [41].



41

6. Anti-bacterial activity

N.C. Desai et al proposed 2-Substitutedamine-5-chlorobenzene-1,3,4-oxadiazole analogues. Out of 9 proposed derivatives, few derivatives showed promising bactericidal action to combat *E. coli* and *S. aureus* at MIC values in the range of 6-18µg/ml. other synthesized compounds were showing moderate activity of inhibition [42a-42c].



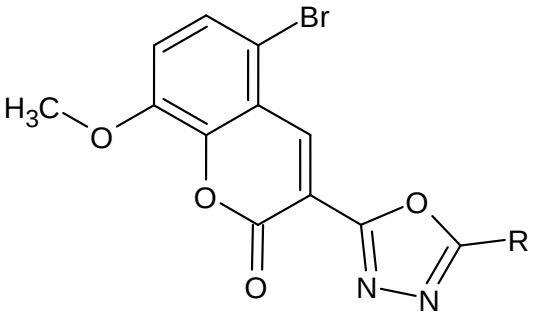
a, **R**= -2-OC_2H_5-C_6H_4

b, **R**= -2,5-$(OCH_3)_2$-C_6H_3

c, **R**= -4-CH_3-C_6H_4

42a-42c

Devki desai et al synthesized 2-Aryl-5-(8'methoxy-5'bromo-3'coumarinyl)-1,3,4-oxadiazole analogues. Few of the proposed derivatives showed moderate activity at 500ppm concentration against *E. coli* [43a-43c].



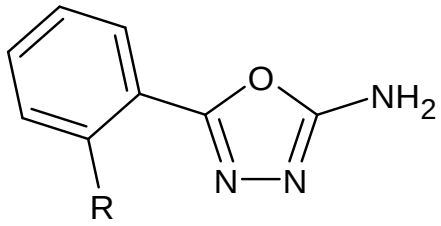
a, **R**=-*p*-CH_3-C_6H_4

b, **R**=-*p*-NO_2-C_6H_4

c, **R**= -*o*-NO_2-C_6H_4

43a-43c

M.S.Y. Khan et al proposed 2-NH-5-Substitutedphenyl-oxadiazolo analogues. Few compounds were exhibiting good antibacterial activity while the others were showing moderate activity against *E. coli* at 100µg/ml with Norfloxacin as reference drug (50µg/ml) [44a-44b].

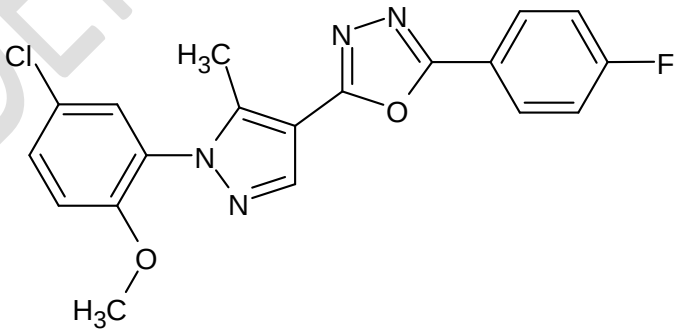


a, **R**= -OH

b, **R**= -F

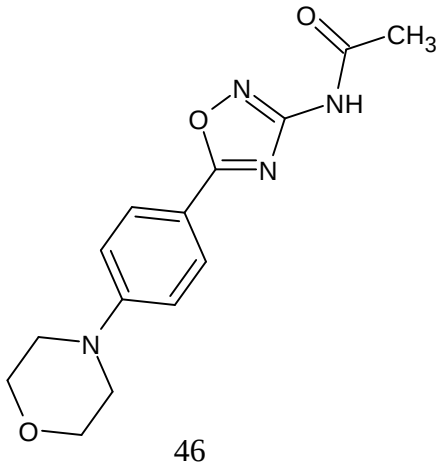
44a-44b

Neithnadka Premsai Rai et al proposed 2-[1-(5-Cl-2- methoxy-phenyl)-5-CH_3-1H-pyrazol-4-yl]-5-(aryl)-oxadiazole analogues. Only one of the synthesized compounds exhibited noticeable bactericidal action with MICs ranging 22.4 to 30.0 mg/mL to combat *Bacillus subtilis* etc. The remaining derivatives displayed moderate activity. Ampicillin was used as standard [45].



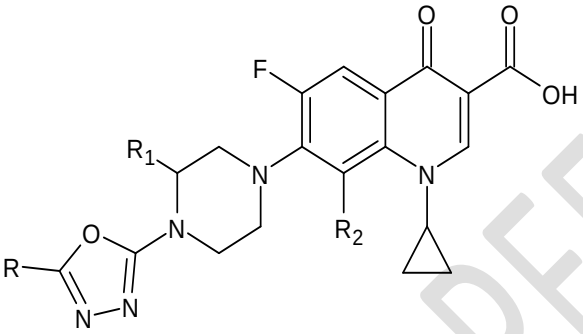
45

Antonio palumbo piccionello et al synthesized two sets of 1,2,4-oxadiazoles, having variant side chains and comprising of a different amount of fluorine atoms. Only one of the proposed compounds was found to exhibit a better activity against *S. pyogenes* (64mg/L). Linezolid and Ceftriaxone were used as standard drugs [46].



46

Rajnish kumar et al synthesized 7-[4-(5-substituted-1,3,4-oxadiazolo-2-yl)piperazine] quinolone-yl analogues. Few compounds was declared as most potent compounds to combat *S. aureus*, *B. subtilis* & *E. coli*. While the other derivatives showed moderate to average potency [47a-47f].



47a-47f

a, **R**=4-nitrophenyl ; $\mathbf{R_1}$= CH_3 ; $\mathbf{R_2}$= OCH_3

b, **R**= Phenyl; $\mathbf{R_1}$= H ; $\mathbf{R_2}$= H

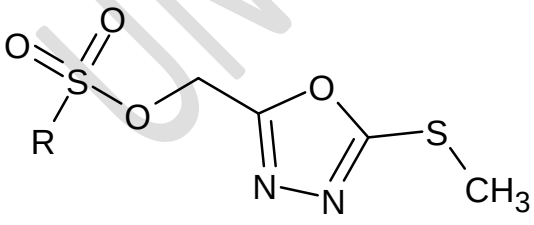
c, **R**= 3-nitrophenyl; $\mathbf{R_1}$= CH_3 ; $\mathbf{R_2}$= OCH_3

d, **R**=3,4-dinitrophenyl ; $\mathbf{R_1}$= H ; $\mathbf{R_2}$= H

e, **R**= Phenyl ; $\mathbf{R_1}$= CH_3 ; $\mathbf{R_2}$= OCH_3

f, **R**= 3,4-dinitrophenyl; $\mathbf{R_1}$= CH_3 ; $\mathbf{R_2}$=OCH_3

Lei Wang et al synthesized 5-phenyl sulfonate methyl-1,3,4-oxadiazoles analogues. Out of the proposed derivatives, few of them demonstrated good activity against *X. axonopodis* with EC_{50} values ranging 95.8-155.2µM. the compounds were also active against rice bacterial leaf blight [48a-48d].



48a-48d

a, **R**= phenyl

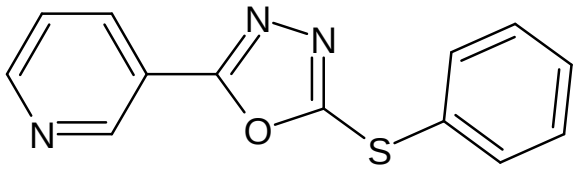
b, **R**=-4-F-phenyl

c, **R**=-4-Cl-phenyl

d, **R**= -4-Br-phenyl

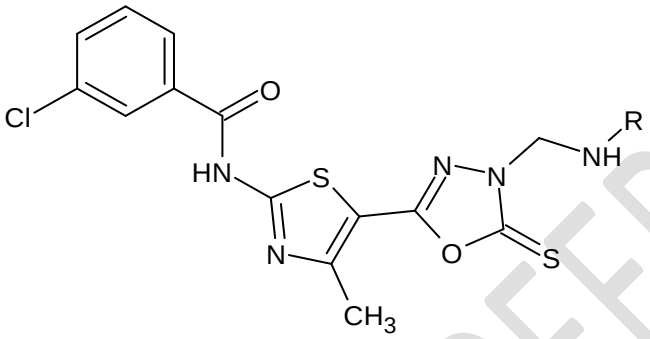
7. Anti-microbial activity

Pattan S.R. et al proposed Novel aryl 5-(Pyridin-4-yl)-1,3,4-oxadiazolo-2-thiols analogues. Only one from the proposed derivatives showed antibacterial action to combat *E. coli*, *B. subtilis*, *S. aureus*, *A. niger* & *C. albicans* at 200µg/ml [49].



49

N.C. Desai et al synthezsized 3-chloro-N-(5-(4-((arylphenyl-amino)methyl)-5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)-4-methylthiazol-2-yl)benzamides analogues. Few of the proposed derivatives displayed proficient potency against all bacterial strains with MICs ranging 12.5-100µg/ml with Ciprofloxacin as the standard drug [50a-50d].



a, **R**=-3-fluorobenzene

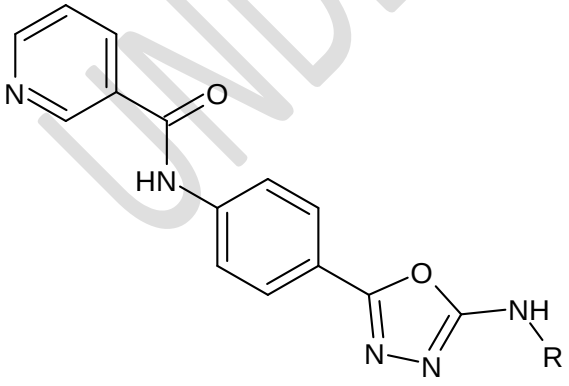
b, **R**=-4-fluorobenzene

c, **R**=-3-nitrobenzene

d, **R**=-4-nitrobenzene

50a-50d

Viral R. shah et al proposed 2-(*p*-Methoxyphenyl) amino-5-p-(nicotinamidophenyl)-l,3,4-oxadiazoles analogues. Few proposed analogues exhibited highest activity against E. coli, S. typhosa, S. citrus and B. megaterium at 50µg/ml concentration with Ampicillin, chloramphenicol, Norfloxacin and Griseofulvin as standard antibiotics [51a-51d].



a, **R**= -C_6H_4

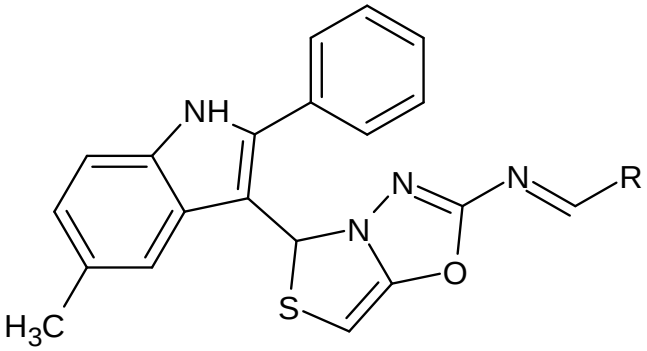
b, **R**= 2,3-(CH_3)-C_6H_4

c, **R**= -2-OCH_3-C_6H_4

d, **R**= -2-C_2H_5-C_6H_4

51a-51d

R. Saundane Anand et al synthesized 2-(Substituted benzylidine)amino-5-(2',5'-diaryl 1*H*-indol-3'-yl)-5*H*-thiazolo[4,3-b]-1,3,4-oxadiazoles derivatives. From screening the compounds revealed that few of the proposed derivatives displayed better zone of inhibition against *S. aureus* and *P. aeroginosa* at concentrations 500 and 1000µg/ml [52a-52b].

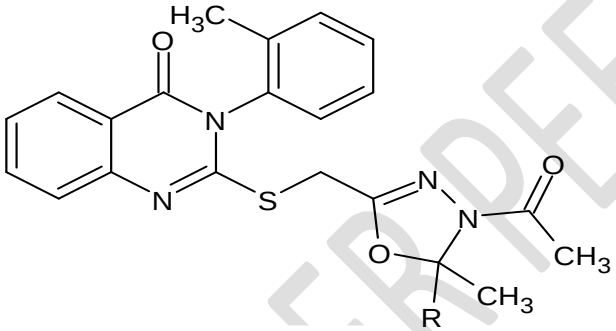


a, **R**= -3-nitrobenzene

b, **R**= -4-methoxybenzene

52a-52b

D.R. Godhani et al synthesized a set of 2-((4-acetyl-5-(substituted)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl) methylthio)-3-*o*-tolylquinazolin-4(3*H*)-one derivatives. Few proposed derivatives showed good potency for *E. coli*, *P. aeruginosa*, *S. aureus* & *S. pyogenus* using Gentamycin, Ampicilin, Chloramphenicol, Ciprofloxacin and Norfloxacin as reference drugs [53a-53b].

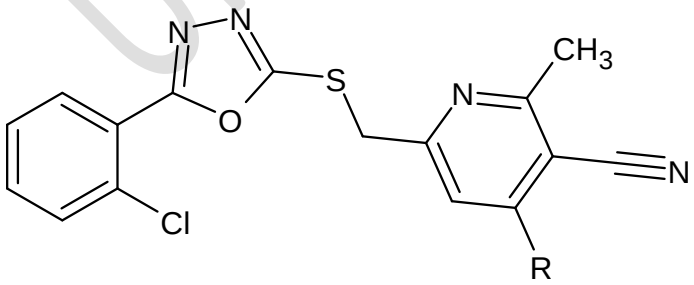


a, **R**= -2-OH-C_6H_4

b, **R**= -4-CH_3-C_6H_4

53a-53b

Niranjan S. Mahajan et al synthesized a set of 2-NH_2-6-[(5-(2-chlorophenyl)-1,3,4-oxaciiazole-2- yl-thio) CH_3]- 4-arylnicotinonitrile derivatives. Few of the synthesized compounds displayed promising inhibitory action for Gram -ve like *E. coli* & *P. aeruginosa* and Gram +ve organisms like B. subtilis having minimum inhibition concentrations of 5-8µg/ml [54a-54b].

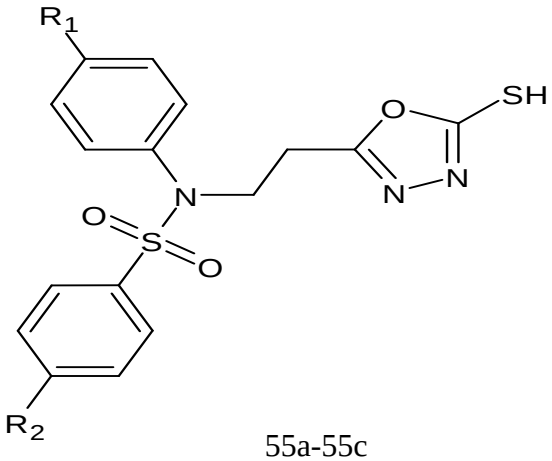


a, **R**= p-OHC_6H_4

b, **R**= m-ClC_6H_4

54a-54b

Desai S.R. et al synthesized series of 5-β-[(N-benzenesulphony/tosyl)-4- alkyl anilino] ethyl-2-mercapto-1,3,4-oxadiazoles derivatives. All the proposed derivatives proved to be showing moderately antibacterial activity against *Escherichia coli* and *Bacillus cirroflagellosus* at 100µg/ml [55a-55c].



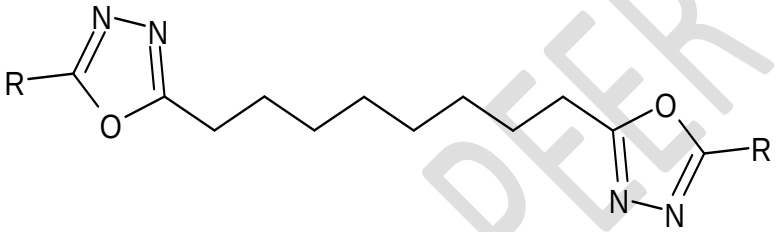
a, $\mathbf{R_1}$= CH_3 ; $\mathbf{R_2}$= H

b, $\mathbf{R_1}$= CH_3 ; $\mathbf{R_2}$= CH_3

c, $\mathbf{R_1}$= Cl ; $\mathbf{R_2}$= CH_3

55a-55c

S.G. patil et al synthesized 1,8-bis (5-aryl-1,3,4-oxadiazol-2-yl) octane analogues. Few of the synthesized derivatives exhibited moderately activity against the bacteria *Staphylococcus aureus* [56a-56b].

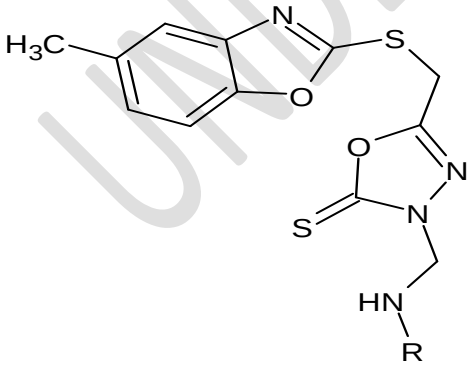


a, **R**= -4-$OCH_3C_6H_4$

b, **R**= -4-$NO_2C_6H_4$

56a-56b

B.M. Basavaraja et al synthesized 5-[(1,3-benzoxazol-2-yl-thio) methyl]-3-{[(4-alkyl phenyl) amino] methyl}-1,3,4-oxadiazolidine-2-thione derivatives. Majority of the compounds showed very good activity against *S. aureus*, *K. pneumonia* and *P. aeruginosa* with Fluoroquinolones as reference [57a-57f].



a, R= -2-Cl

b, R= -3-Cl

c, R= -2-CH_3

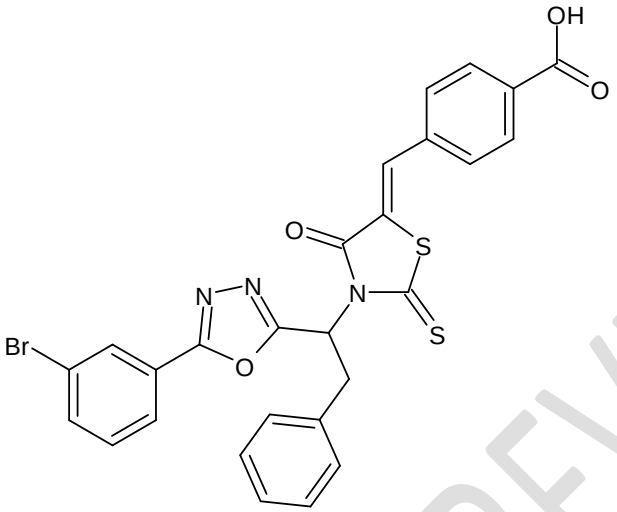
d, R=-3-CH_3

e, R=-2-Cl; -4-Cl

f, R= -4-OCH_3

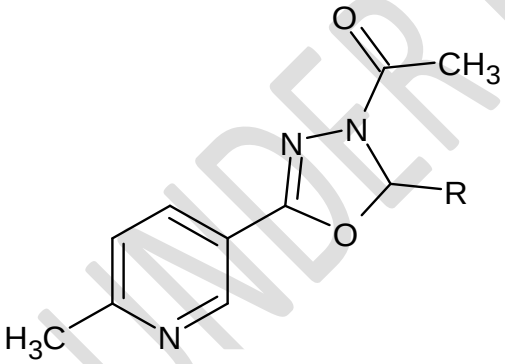
57a-57f

Jia-Chun Liu et al synthesized set of 3-((5-phenyl-1,3,4-oxadiazol-2-yl)methyl)-2-thioxothiazolidin-4-one analogues. The antibacterial evaluation of proposed analogues proved that one derivative displayed better potency with minimum inhibitory concentration values of 1µg/ml to combat MRSA (3167 and 3506) strains. For reference, Fluoroquinolones were used as standard drugs for comparison [58].



58

Shyma P.C. et al synthesized set of 3-acetyl-2-substituted-2H/methyl-5-[3-(6-methylpyridinyl)]-2,3-dihydro-[1,3,4]- oxadiazoles analogues. Few of the derivatives exhibited good to moderate potency for E. coli, *S. aureus* and *P. aeruginosa* with MIC concentration 0.5-1.5mg/ml. Streptomycin was taken as reference drug for correlation [59a-59d]



a, **R**= *p*-bromophenyl

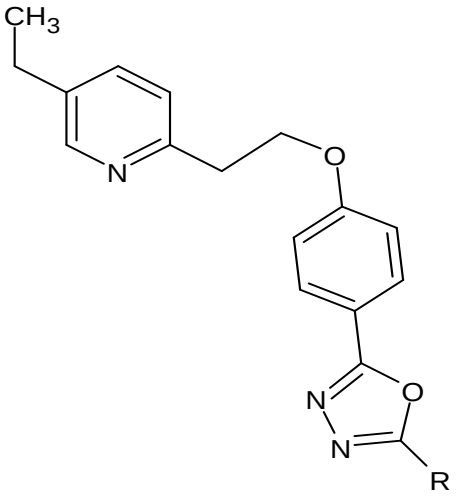
b, **R**= *p*-chlorophenyl

c, **R**= 2,4-dichlorophenyl

d, **R**= 2-fluoro-3-chlorophenyl

59a-59d

S.L. Gaonkar et al innovated a set of 2-{4-[2-(5-ethylpyridin-2-yl) ethoxy] phenyl}-5-aryl-1,3,4-oxadiazolo analogues. The proposed derivatives were found to display good to less potent antimicrobial action. Few of the synthesized derivatives displayed good inhibitory action while some of them showed moderate action with MIC values ranging 8-26µg/ml [60a-60f].



a, **R**= 4-chlorophenyl

b, **R**= 2,3-dichlorophenyl

c, **R**= 2,4-dichlorophenyl

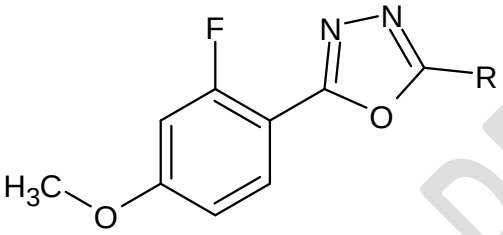
d, **R**= 4-methoxyphenyl

e, **R**= 4-nitrophenyl

f, **R**= 4-pyridinyl

60a-60f

B. Chandrakantha et al synthesized novel 1,3,4-oxadiazole ring tethered with 2-F-4-OCH_3 phenyl group. Few of the proposed derivatives displayed significant antibacterial action against *E. coli* & *P. aeruginosa* at quite less minimum inhibitory concentration 3µg/ml [61a-61b].

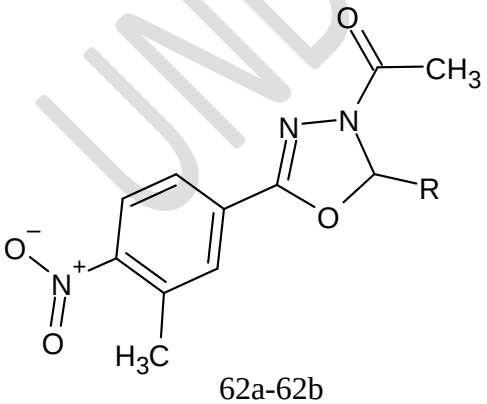


a, **R**= -3-bromo-2-methylphenyl

b, **R**= 2,3,4-trifluorophenyl

61a-61b

Kinga paruch et al synthesized novel 3-Acetyl-2,5-diaryl-1,3,4-oxadiazoline analogues. Most of proposed analogues exhibited bactericidal effect for Gram +ve organism. Two of the proposed derivatives exhibited the significant antibacterial action with minimal inhibitory concentrations (MICs) ranging 0.48µg/ml to 500µg/ml. other compounds showed moderate to poor antibacterial activity [62a-62b].

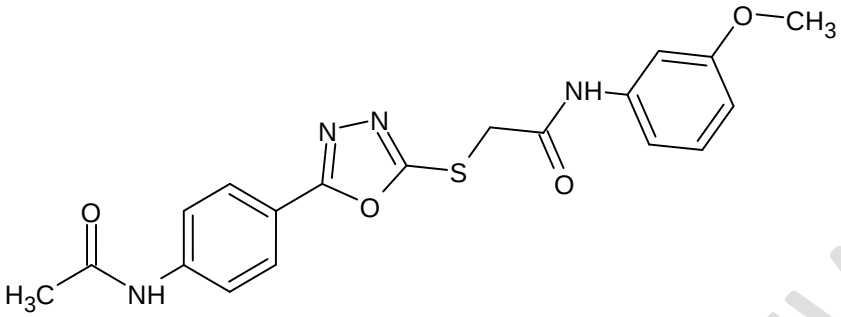


a, **R**= -(-5-iodofuran-2-yl)

b, **R**= quinolin-4-yl

62a-62b

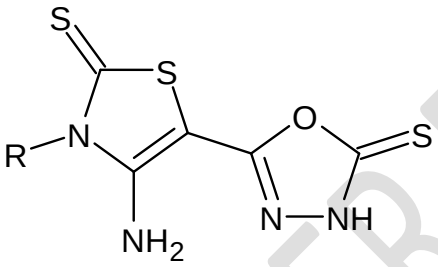
Shah H.P. et al innovated set of 2-{[5-(4-acetamidophenyl)-1,3,4-oxadiazol-2-yl]sulfanyl}-*N*-aryl)acetamide derivatives. Out of synthesized derivatives, one exhibited excellent action against *S. sureus* [63].



63

8. Anti-viral activity

Mohammed albratty et al synthesized thiazole bearing 1,3,4-oxadiazoles analogues. Both the proposed derivatives exhibited promising antivial actions against various viral strains possibly under the influence of the presence of amino thiazole substituent [64a-64b].



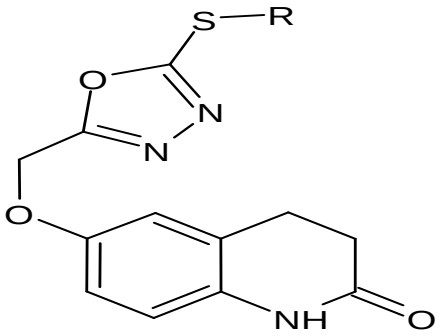
a, **R**= C_2H_5

b, **R**= C_6H_5

64a-64b

9. Anti-convulsant activity

Shiben wang et al innovated Dihydroquinoline bearing 1,3,4-oxadiazoles analogues. One of the synthesized compound was showing the significant anticonvulsant action better from the actions of carbamazepine and ethosuximide [65].

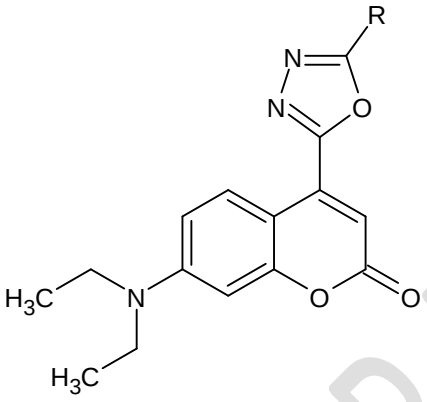


R= n-C_5H_{11}

65

10. Anti-cholinestrase activity

Xiang Yu et al innovated a set of novel 7-diethylaminocoumarin-based 1,3,4-oxadiazoles analogues. Among the derivatives, two of them showed moderate inhibitory activities positively correlated to the concentration [66a-66b].



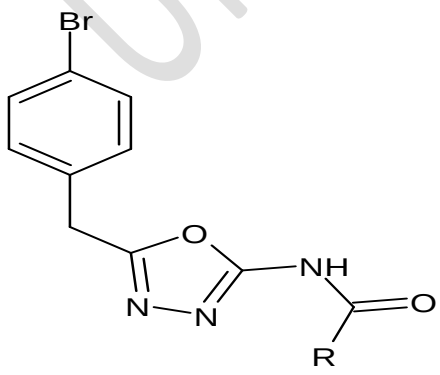
a, **R**= -4-chlorophenyl

b, **R**= -4bromophenyl

66a-66b

11.Anti-salmonella typhii

Eid E. Salama et al innovated 5-subastituted-2-NH_2-1,3,4-oxadiazolo analogues. Out of the proposed derivatives few of them displayed great inhibitory activity against *salmonella typhii* whereas the other compounds displayed moderate activity [67a-67b].



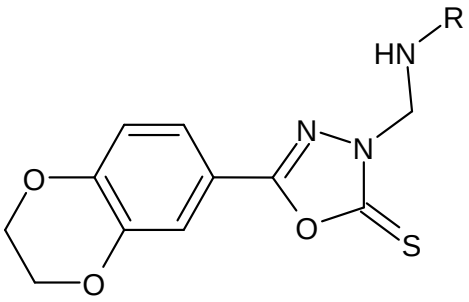
a, **R**= -(4-$COCH_3$)C_6H_4

b, **R**= -(3-NO_2)C_6H_4

67a-67b

12. Antioxidant

Liang Ma et al innovated novel set of oxadiazole analogues having 1,4-benzodioxane moiety. Few of the proposed derivatives were exhibiting excellent radical scavenging action compared to the exhisting antioxidants, like BHT and Trolox. The synthesized derivatives were assayed using (DPPH), (ABTS+ •) and (FRAP) scavenging assays [68a-68b].

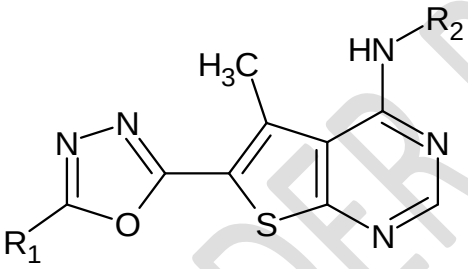


a, **R**= 2,6-Difluorophenyl

b, **R**= 3,4,5-Trifluorophenyl

68a-68b

Y. Kotaiah et al innovated set of novel N-substitutedaryl phenyl-1,3,4-oxadiazole-thiazole- pyrimidine amine analogues. Few of these synthesized derivatives displayed good radical scavenging under the influence of EDGs like -CH_3 on either ends of the thienopyrimidine moiety. These synthesized compounds were screened by using DPPH, Hydrogen peroxide and nitric oxide radical scavenging assays [69a-69d].



a, $\mathbf{R_1}$= phenyl ; $\mathbf{R_2}$= 4-fluorophenyl

b, $\mathbf{R_1}$= 4-chlorophenyl ; $\mathbf{R_2}$= 4-fluorophenyl

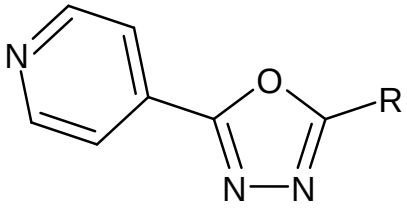
c, $\mathbf{R_1}$= phenyl ; $\mathbf{R_2}$= 2,4-difluorophenyl

d, $\mathbf{R_1}$= 4-chlorophenyl ; $\mathbf{R_2}$= 2,4-difluorophenyl

69a-69d

13. Analgesic activity

Ilango K. et al innovated 2-substituted-5-(4-pyridyl)-1,3,4-oxadiazoles analogues. Among these proposed analogues, few of them showed good analgesic activity at a concentration of 500mg/ml using Aspirin for reference comparison (40mg/ml) [70a-70b].



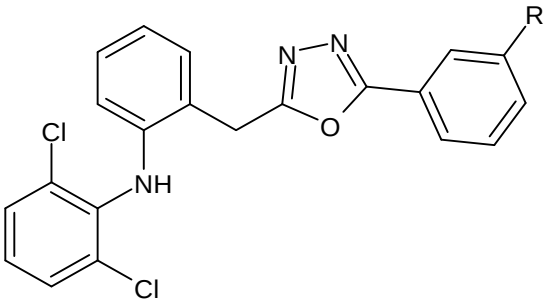
a, **R**= 4-methoxy phenyl

b, **R**= 4-hydroxy phenyl

c, **R**= 4-hydroxy-3,5-Dimethoxyphenyl

70a-70c

Ilango K. et al synthesized 2, 6-diCl-N-(2-((5-(alkyl)-1, 3, 4- oxadiazol-yl) methyl) phenyl) benzenamines analogues. Few of the proposed derivatives showed analgesic action while few of them showed central analgesic activity using the acetic acid induced writhing response methods [71a-71d].



71a-71d

a, **R**= NO_2

b, **R**= NH_2

c, **R**= OCH_3

d, **R**= Cl

CONCLUSION

This review is focused on the Diversified Pharmacological Properties possessed by and associated with the derivatives of Oxadiazole moiety in last two and a half decades. Synthetic compounds possessing Oxadiazole ring in their chemical structure have been studied for multiple number of biological activities such as antifungal, anticancer, anti HIV, antihypertensive, antibacterial, antimicrobial, anticholinesterase, anticonvulsant, antiviral etc. The studied literatures resulted in getting a conclusion that the Oxadiazole ring has been used in multiple number of synthetic studies now-a-days. Oxadiazole moiety has grabbed the attention of many researchers due to its biological versatility.

COMPETING INTERESTS DISCLAIMER:

Authors have declared that no competing interests exist. The products used for this research are commonly and predominantly use products in our area of research and country. There is absolutely no conflict of interest between the authors and producers of the products because we do not intend to use these products as an avenue for any litigation but for the advancement of knowledge. Also, the research was not funded by the producing company rather it was funded by personal efforts of the authors.

REFERENCES

1. Desai NC, Bhavsar AM, Shah MD and Saxena Anil K, Synthesis and QSAR studies of thiosemicarbazides, 1,2,4-triazoles, 1,3,4-thiadiazoles and 1,3,4-oxadiazoles derivatives as potential antibacterial agents, Indian Journal of Chemistry- section B, 2008; 47B(04); 579-589.
2. Desai D and Mehta RM, Synthesis and antibacterial activity of some new hydrazides and 1,3,4-oxadiazoles of coumarin derivatives, Indian Journal of Heterocyclic chemistry, 2002; 12(2); 171-172.

3. Khan MSY, Khan RM and Drabu S, Anticonvulsant and antibacterial activity of some new 1,3,4-oxadiazole derivatives, Indian Journal of Heterocyclic Chemistry, 2001; 11(2); 119-122.
4. Rai NP, Narayanswamy VK, Shashikanth S and Arunachalam PN, Synthesis, characterization and antibacterial activity of 2-[1-(5-chloro-2-methoxy-phenyl)-5-methyl-1H-pyrazol-4-yl]-5-(substituted-phenyl)-[1,3,4]oxadiazoles, European Jopurnal of Medicinal Chemistry, 2009; 44(11); 4522-4527.
5. Piccionello AP, Masumeci R, Cocuzza CE and Fortuna CG, Synthesis and preliminary antibacterial evaluation of Linezolid-like 1,2,4-oxadiazole derivatives, European Journal of Medicinal Chemistry, 2012; 50; 441-448.
6. Rajnish K, Ashwani K, Jain S and Kaushik D, Synthesis ,antibacterial evaluation and QSAR Studies of 7-[4-(5-aryl-1,3,4-oxadiazole-2-yl)piperazinyl]quinolone derivatives, European Journal of Medicinal Chemistry, 2011; 46(9); 3543-3550.
7. Wang L, Zhou X, Hui L and Mu X, Synthesis and Antibacterial Evaluation of Novel 1,3,4-Oxadiazole Derivatives Containing Sulfonate/Carboxylate Moiety, Molecules, 2020; 25(7).
8. Pattan SR, Pattan JS, Gadhave PP and Dighe SB, Synthesis, Antimicrobial and Antitubercular Activity of Some Novel [3-Isonicotinoyl-5-(4-substituted)-2,3-dihydro-1,3,4-oxadiazol-2-yl] and Substituted 5-(Pyridin-4-yl)-1,3,4-oxadiazole-2-thiol Derivatives, Indian Drugs, 2011; 48(6), 19-25.
9. Rane R, Banglore PV, Borhade SD and Khandare PK, Synthesis and evaluation of novel 4-nitropyrrole-based 1,3,4-oxadiazole derivatives as antimicrobial and anti-tubercular agents, European Journal of Medicinal Chemistry, 2013; 70C; 49-58.
10. Desai NC, Bhatt NB, Somani HC and Bhatt KA, Synthesis and antimicrobial activity of some thiazole and 1,3,4-oxadiazole hybrid heterocycles, Indian Journal of Chemistry-Section B, 2016; 55B(01); 94-101.
11. Shah VR, Vadodaria M and Parikh AR, Synthesis of 1,3,4-oxadiazoles having nicotinamide moiety as potential antimicrobial agents, Indian Journal of Chemistry-Section B, 1997; 36B(01); 101-103.
12. Saundane AR, kalpana R and Manjunatha Y, Synthesis, antioxidant and antimicrobial activities of indolyl-thiazolo [4,3-b]-1,3,4-oxadiazol-2-amines and its Schiff's bases, Indian Journal of Heterocyclic Chemistry, 2012; 21(3); 193-200.
13. Godhani DR, Dobariya PB and Sanghani AM, Synthesis and Antimicrobial evaluation of some new 1,3,4- Oxadiazoles, Indian Journal of Heterocyclic Chemistry, 2012; 21(3); 259-262.
14. Mahajan N, Dhavale SC, Jawarkar R and Manikrao AM, Synthesis and antimicrobial evaluation of 2-amino-6-[(5-(2-chlorophenyl)-1,3,4-oxadiazole-2-ylthio) methyl-13 4-arylnicotinonitriles, Indian Journal of Heterocyclic Chemistry, 2012; 22(1); 13-16.
15. Desai SR, Laddi U, Bennur RS and Patil PA, Synthesis and Pharmacological Activities of Some New 5-Substituted-2-mercapto-1,3,4-oxadiazoles, Indian Journal of Pharmaceutical Sciences, 2011; 73(5); 593-596.
16. Laddi UV, Talawar MB and Bennur SC, Synthesis and antimicrobial activity of some new 1,3,4-Oxadiazoles and 1,2,4-Triazoles, Indian Journal of Heterocyclic Chemistry, 1994; 4(4); 111-116.
17. Pattan SR, Pattan JS, Musmade Deepak and Vetal SS, Synthesis and evaluation of some substituted aryl Oxadiazole and mercapto ocadiazole derivatives for antifungal, antimicrobial and antitubercular activities, Indian Drugs, 2012; 49(4); 12-18.
18. Desai JM and Shah VM, Synthesis and antimicrobial profile of 1,3,4-oxadiazoles, sulphonamides, 5-imidazolinones, azomethines, 4-thiazolidinones, 2-azetidinones, formazans and tetrazolium chlorides, Indian Journal of Heterocyclic Chemisty, 1999; 8; 329-334.
19. Desai SR, Laddi U, Bennur RS and Patil PA, Synthesis and Pharmacological Activities of Some New 5-Substituted-2-mercapto-1,3,4-oxadiazoles, Indian Journal of Pharmaceutical Sciences, 2011; 73(5); 593-596.
20. Patil SG, Girisha M, Badiger J and Kudari SM, Synthesis and anticonvulsat,antimicrobial activity of some bis -1,3,4-oxadiazole and bis-1,2,4-triazole derivatives from sebacic acid, Indian Journal of Heterocyclic Chemisty, 2007; 17(1); 37-40.

21. Basavaraja BM, Vagdevi HM, Srikrishna LP and Shubha BS, Synthesis and antimicrobial activity of 1,3,4-oxadiazole incorporated benzoxazoles, Indian Journal of Heterocyclic Chemisty, 2008; 18(1); 05-08.
22. Jia-chun liu, Chang-ji zheng, Meng-xiao wang and Ya-ru li, Synthesis and evaluation of the antimicrobial activities of 3-((5-phenyl-1,3,4-oxadiazol-2-yl)methyl)-2-thioxothiazolidin-4-one derivatives, European Journal of Medicinal Chemistry, 2014; 74; 54.
23. Shyma PC, Kalluraya balakrishna, Peethambar SK and Telkar Sandeep, Synthesis, characterization and molecular docking studies of some new 1,3,4-oxadiazolines bearing 6-methylpyridine moiety for antimicrobial property, European Journal of Medicinal Chemistry,2013; 68C(12); 394-404.
24. Padmavathi V, Reddy GS, Padmaja A and Kondaiah P, Synthesis, antimicrobial and cytotoxic activities of 1,3,4-oxadiazoles, 1,3,4-thiadiazoles and 1,2,4-triazoles, European Journal of Medicinal Chemistry, 2008; 44(5); 2106-2112.
25. Gaonkar SL, Rai KML and Prabhswamy B, Synthesis and antimicrobial studies of a new series of 2-[4-[2-(5-ethylpyridin-2-yl)ethoxy]phenyl]-5-substituted-1,3,4-oxadiazoles, European Journal of Medicinal Chemistry, 2006; 41(7); 841-846.
26. Sravya G, Yamini G, Padmavathi V and Padmaja A, Synthesis and antimicrobial activity of styryl/ pyrrolyl/ pyrazolyl sulfonylmethyl-1,3,4-oxadiazolyl amines, European Journal of Medicinal Chemistry, 2016; 21; 647 655.
27. Chandrakantha B, Shetty Prakash, Nambiyar vijesh and Isloor nishitha, Synthesis, characterization and biological activity of some new 1,3,4-oxadiazole bearing 2-flouro-4-methoxy phenyl moiety, European Journal of Medicinal Chemistry, 2009; 45(3); 1206-1210.
28. Kinga paruch, Popiolek Lukasz, Biernasiuk anna and Hordyjewska anna, Novel 3-Acetyl-2,5-disubstituted-1,3,4-oxadiazolines: Synthesis and Biological Activity, Molecules, 2020; 25(24); 5844.
29. Shah HP, Shah B, Bhatt JJ and Desai NC, Synthesis of 2,5-disubstituted 1, 3, 4- oxadiazoles as potential antimicrobial, anticancer and anti-HIV agnets, Cheminform, 2010; 29(39); 58.
30. Pattan SR, Chavan PA, Muluk RA and Dengale SS, Synthesis and biological evaluation of some heterocycles containing oxadiazole and pyrazole ring for antibacterial, antifungal and antitubercular activities, Indian Drugs, 2012; 49(3); 18-24.
31. Rahul V. Patel, Patel PK, Premlata kumari and Kishor H Chikhalia, Synthesis of benzimidazolyl-1,3,4-oxadiazol-2ylthio-N-phenyl (benzothiazolyl) acetamides as antibacterial, antifungal and antituberculosis agents, European Journal of Medicinal Chemistry; 2012; 53; 41-51.
32. Nadagouda SG, Atul khochage, MR pradeep kumar and Karot haresh, Synthesis, antibacterial and antifungal activities of 2,5-disubstituted -1,3,4-oxadiazoles, Indian Journal of Heterocyclic Chemisty, 2006; 41(7); 841-846.
33. Joshi SD, Unale YP, Parkale DB and Nadagouda SG, Synthesis and evaluation of antibacterial and antifungal activities of some novel 2,5-disubstituted-1,3,4 oxadiazoles, Indian Journal of Heterocyclic Chemisty, 2012; 21(4); 319-322.
34. Gaurav grover and kini suvarna, Synthesis and evaluation of new 1,3,4-oxadiazoles and 1,3,4-oxadiazole-2-thione derivatives of nalidixic acid as potential antibacterial and antifungal agents, Indian Journal of Heterocyclic Chemisty, 2003; 12(3); 289-290.
35. Dayashankar tripathi, nishra AR, Singh D and Dwivedi AK, Synthesis of new fungitoxic 2-aryl -1,3,4-oxadiazolo[3,2-a]-s-triazine -5,7-dithiones and their 6-aryl sulphonyl derivatives, Indian Journal of Heterocyclic Chemisty, 2007; 16(3); 239-242.
36. DV singh, Mishra AR and Mishara RM, Synthesis and antifungal activity of new 1,3,4-oxadiazolo [3,2-b]-s-triazine-5-ones and their thiones analogues, Indian Journal of Heterocyclic Chemisty, 2005; 14(4); 289-292.
37. Arunkumar S, Ilango K, Manikandan RS, Sudha M and Ramalakshmi N, Synthesis, Characterisation and BiologicalEvaluation of some novel 2,5-Disubstituted1,3,4-oxadiazole derivatives of Gallic acid, International Journal of Pharm.Tech Research, 1(4); 1094-1099.

38. Gangapuram M and Kinfe K Redda, Synthesis of substituted N -[4(5-methyl/phenyl-1,3,4-oxadiazol-2-yl)-3,6-dihydropyridin-1(2H)-yl]benzamide/benzene sulfonamides as anti-inflammatory and anti-cancer agents, Indian Journal of Heterocyclic Chemisty, 2009; 46(2); 309-316.
39. Subrahmanya BK, Karthikeyan MS, Holla BS and Shetty NS, Synthesis of some new fluorine containing 1,3,4 oxadiazole derivatives as potential antibacterial and anticancer agents, Indian Journal of Chemistry- Section B, 2004; 43B(8); 1765-1769.
40. Kundu mrityunjoy, jagdish singh Brijesh singh and Ghosh tirtha, Synthesis and anticancer activity of 3,5-diaryl-1,2,4- oxadiazole derivatives, Indian Journal of Chemistry- Section B, 2012; 51B(03); 493-497.
41. Fatma AFR, Sahar MAS, Alfayomy AM and Mohamed aboelmagd, Design, synthesis and anticancer activity of new monastrol analogues bearing 1,3,4-oxadiazole moiety, European Journal of Medicinal Chemistry, 2017; 138; 140-151.
42. Dora Kovacs, Janos wolfling, Nikoletta szabo and Mihaly szecsi, An efficient approach to novel 17-5'-(1',2',4')-oxadiazolyl androstenes via the cyclodehydration of cytotoxic O-steroidacylamidoximes, and an evaluation of their inhibitory action on 17α-hydroxylase/$C_{17,20}$-lyase, European Journal of Medicinal Chemistry, 2013; 70; 649-660.
43. Juan sun, Hui zhu, Zhong-ming yang and Hai-liang zhu, Synthesis, molecular modeling and biological evaluation of 2-aminomethyl-5-(quinolin-2-yl)-1,3,4-oxadiazole-2(3H)-thione quinolone derivatives as novel anticancer agent, European Journal of Medicinal Chemistry, 2013; 60; 23-28.
44. Pathiyapurayil P, Poojary B, Chikkanna C and Buridipad SK, Design, synthesis and biological evaluation of a novel series of 1,3,4-oxadiazole bearing N-methyl-4-(trifluoromethyl)phenyl pyrazole moiety as cytotoxic agents, European Journal of Medicinal Chemistry, 2012; 53; 203-210.
45. Mohd rashid, Asif Husain and Ravinesh Mishra, Synthesis of benzimidazoles bearing oxadiazole nucleus as anticancer agents, European Journal of Medicinal Chemistry, 2012; 54; 855-866.
46. Liu K, Lu X, Zhang Hj and Sun J, Synthesis, molecular modeling and biological evaluation of 2-(benzylthio)-5-aryloxadiazole derivatives as anti-tumor agents, European Journal of Medicinal Chemistry, 2011; 47(1); 473-478.
47. Samir bondock, Shymaa Adel, Hassan A Etman and Farid A Badria, Synthesis and antitumor evaluation of some new 1,3,4-oxadiazole-based heterocycles, European Journal of Medicinal Chemistry, 2012; 48; 192-199.
48. Dalip kumar, Gautam patel, Angela K Chavers and Kavita shah, Synthesis of novel 1,2,4-oxadiazoles and analogues as potential anticancer agents, European Journal of Medicinal Chemistry, 2011; 46(7); 3085-3092.
49. Bajaj S, Asati V, Jagdish singh and Partha pratim roy, 1,3,4-Oxadiazoles: An emerging scaffold to target growth factors, enzymes and kinases as anticancer agents, European Journal of Medicinal Chemistry, 2015; 97; 124-141.
50. Maftei CV, Fodor E, Jones PG and Matthias F, N-heterocyclic carbenes (NHC) with 1,2,4-oxadiazole-substituents related to natural products: synthesis, structure and potential antitumor activity of some corresponding gold(I) and silver(I) complexes, European Journal of Medicinal Chemistry, 2015; 101; 431-441.
51. Caneschi W, Enes KB, Mendonca CCD and Fernandes FDS, Synthesis and anticancer evaluation of new lipophilic 1,2,4 and 1,3,4-oxadiazoles, European Journal of Medicinal Chemistry, 2019; 165; 18-30.
52. Lakshmithendral K, Sarvanan K, Elancheran R and Archana K, Design, synthesis and biological evaluation of 2-(phenoxymethyl)-5-phenyl-1,3,4-oxadiazole derivatives as anti-breast cancer agents, European Journal of Medicinal Chemistry, 2019; 16(8); 1-10.
53. Yang Z, Shen M, Tang M and Zhang W, Discovery of 1,2,4-oxadiazole-Containing hydroxamic acid derivatives as histon deacetylase inhibitors potential application in cancer therapy, European Journal of Medicinal Chemistry, 2019; 17(8); 116-130.

54. Biju CR and Ilango K, Insilico docking investigation, synthesis and cytotoxic studies of coumarin substituted 1, 3, 4-oxadiazole derivatives, International Journal of Pharmacy and Pharmaceutical Sciences; 2012; 4; 262-265.
55. Unnissa HS, Ravi TK and Sonia George, Drug design and synthesis of 1, 3, 4-oxadiazolo cinnoline analogs as potent antitubercular agents, World Journal of Pharmaceutical Sciences, 2015; 3(11); 54-60.
56. Almansour AI, Raju SK, Arumugam N and Sriram D, A solvent free, four-component synthesis and 1,3-dipolar cycloaddition of 4(H)-pyrans with nitrile oxides: synthesis and discovery of antimycobacterial activity of enantiomerically pure 1,2,4-oxadiazoles, European Journal of Medicinal Chemistry, 2012; 53; 416-423.
57. Ravi LB and Surendra GG, Identification and development of 2,5-disubstituted oxadiazole as potential candidate for treatment of XDR and MDR tuberculosis, European Journal of Medicinal Chemistry, 2012; 47(1); 278-282.
58. Galina K, Jan N, Valaskova L and Carazo A, S-substituted 3,5-dinitrophenyl 1,3,4-oxadiazole-2-thiols and tetrazole-5-thiols as highly efficient antitubercular agents, European Journal of Medicinal Chemistry, 2017; 12(6); 369-383.
59. Vosatka R, Kratky M, Svarcova M and Janousek J, New lipophilic isoniazid derivatives and their 1,3,4-oxadiazole analogues: Synthesis, antimycobacterial activity and investigation of their mechanism of action, European Journal of Medicinal Chemistry, 2018; 15(1); 824-835.
60. Somnath gholap, Tambe M, Nawale L and Sarkar D, Design, synthesis, and pharmacological evaluation of fluorinated azoles as anti-tubercular agents, Arch Pharma, 2018; 351(2); 1-10.
61. Peraman R, Varma RV and Reddy YP, Re-engineering nalidixic acid's chemical scaffold: A step towards the development of novel anti-tubercular and anti-bacterial leads for resistant pathogens, Bioorganic Medicinal Chemistry, 2015; 25(19); 4314-4319.
62. Ambhore AN, Kamble SS, Kadam SN and Kamble RD, Design, synthesis and in silico study of pyridine based 1,3,4-oxadiazole embedded hydrazinecarbothioamide derivatives as potent anti-tubercular agents, Computational Biology and Chemistry, 2019; 80; 54-65.
63. Wagle S, Adhikari AV and Kumari NS, Synthesis of some new 2-(3-methyl-7-substituted- 2-oxoquinoxalinyl)-5-(aryl)-1,3,4-oxadiazoles as potential non-steroidal antiinflammatory and analgesic agents, Indian Journal of Chemistry-Section B, 2008; 47B(03); 439-448.
64. Mohd Amir, Javed SA and Harish K, Synthesis of some 1,3,4-oxadiazole derivatives as potential anti-inflammatory agents, Indian Journal of Chemistry-Section B, 2007; 46B(06); 1014-1019.
65. Ravindra KC, Vagdevi HM, Vaidya VP and Padmashali B, Synthesis, antimicrobial and antiinflammatory activities of 1,3,4-oxadiazoles linked to naphtho[2,1-b]furan, Indian Journal of Chemistry-Section B, 2006; 45B(11); 2506-2511.
66. Mohd Amir, Saifullah Khalid and Wasim Akhter, Design, synthesis and pharmacological evaluation of 1,3,4-oxadizole derivatives of aryl acetic acid as anti-inflammatory and analgesic agents, Indian Journal of Chemistry-Section B, 2011; 50B(08); 1107-1111.
67. Kittur BS, Sastry BS, Pattan SR and Parag Rabara, Synthesis and Antiinflammatory activity ofsome novel 1,3,4- Oxadiazole and pyrazole derivatives, Indian Drugs, 2009; 46(5); 404-408.
68. Somani RR and Bhanushali UV, Syntheis and evaluation of anti-inflammatory , analgesic and ulcerogenic potential of NSAIDs Bearing 1,3,4- oxadiazole Scaffold, Indian Journal Pharmaceutical Sciences, 2011; 73(6); 634-640.
69. Banerjee AG, Nirupam das, Shengule SA and Srivastava RS, Synthesis, characterization, evaluation and molecular dynamics studies of 5, 6-diphenyl-1,2,4-triazin-3(2H)-one derivatives bearing 5-substituted 1,3,4-oxadiazole as potential anti-inflammatory and analgesic agents, European Journal of Medicinal Chemistry, 2015; 10(1); 81-95.
70. Glomb T, Wiatrak B, Gebczak K and Gebarowski T, New 1,3,4-Oxadiazole Derivatives of Pyridothiazine1,1-Dioxide with Anti-Inflammatory Activity, International Journal of Molecular Sciences, 2020; 21(23); 9122

71. Ilango K, Valentina p, Umarani N and Kumar T, Synthesis and Characterization of 2, 5-Disubstituted- 1, 3, 4-oxadiazoles as Potential Anti-infl ammatory Agents, Journal of Young Pharmacists, 2009; 1(1); 72-76.

72. Majid Nazir, Mohd Athar A, Aziz-ur-rehman and Sabahat Z Siddiqui, New indole based hybrid oxadiazole scaffolds with N- substituted acetamides: As potent anti-diabetic agents, Bioorganic Chemistry, 2018; 81; 253-263.

73. Ramesh SG, Avinash KK, Timanagouda K and Raghuveer, Synthesis of novel 5-(2,5-bis(2,2,2-trifluoroethoxy) phenyl)-1,3,4-oxadiazole-2-thiol derivatives as potential glucosidase inhibitors, Bioorganic Chemistry, 2021; 114; 105046

74. Mohd Albaratty, Karam AES and Hassan Ahmed Alhazmi, Synthesis and evaluation of some new 1,3,4-oxadiazoles bearing thiophene, thiazole, coumarin, pyridine and pyridazine derivatives as antiviral agents, Acta Pharma, 2019; 69(2); 261-276.

75. Shiben Wang, Hui Liu, Wang X and Kanh lei, Synthesis of 1,3,4-oxadiazole derivatives with anticonvulsant activity and their binding to the $GABA_A$ receptor, European Journal of Medicinal Chemistry, 2020; 206; 112672

76. Xiang Yu, You-Fang Zhao, Guo-Juan Huang and Ya-Fang Chen, Design and synthesis of 7-diethylaminocoumarin- based 1,3,4-oxadiazole derivatives with anti- acetylcholinesterase activities, journal of Asian Natural Products research, 2020; 1-11

77. Liang Ma, Yu Xiao, Cong li and Zheng-Lu Xie, Synthesis and antioxidant activity of novel Mannich base of 1,3,4-oxadiazole derivatives possessing 1,4-benzodioxan, Bioorganic Medicinal Chemistry, 2013; 21(21); 6763-6770.

78. Kotaiah Y, Harikrishna N, Nagaraju K and C Venkata Rao, Synthesis and antioxidant activity of 1,3,4-oxadiazole tagged thieno[2,3-d] pyrimidine derivatives, European Journal of Medicinal Chemistry, 2012; 58; 340-345.

79. Biju CR, Ilango K, Manju Prathap and Rekha K, Design and Microwave-assisted Synthesis of 1,3,4-Oxadiazole derivatives for analgesic and Anti-inflammatoery activity, Journal of Young Pharmacists, 2012; 4(1); 33-37.

80. Ilango K, Valetina P, Gajendra kumar and Dushyant dixit, Design, Synthesis and QSAR Studies on a Series of 2, 5-Disubstituted1,3,4-oxadiazole Derivatives of Diclofenac and Naproxen for Analgesic and Anti-inflammatory Activity, Medicinal Chemistry, 2015; 11(8); 753-763.