



A Review on Oxadiazoles as a Pharmacologically Active Nucleus

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Authors' contributions

This work was carried out in collaboration between both authors. Both authors read and approved the final manuscript.

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Review Article

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ABSTRACT

The structure of the oxadiazole skeleton is a biologically and biochemically active nucleus that has a multiple number of biological activities. The oxadiazole structure is a five-membered aromatic ring that has been used in numerous studies and molecules synthesised in laboratories. The principle structure of the Oxadiazole ring with a pair of Pyridine-type nitrogen atoms has been confirmed to be valuable for Oxadiazole analogues for having efficacious protein interactions with a large number of enzyme proteins and receptor proteins present in the organ system of the human body through different types of interactions, like Vander Wall interactions, thereby producing a huge variety of biological activities or pharmacological properties. Due to the variety in the pharmacological activity of Oxadiazole and their derivatives and analogues, they have been termed as one of the important pharmacological aspects to study. Multiple numbers of oxadiazole related synthetic compounds possessing high potent action and therapeutic activity are being widely incorporated for treatment and management of multiple diseases and disorders, giving immeasurable progression and establishment value. Oxadiazole derivatives express a multiple number of pharmacological activities like antimicrobial, anti-inflammatory, analgesic, antifungal, antipyretic, antidepressant, anti-tubercular, 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, and scientists to explore the Oxadiazole nucleus as a biologically active molecule having promising potency. This review article

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mainly focuses on the pharmacological profile of 1,3,4-Oxadiazole with various activities and examples (in the form of figures and structures). Expectations are that this article will be like a path showing torch to help and serve as guidance for new innovations/ideas along the progression of research for the evolution of more active/potent and less poisonous/toxic Oxadiazole-based derivatives.

Keywords: Oxadiazole; antifungal; pharmacological activity; antimicrobial; antitumor; antitubercular.

1. INTRODUCTION

Compounds having different heterocyclic moieties have earned a special interest in drug discovery. Among all the heterocyclic compounds, oxadiazoles have influenced remarkable engrossment in medicinal and pharmaceutical chemistry and have exhibited a huge scope of biological and pharmacological properties and actions. 1,3,4-oxadiazole derivatives represent an array of synthetic compounds with significant medicinal importance. Oxadiazole analogues are an intriguing moiety that has been the primary focus of a plethora of recent studies and research. This present article narrates some of the numerous biological and pharmacological activities incorporated into the Oxadiazole structural system.

The molecular skeleton of the Oxadiazole ring consists of a 5 atom structure with a couple of pyridine-type Nitrogen (N) and a 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 the 1,2,4-oxadiazoles variant have been more focused and prominently studied due to their possessing influential chemical, biological and pharmacological properties. The 1,2,5-oxadiazoles (furazan) have also been studied to some extent and they 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. [Fig. 1].

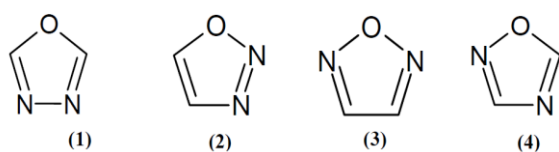


Fig. 1. Structures of the regioisomeric oxadiazole rings

Oxadiazole is 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 furan structure are exchanged for a couple of pyridine nitrogen atoms (-N), the aromaticity property of the emerging oxadiazole ring decreases significantly, and the resulting oxadiazole moiety shows/displays the characteristics/properties of conjugated diene. Because of the presence of a comparatively less e-(negative charge) cloud over the available carbon atoms (at different positions for different isomers), the Oxadiazole ring is extremely unfavorable for electrophilic substitutions at the two carbon atoms present, despite the attack of electrophile or electrophilic groups on the pyridine variety of nitrogen atoms when Oxadiazole moiety hydrogens are swapped with EDGs like (-CH₃). Nucleophile-based attack is exceptionally impossible in the Oxadiazole moiety due to the 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.

The Oxadiazole moiety is very resourceful and has continuously been an area of large scale and vast study in recent years. Compounds possessing an Oxadiazole 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 as intermediates in the organic manufacturing of various compounds and are largely used as transporting agents for electrons.

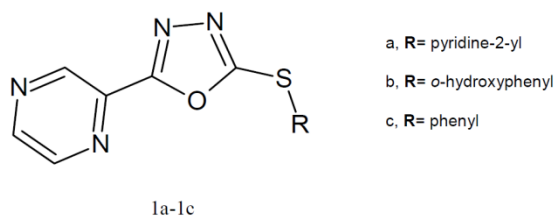
In this present review, emphasis is on the diverse pharmacological properties that have been associated with and contributed to by substituted or derivatized oxadiazoles in the past two and a half decades. (1995-2020).

2. PHARMACOLOGICAL SCAFFOLDS OF OXADIAZOLES

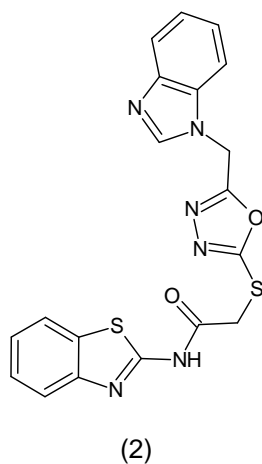
Oxadiazoles have been included in a domain of well-known biologically and pharmacologically active compounds, like, either as a side chain group or in the form of a modification of another heterocyclic ring. There are multiple reports in the literature available describing the oxadiazole derivatives with a multitude of pharmacological and biological effects and a few of them are covered in this review.

3. ANTIFUNGAL ACTIVITY

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

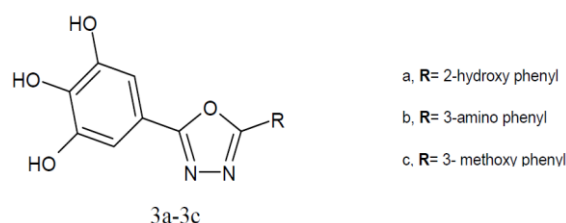


V.P. Rahul et al. [2] innovated the benzimidazole oxadiazole thio-N-phenyl benzothiazole acetamides analogues. Two compounds showed better activity against *Aspergillus niger* at 12.5µg/ml of minimum inhibitory concentration (MIC) (2).

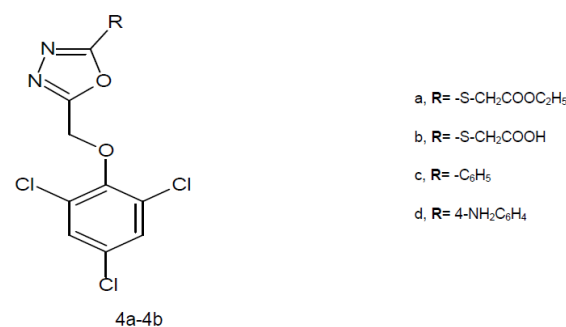


K. Ilango et al. [3] proposed novel set of 2-(trihydroxy phenyl)-5-substituted oxadiazole

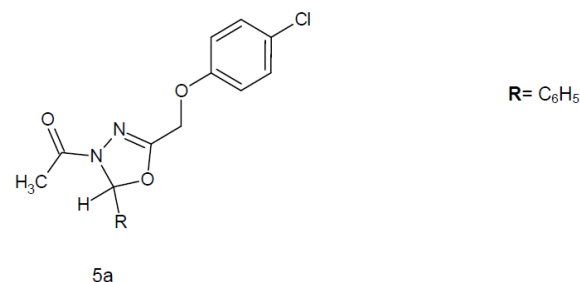
analogues. Each of the proposed analogues was screened for antibacterial as well as antifungal activity. A few of the synthesised compounds displayed moderate antifungal action at an MIC value of 100µg/ml against *Aspergillus niger* while Ketoconazole was used as a standard/reference drug (3a-3c).



S.G. Nadagouda et al. (2009) synthesized 2-substitute-5-[(2,4,6-trichlorophenoxy) 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).

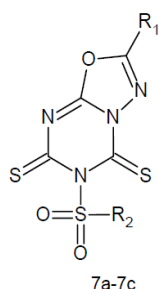


S.D. Joshi et al. [4] synthesized 2-aryl-3-acetyl-5-[4-chlorophenoxymethyl]-2,3-H-oxadiazoles analogues. One compound showed better antifungal activity against *Aspergillus niger* (5a).

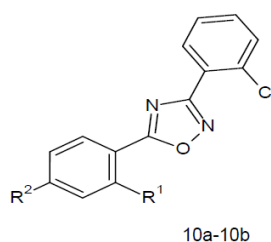


Dayashankar Tripathi et al. [5] synthesised 2-arylsulphonyl-oxadiazole-triazine-5,7-dithione derivatives. Three compounds exhibited antifungal activity nearly parallel to that of

Dithane M-45 (standard) at 100 ppm conc. against *Aspergillus niger* (7a-7c).

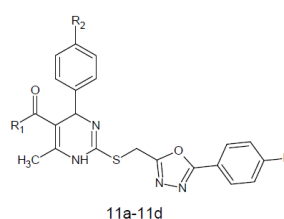


- a. $R_1 = 4\text{-ClC}_6\text{H}_4$; $R_2 = 4\text{CH}_3\text{OC}_6\text{H}_4$
 b. $R_1 = 4\text{-ClC}_6\text{H}_4$; $R_2 = 2\text{-ClC}_6\text{H}_4$
 c. $R_1 = 4\text{-ClC}_6\text{H}_4$; $R_2 = 2\text{-BrC}_6\text{H}_4$



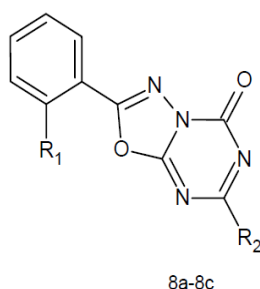
- a. $R^1 = \text{H}$; $R^2 = \text{Cl}$
 b. $R^1 = \text{Cl}$; $R^2 = \text{Cl}$

Fatma A.F. Ragab et al. [9] synthesized Dihydropyrimidine analogues having oxadiazole ring as monastrol derivatives. Some derivatives displayed action to combat various cancer cell lines (11a-11d).



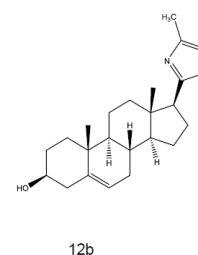
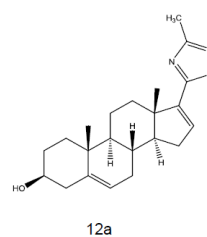
- a. $R = \text{Cl}$; $R_1 = \text{OC}_2\text{H}_5$; $R_2 = 4\text{-Cl}$
 a. $R = \text{Cl}$; $R_1 = \text{OC}_2\text{H}_5$; $R_2 = 4\text{-Br}$
 a. $R = \text{Cl}$; $R_1 = \text{OC}_2\text{H}_5$; $R_2 = 3\text{-Cl}$
 a. $R = \text{Cl}$; $R_1 = \text{OC}_2\text{H}_5$; $R_2 = 2,4\text{-diCl}$

D.V. Singh et al. [6] synthesised 2-Aryl-7-alkyl or aryl-1,3,4-oxadiazole-triazine-5-thione derivatives. A few compounds had similar activity to Mancozeb at 1000 ppm and showed 53–49% growth inhibition against *Aspergillus niger* (8a–8c).



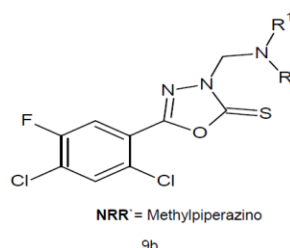
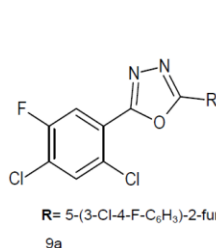
- a. $R_1 = \text{Cl}$; $R_2 = \text{methyl}$
 b. $R_1 = \text{Cl}$; $R_2 = \text{ethyl}$
 c. $R_1 = \text{Cl}$; $R_2 = \text{phenyl}$

Dora kovacs et al. [10] synthesized novel series of Oxadiazole ring in the steroidal structure. Two compounds found to be having anti-proliferative activity against 4 cell lines (HeLa, MCF7, A2780 and A431) and inhibition action over rat testicular $C_{17,20}$ -lyase (12a-12b).



4. ANTICANCER ACTIVITY

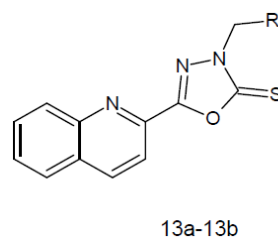
K. Subrahmanya Bhat et al. [7] synthesized 3-(methylamino substituted)-5-(2,4-diCl-5-fluorobenzene)-oxadiazolo derivatives. Two compounds emerged as active in the primary anticancer assay against the breast cancer MCF-7 cell line (9a-9b).



$R = 5\text{-(3-Cl-4-F-C}_6\text{H}_3\text{)-2-furanyl-}$

$\text{NRR} = \text{Methylpiperazino}$

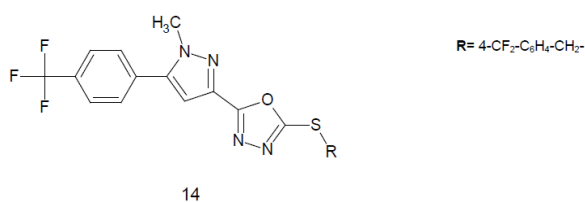
J. sun et al. [11] synthesized 2-aminomethyl-5-quinoline-oxadiazole-thione quinolone analogues. Two of these innovated compounds showed promising antiangiogenic activity against various cell lines like HepG2, SGC-7901 and MCF-7 (13a-13b).



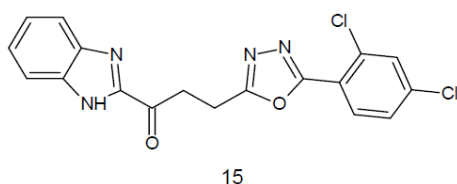
- a. $R = \text{-NH-C}_6\text{H}_4\text{(2-F)}$
 b. $R = \text{-NH-C}_6\text{H}_4\text{(4-Cl)}$

Mrityunjay Kundu et al. [8] synthesized 3-(2-Chlorophenyl)-5-substituted-1,2,4-Oxadiazole analogues. Two analogues showed potent anticancer property on Swiss albino mice (10a-10b).

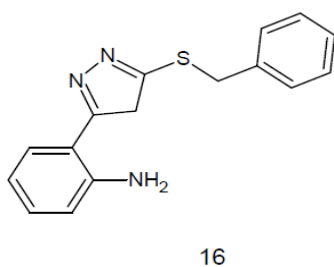
P. Pushpan et al. (2012) synthesized a series of oxadiazole having N-methyl-4-(CF₃) phenyl pyrazole group. One compound showed most potent cytotoxic activity with MIC values 15.54 mm in MCF-7 cells (14).



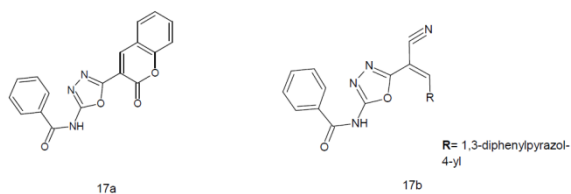
Mohd. Rashid et al. [12] synthesized novel series of 1-(1*H*-benzimidazole)-3-(5-(aryl)-oxadiazole)-propanone derivatives. One of the derivative exhibited maximum growth inhibition and was screened at 5 different dose concentrations (0.01, 0.1, 1, 10 and 100 MM) (15).



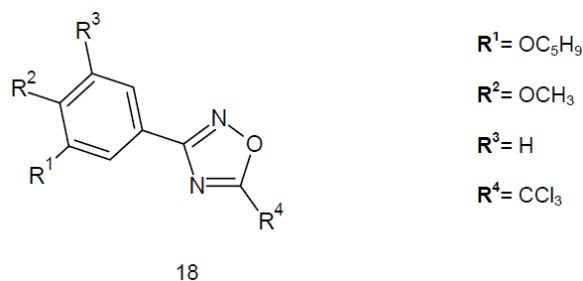
Kia liu et al. [13] innovated a novel set of 2-(benzylthio)-5-aryloxadiazoles. One derivative was found to have most anti-tumor activity while the evaluation on cell lines like MCF-7 and A549, B16-F10. For reference, Gefitinib was used as standard drug (16).



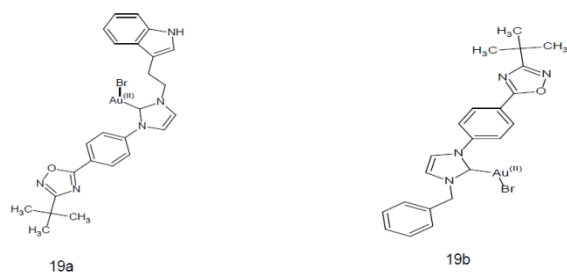
Samir Bondock et al. [14] put forward few oxadiazoles related heterocyclic moiety. Five compounds exhibited prominent potency against HepG2, WI 38, MCF-7, & VERO at different MIC concentrations ranging from 10 to 1000µg/ml (17a-17b).



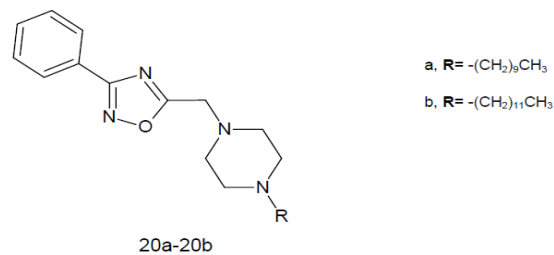
Dalip kumar et al. [15] innovated a series of 1,2,4-oxadiazolo analogues. The trichloromethyl analogues which were proved to have best activity among the derivatives of the set with significant potent action to combat PC3, DU145, LnCaP, MCF7 MDA-MB-231, PaCa2 and DUP145 with IC₅₀ 9.2 µM (18).



Catalin V. Maffei et al. [16] 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 IC₅₀ < 0.1µM against a 12 cancer cell lines (19a -19b).

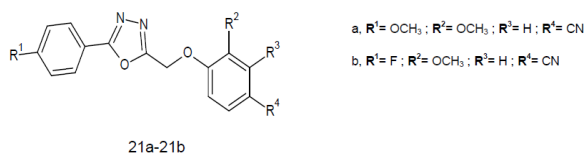


Wiliam Caneschi et al. [17] innovated a series of 1,2,4 and 1,3,4-oxadiazoles consisting of a lipophilic moiety. Two compounds of 1,2,4-oxadiazole derivative was selectively most potent against 4T¹ cell line. Few compounds of 1,3,4-oxadiazole analogues with aryl substitutes associated showed quite potent in anticancer assays (20a-20b).

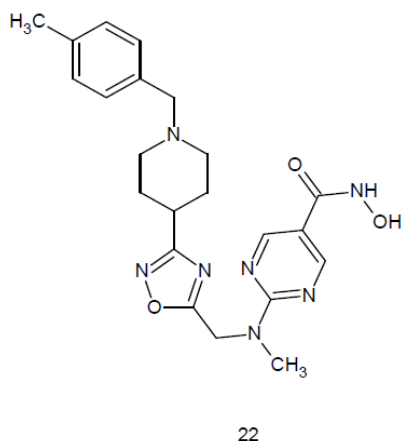


K. Lakshmithendral et al.. [18] innovated 2-(phenoxyethyl)-5-phenyl-1,3,4-oxadiazoles.

Two analogues showed good to moderate anti-breast cancer action in MDA-MB-453 and MCF-7 cell lines (21a-21b).

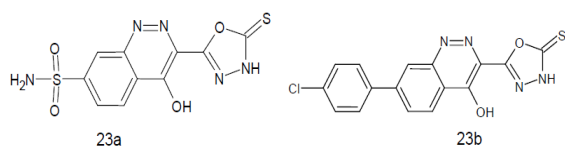


Zhuang yang et al. [19] synthesized 1,2,4-oxadiazoles comprising of hydroxamic acid analogues regarding a histone deacetylase inhibitor. The most active derivative exhibited optimum HDAC inhibition action, mostly towards HDAC with MIC values ranging from 1.8 to 3.0 nm, with the antiangiogenic MIC values range of 9.8–44.9 nM to combat 12 different cancer cell lines (22).



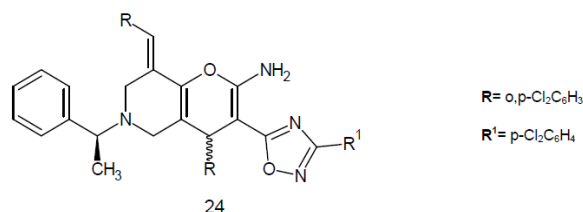
5. ANTI-TUBERCULAR ACTIVITY

Hurmath Unnissa S et al. [20] 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 *Mycobacterium tuberculosis* through MABA using Isoniazid as standard (23a-23b).

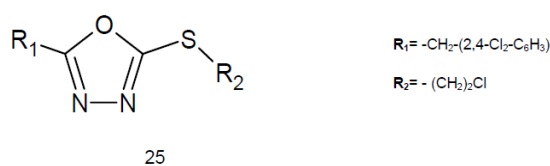


Abdulrahman I. Almansour et al [21] synthesized enantiomerically pure 1,2,4-oxadiazoles through a solvent independent, synthesis based on 4 components and 1,3-dipolar cycloaddition of

4(H)-pyrans having R-CNO. Few compounds showed promising anti-mycobacterial activity and others showed moderate activity using Isoniazid as a standard (24).



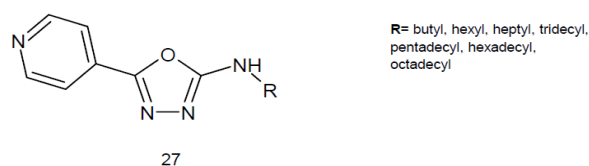
L.B. Ravi et al. [22] innovated 2-(alkyl-thio)-5-(substituted aryl-methyl)-1,3,4-oxadiazole analogues. One of the proposed compounds showed almost equipotent anti-mycobacterial activity as that of Isoniazid against nine multidrug-resistant (MDR) & two poly-drug resistant MTB strains (25).



Galina karabanovich et al. [23] 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).

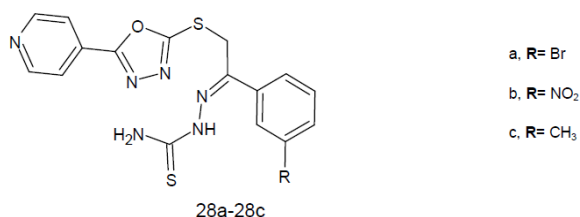


Rudolf Vosatka et al. [24] innovated 1,3,4-oxadiazole analogues of Isoniazid analogues. Results of pharmacological activities were not that promising. The oxadiazole analogues showed very moderate anti-TB activity (27).

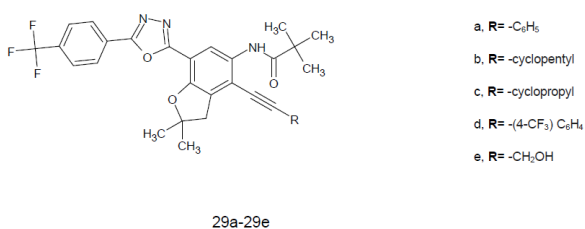


Ajay N. Ambhore et al. [25] synthesised pyridine-oxadiazole-thio-ethylidene-hydrazine

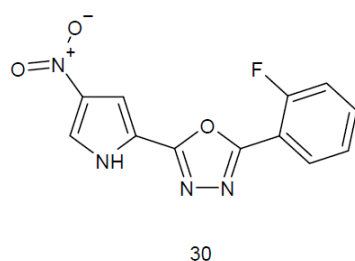
carbothioamide analogues. A few compounds showed potent growth inhibition and antimycobacterium activity and the others showed moderate activities as compared to the drugs Rifampicin and Isoniazid as standard (28a-28c).



Somnath Gholap et al. [26] synthesized 2,2-dimethyl-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 *Mycobacterium 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).



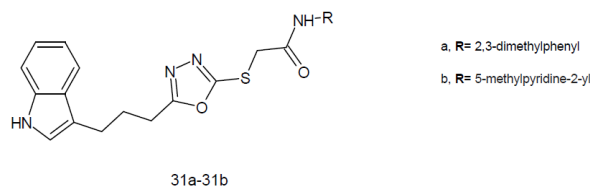
Rajesh A. Rane et al. (2012) synthesised 4-nitropyrole-based 1,3,4-oxadiazole (2-(4-NO₂-pyrrol-2-yl)-5-substituted-1,3,4-oxadiazolo) analogues. One of the synthesised compounds showed anti-mycobacterial activity (0.46µg/ml) equivalent to that of reference Isoniazid (0.40µg/ml) against the VERO cell line and was proved non-harmful (30).



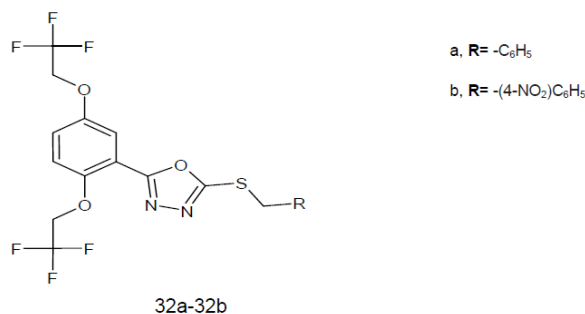
6. ANTI-DIABETIC ACTIVITY

Majid Nazir et al. [27] synthesized 5-[3-(1*H*-indol-3-yl) propyl]-1,3,4-oxadiazolo-2-thiol analogues. Two of the synthesised compounds were most

potent with MIC values ranging 9.46 ± 0.03 µM to 9.37 ± 0.03 µM. Remaining derivatives displayed non-significant 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).

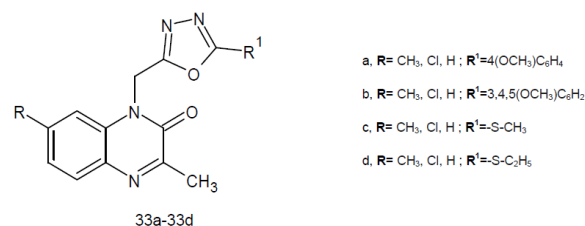


Ramesh S. Gani et al. [28] synthesized new set of 5-(2,5-bis(2,2,2-trifluoroethoxy) phenyl)-1,3,4-oxadiazolo-2-thiols analogues. Two of the synthesised derivatives showed better activity both in vitro as well as in vivo at MIC=40.00-80.00µg/ml as compared to the reference acarbose (MIC=34.72µg/ml) (32a-32b).



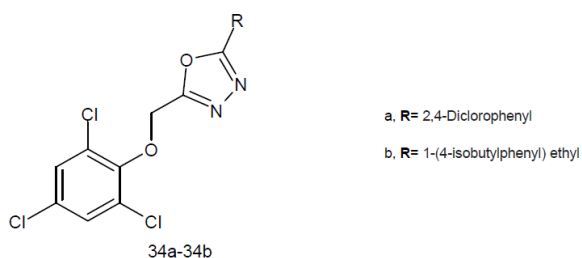
7. ANTI-INFLAMMATORY ACTIVITY

Shivananda Wagle et al. [29] synthesized 2-(3-methyl-7-aryl-2-oxoquinoxaliny)-5-(substituted)-1,3,4-oxadiazoles analogues. Few compounds exhibited good anti-inflammatory action at 50mg/kg dose using carrageenan-induced paw oedema method. Indomethacin was taken for reference (33a-33d).

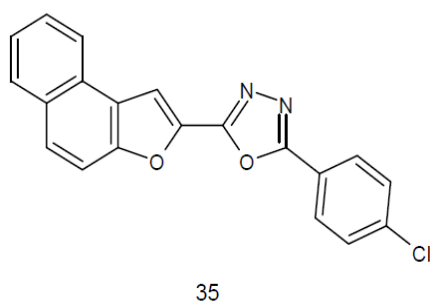


Mohd Amir et al. [30] synthesized 2-Substitutedaryl-5-(2,4,6-trichlorophenoxy methyl)-1,3,4-oxadiazole analogues. Two of the proposed derivatives displayed maximum anti-

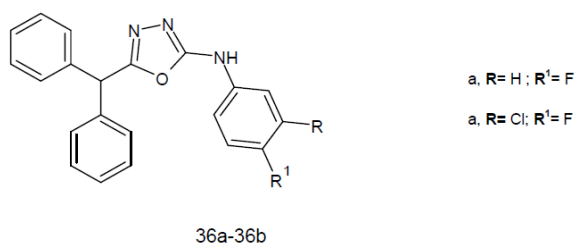
inflammatory action while being checked by carrageenan-induced rat paw oedema method with NSAIDs for reference (34a-34b).



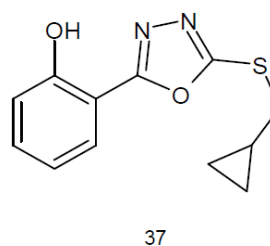
K.C. Ravindra et al. [31] innovated 2-Naphtho [2,1-b]furan-2-yl-5-substituted-1,3,4-oxadiazole derivatives. One of the synthesized compounds was displaying higher anti-inflammatory potency while compared with the reference drug using Ibuprofen for reference by carrageenan-induced rat paw oedema (35).



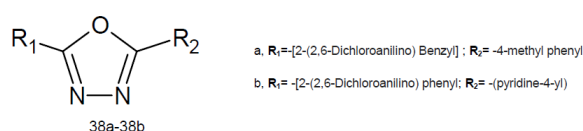
Mohd Amir et al. [32] synthesized 5-(diphenylmethyl)-2-(4-halogenated phenyl) amino-1,3,4-oxadiazole analogues. Two of the proposed derivatives emerged as most potent compounds (70mg/kg body weight) of the synthesis and were moderate potent, while compared with the reference Ibuprofen, using the carrageenan-induced rat paw oedema method in albino rats (36a-36b).



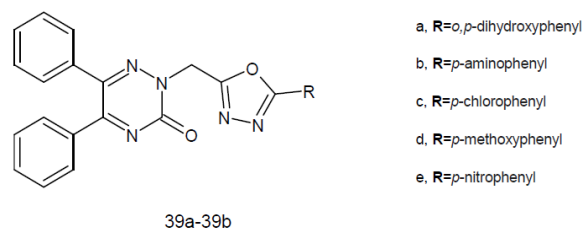
B.S. Kittur et al. [33] innovated 2-mercapto-1,3,4-oxadiazole analogues. Out of three proposed derivatives, only one of them was showing promising anti-inflammatory activity while the others were exhibiting moderate activity (37).



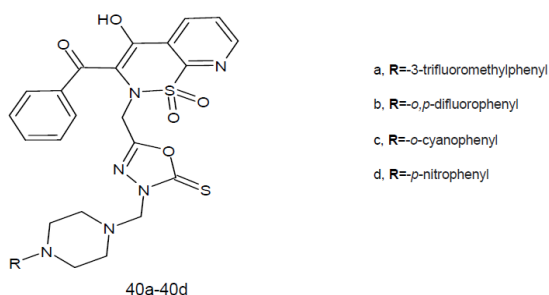
R.R. Somani et al. [34] proposed 2,5-Disubstitutedaryl-1,3,4-oxadiazole scaffolds. All the synthesized derivative was showing inhibitory effects towards the induced inflammation. Few of the synthesized compounds were exhibiting great percentages of inhibition (38a-38b).



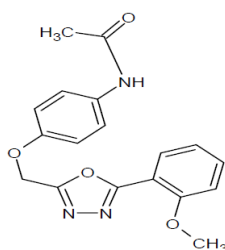
Anupam G. Banerjee et al. [35] synthesized 5, 6-diphenyl-1,2,4-triazin-3(2H)-one analogues having 5-aryl Oxadiazole analogues. Few of the proposed analogues were showing decent inhibition percentage of the denaturation (80.81-76.70%) of the Bovine serum albumin (BSA) compared to the standard Indomethacin (84.88%) (39a-39e).



Teresa Glomb et al. [36] 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-40d).



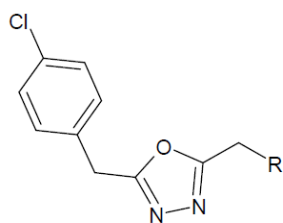
K. Ilango et al. [37] synthesized 2- (4-Acetamido phenoxy methyl) - 5-substituted- oxadiazole analogues. One of the synthesized compounds displayed the highest anti-inflammatory activity while few of the derivatives exhibited moderate activities against carrageenan induced paw oedema in rats at the concentration of 50mg/ml using Diclofenac sodium as standard drug (41).



41

8. ANTI-BACTERIAL ACTIVITY

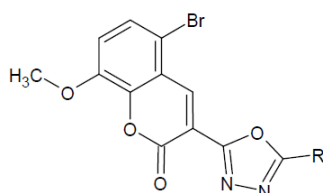
N.C. Desai et al. [38] proposed 2-Substitutedamine-5-chlorobenzene-1,3,4-oxadiazole analogues. Out of 9 proposed derivatives, few derivatives showed promising bactericidal action to combat *Escherichia coli* and *S. aureus* at MIC values in the range of 6-18µg/ml. other synthesized compounds were showing moderate activity of inhibition (42a-42c).



42a-42c

- a, R= -2-OC₂H₅-C₆H₄
 b, R= -2,5-(OCH₃)₂-C₆H₃
 c, R= -4-CH₃-C₆H₄

Devki Desai et al. [39] 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).

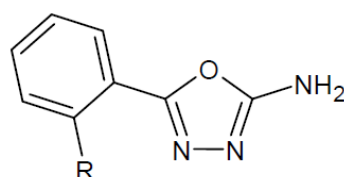


43a-43c

- a, R= -p-CH₃-C₆H₄
 b, R= -p-NO₂-C₆H₄
 c, R= -o-NO₂-C₆H₄

M.S.Y. Khan et al. [40] proposed 2-NH-5-Substitutedphenyl-oxadiazole analogues. Few

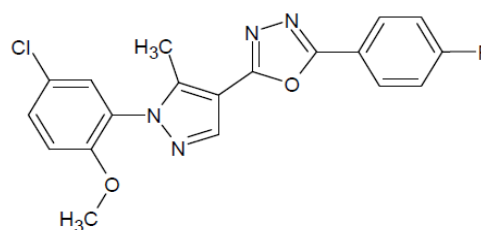
compounds were exhibiting good antibacterial activity while the others were showing moderate activity against *E. coli* at 100µg/ml with Norfloxacin as reference drug (50µg/ml) [44a-44b].



44a-44b

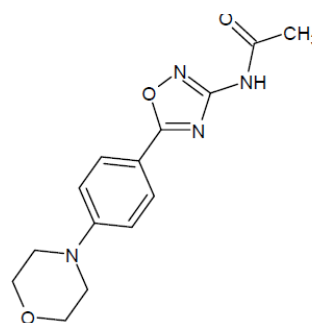
- a, R= -OH
 b, R= -F

Neithnadka Premsai Rai et al. [41] proposed 2-[1-(5-Cl-2- methoxy-phenyl)-5-CH₃-1H-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].



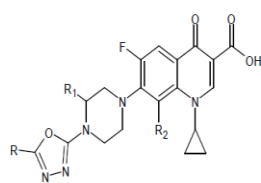
45

Antonio Palumbo Piccionello et al. [42] 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

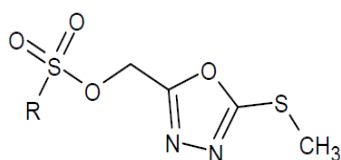
Rajnish kumar et al. (2011) synthesized 7-[4-(5-substituted-1,3,4-oxadiazolo-2-yl) piperazine] quinolone-yl analogues. Few compounds were declared as most potent compounds to combat *S. aureus*, *B. subtilis* & *E. coli*. While the other derivatives showed moderate to average potency (47a-47f).



47a-47f

- a, R=4-nitrophenyl; R₁=CH₃; R₂=OCH₃
- b, R=Phenyl; R₁=H; R₂=H
- c, R=3-nitrophenyl; R₁=CH₃; R₂=OCH₃
- d, R=3,4-dinitrophenyl; R₁=H; R₂=H
- e, R=Phenyl; R₁=CH₃; R₂=OCH₃
- f, R=3,4-dinitrophenyl; R₁=CH₃; R₂=OCH₃

Lei Wang et al. [43] 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 EC₅₀ values ranging 95.8-155.2µM. the compounds were also active against rice bacterial leaf blight (48a-48d).

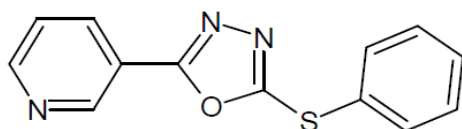


48a-48d

- a, R= phenyl
- b, R=-4-F-phenyl
- c, R=-4-Cl-phenyl
- d, R= -4-Br-phenyl

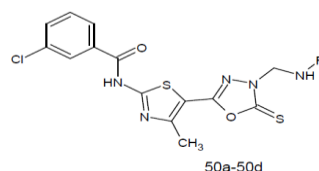
9. ANTI-MICROBIAL ACTIVITY

S.R. Pattan et al. [44] 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

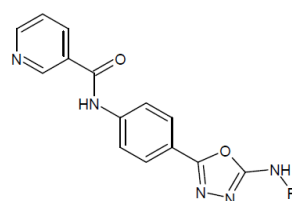
N.C. Desai et al. [45] synthesized 3-chloro-N-(5-(4-(arylphenyl-amino) methyl)-5-thioxo-4,5-dihydro-1,3,4-oxadiazol-2-yl)-4-methylthiazol-2-yl)benzamides analogues. Few of the proposed derivatives displayed proficient potency against all bacterial strains with MICs ranging 12.5-100µg/ml with Ciprofloxacin as the standard drug (50a-50d).



50a-50d

- a, R=-3-fluorobenzene
- b, R=-4-fluorobenzene
- c, R=-3-nitrobenzene
- d, R=-4-nitrobenzene

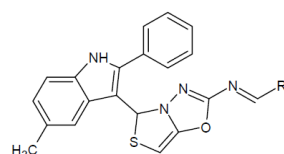
Viral R. shah et al. [46] proposed 2-(p-Methoxyphenyl) amino-5-p-(nicotinamidophenyl)-1,3,4-oxadiazoles analogues. Few proposed analogues exhibited highest activity against *E. coli*, *S. typhosa*, *S. citrus* and *B. megaterium* at 50µg/ml concentration with Ampicillin, chloramphenicol, Norfloxacin and Griseofulvin as standard antibiotics (51a-51d).



51a-51d

- a, R=-C₆H₄
- b, R=2,3-(CH₃)-C₆H₄
- c, R=-2-OCH₃-C₆H₄
- d, R=-2-C₂H₅-C₆H₄

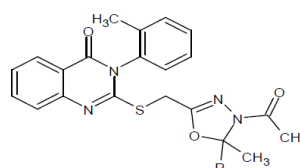
R. Saundane Anand et al. [47] synthesized 2-(Substituted benzylidene)amino-5-(2',5'-diaryl 1H-indol-3'-yl)-5H-thiazolo[4,3-b]-1,3,4-oxadiazoles derivatives. From screening the compounds revealed that few of the proposed derivatives displayed better zone of inhibition against *S. aureus* and *P. aeruginosa* at concentrations 500 and 1000µg/ml (52a-52b).



52a-52b

- a, R= -3-nitrobenzene
- b, R= -4-methoxybenzene

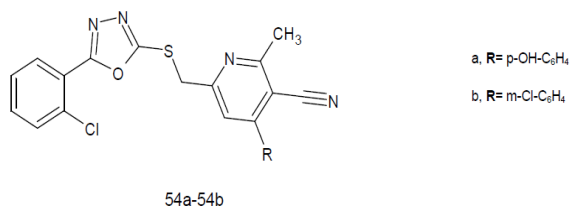
D.R. Godhani et al. [48] synthesized a set of 2-((4-acetyl-5-(substituted)-5-methyl-4,5-dihydro-1,3,4-oxadiazol-2-yl) methylthio)-3-otolylquinazolin-4(3H)-one derivatives. Few proposed derivatives showed good potency for *E. coli*, *P. aeruginosa*, *S. aureus* & *S. pyogenes* using Gentamycin, Ampicillin, Chloramphenicol, Ciprofloxacin and Norfloxacin as reference drugs (53a-53b).



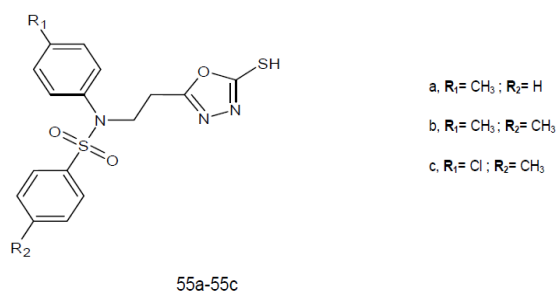
53a-53b

- a, R= -2-OH-C₆H₄
- b, R= -4-CH₃-C₆H₄

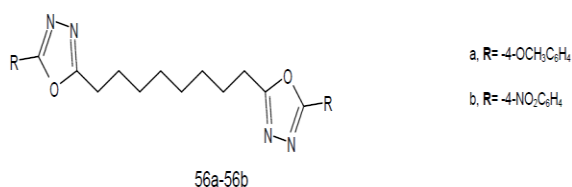
Niranjan S. Mahajan et al. [49] synthesized a set of 2-NH₂-6-[(5-(2-chlorophenyl)-1,3,4-oxadiazol-2-yl-thio) CH₃]-4-arylnicotinonitrile derivatives. Few of the synthesized compounds displayed promising inhibitory action for Gram negative like *E. coli* & *P. aeruginosa* and Gram positive organisms like *B. subtilis* having minimum inhibition concentrations of 5-8µg/ml (54a-54b).



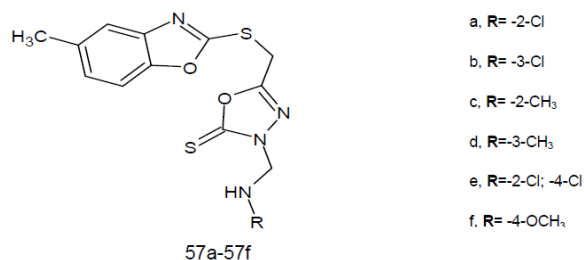
Desai S.R. et al. [50] synthesized series of 5-β-[(N-benzenesulphonyl/tosyl)-4-alkyl anilino] ethyl-2-mercapto-1,3,4-oxadiazoles derivatives. All the proposed derivatives proved to be showing moderately antibacterial activity against *Escherichia coli* and *Bacillus cirroflagellosus* at 100 µg/ml (55a-55c).



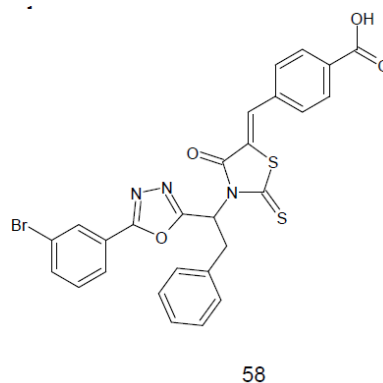
S.G. patil et al. [51] synthesized 1,8-bis (5-aryl-1,3,4-oxadiazol-2-yl) octane analogues. Few of the synthesized derivatives exhibited moderately activity against the bacteria *Staphylococcus aureus* [(56a-56b).



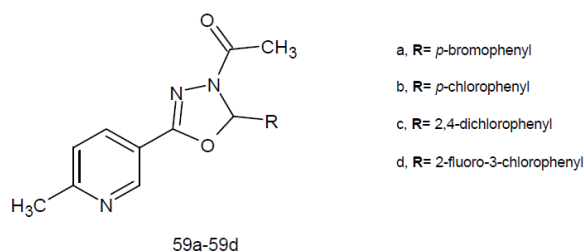
B.M. Basavaraja et al. [52] synthesized 5-[(1,3-benzoxazol-2-yl-thio) methyl]-3-[(4-alkyl phenyl) amino] methyl-1,3,4-oxadiazolidine-2-thione derivatives. Majority of the compounds showed very good activity against *S. aureus*, *K. pneumoniae* and *P. aeruginosa* with Fluoroquinolones as reference (57a-57f).



Jia-Chun Liu et al. [53] 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).

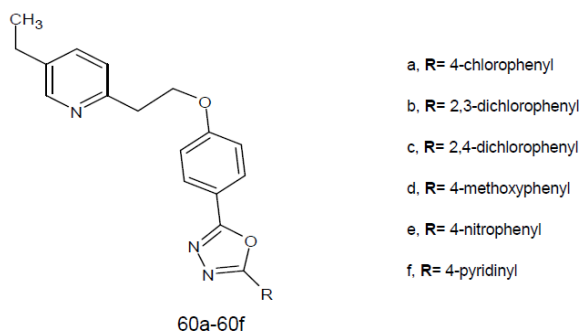


P.C. Shyma et al. [54] synthesized set of 3-acetyl-2-substituted-2H/methyl-5-[3-(6-methylpyridinyl)]-2,3-dihydro-[1,3,4]-oxadiazole analogues. Few of the derivatives exhibited good to moderate potency for *E. coli*, *S. aureus* and *P. aeruginosa* with MIC concentration 0.5-1.5mg/ml. Streptomycin was taken as reference drug for correlation (59a-59d).

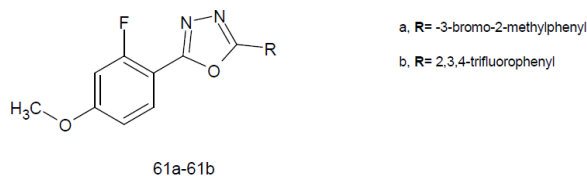


S.L. Gaonkar et al. [55] innovated a set of 2-[4-[2-(5-ethylpyridin-2-yl) ethoxy] phenyl]-5-aryl-1,3,4-oxadiazole analogues. The proposed derivatives were found to display good to less

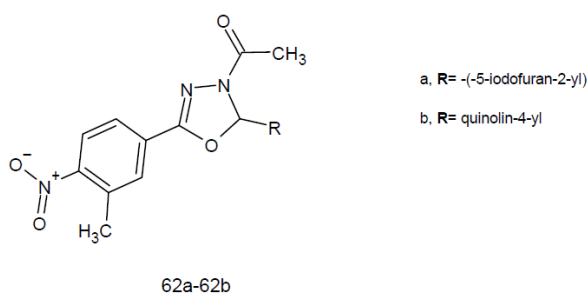
potent antimicrobial action. Few of the synthesized derivatives displayed good inhibitory action while some of them showed moderate action with MIC values ranging 8-26 μ g/ml (60a-60f).



B. Chandrakantha et al. [56] synthesized novel 1,3,4-oxadiazole ring tethered with 2-F-4-OCH₃ phenyl group. Few of the proposed derivatives displayed significant antibacterial action against *E. coli* & *P. aeruginosa* at quite less minimum inhibitory concentration 3 μ g/ml (61a-61b).

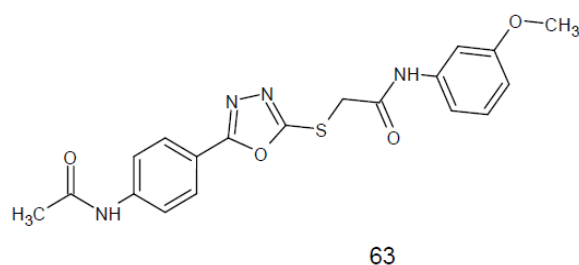


Kinga Paruch et al. [57] synthesized novel 3-Acetyl-2,5-diaryl-1,3,4-oxadiazoline analogues. Most of proposed analogues exhibited bactericidal effect for Gram positive organism. Two of the proposed derivatives exhibited the significant antibacterial action with minimal inhibitory concentrations (MICs) ranging 0.48 μ g/ml to 500 μ g/ml. other compounds showed moderate to poor antibacterial activity (62a-62b).



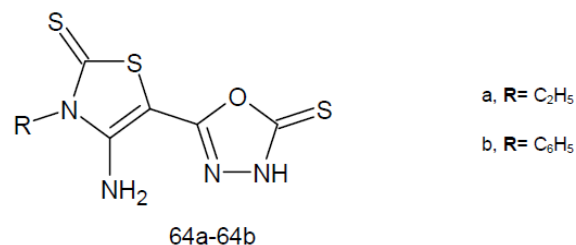
H.P. Shah et al. [58] innovated set of 2-[[5-(4-acetamidophenyl)-1,3,4-oxadiazol-2-yl]sulfanyl]-N-aryl)acetamide derivatives. Out of synthesized

derivatives, one exhibited excellent action against *S. aureus* (63).



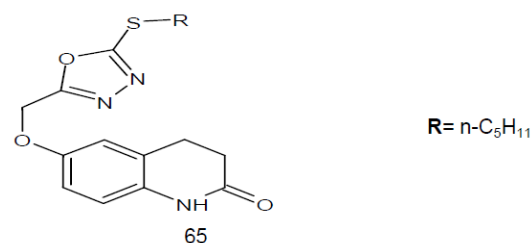
10. ANTI-VIRAL ACTIVITY

Mohammed Albratty et al. (2019) synthesized thiazole bearing 1,3,4-oxadiazole analogues. Both the proposed derivatives exhibited promising antiviral actions against various viral strains possibly under the influence of the presence of amino thiazole substituent (64a-64b).



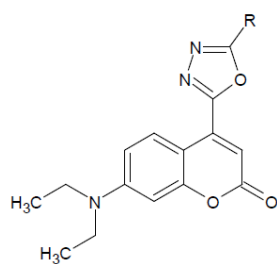
11. ANTI-CONVULSANT ACTIVITY

Shiben wang et al.. [59] innovated Dihydroquinoline substituted 1,3,4-oxadiazole analogues. One of the synthesized compounds was showing the significant anticonvulsant action better from the actions of carbamazepine and ethosuximide [65].



12. ANTI-CHOLINESTERASE ACTIVITY

Xiang Yu et al. [60] innovated a set of novel 7-diethylaminocoumarin-based 1,3,4-oxadiazole analogues. Among the derivatives, two of them showed moderate inhibitory activities positively correlated to the concentration (66a-66b).



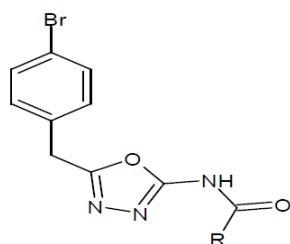
66a-66b

a, R= -4-chlorophenyl

b, R= -4-bromophenyl

13. ANTI-SALMONELLA TYPHI

Eid E. Salama et al. innovated 5-substituted-2-NH₂-1,3,4-oxadiazolo analogues. Out of the proposed derivatives few of them displayed great inhibitory activity against *Salmonella typhi* whereas the other compounds displayed moderate activity (67a-67b).

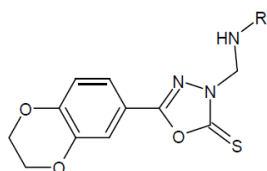


67a-67b

a, R= -(4-COCH₃)C₆H₄b, R= -(3-NO₂)C₆H₄

14. ANTIOXIDANT

Liang Ma et al. [61] 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 exhibiting antioxidants, like BHT and Trolox. The synthesized derivatives were assayed using (DPPH), (ABTS+ •) and (FRAP) scavenging assays (68a-68b).



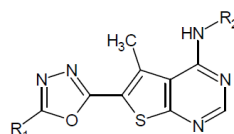
68a-68b

a, R= 2,6-Difluorophenyl

b, R= 3,4,5-Trifluorophenyl

Y. Kotaiah et al. [62] innovated set of novel N-substituted aryl phenyl-1,3,4-oxadiazole-thiazole-pyrimidine amine analogues. Few of these synthesized derivatives displayed good radical scavenging under the influence of EDGs like -CH₃ 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).

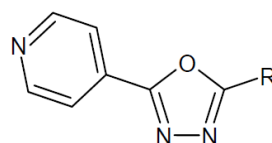


69a-69d

a, R₁= phenyl ; R₂= 4-fluorophenylb, R₁= 4-chlorophenyl ; R₂= 4-fluorophenylc, R₁= phenyl ; R₂= 2,4-difluorophenyld, R₁= 4-chlorophenyl ; R₂= 2,4-difluorophenyl

15. ANALGESIC ACTIVITY

K. Ilango et al. [63] 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).



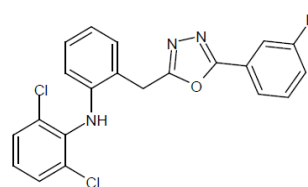
70a-70c

a, R= 4-methoxy phenyl

b, R= 4-hydroxy phenyl

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

K. Ilango et al. [64] 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= NO₂b, R= NH₂c, R= OCH₃

d, R= Cl

16. CONCLUSION

This review is focused on the diverse pharmacological properties possessed by and associated with the derivatives of Oxadiazole moiety in the last two and a half decades. Synthetic compounds possessing Oxadiazole ring in their chemical structure have been studied for multiple biological activities such as antifungal, anticancer, anti-HIV, antihypertensive, antibacterial, antimicrobial, anticholinesterase, anticonvulsant, antiviral etc. The studied

literature 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.

DISCLAIMER

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.

CONSENT

It is not applicable.

ETHICAL APPROVAL

It is not applicable.

COMPETING INTERESTS

Authors have declared that no competing interests exist.

REFERENCES

1. Pattan SR, Pattan JS, Musmade Deepak, Vetal SS. Synthesis and evaluation of some substituted aryl Oxadiazole and mercapto oxadiazole derivatives for antifungal, antimicrobial and antitubercular activities. *Indian Drugs*. 2012;49(4):12-18.
2. Rahul V. Patel, Patel PK, Premlata kumara, Kishor H Chikhaliya. 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.
3. Biju CR, 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.
4. Joshi SD, Unale YP, Parkale DB, Nadagouda SG. Synthesis and evaluation of antibacterial and antifungal activities of some novel 2,5-disubstituted-1,3,4 oxadiazoles. *Indian Journal of Heterocyclic Chemistry*. 2012;21(4):319-322.
5. Dayashankar tripathi, nishra AR, Singh D, 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 Chemistry*. 2007;16(3):239-242.
6. DV singh, Mishra AR, 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 Chemistry*. 2005;14(4):289-292.
7. Subrahmanya BK, Karthikeyan MS, Holla BS, 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.
8. Kundu Mrityunjoy, Jagdish Singh Brijesh Singh, 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.
9. Fatma AFR, Sahar MAS, Alfayomy AM, 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.
10. Dora Kovacs, Janos wolfling, Nikoletta szabo, 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 17 α -hydroxylase/C_{17,20}-lyase. *European Journal of Medicinal Chemistry*. 2013;70:649-660.
11. Juan sun, Hui zhu, Zhong-ming yang, 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.
12. Mohd rashid, Asif Husain, Ravinesh Mishra. Synthesis of benzimidazoles bearing oxadiazole nucleus as anticancer

- agents. *European Journal of Medicinal Chemistry*. 2012;54:855-866.
13. Liu K, Lu X, Zhang H, 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.
 14. Samir bondock, Shymaa Adel, Hassan A Etman, 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.
 15. Dalip kumar, Gautam patel, Angela K Chavers, 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.
 16. Maftai CV, Fodor E, Jones PG, 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.
 17. Caneschi W, Enes KB, Mendonca CCD, 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.
 18. Lakshmithendral K, Sarvanan K, Elancheran R, 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.
 19. Yang Z, Shen M, Tang M, Zhang W. Discovery of 1,2,4-oxadiazole-Containing hydroxamic acid derivatives as histone deacetylase inhibitors potential application in cancer therapy. *European Journal of Medicinal Chemistry*. 2019;17(8):116-130.
 20. Unnissa HS, Ravi TK Sonia George. Drug design and synthesis of 1, 3, 4-oxadiazole cinnoline analogs as potent antitubercular agents. *World Journal of Pharmaceutical Sciences*. 2015;3(11):54-60.
 21. Almansour AI, Raju SK, Arumugam N, 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.
 22. Ravi LB, 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.
 23. Galina K, Jan N, Valaskova L, 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.
 24. Vosatka R, Kratky M, Svarcova M, 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.
 25. Ambhore AN, Kamble SS, Kadam SN, 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.
 26. Somnath gholap, Tambe M, Nawale L, Sarkar D. Design, synthesis, and pharmacological evaluation of fluorinated azoles as anti-tubercular agents. *Arch Pharma*. 2018;351(2):1-10.
 27. Majid Nazir, Mohd Athar A, Aziz-ur-rehman, Sabahat Z Siddiqui. New indole based hybrid oxadiazole scaffolds with N-substituted acetamides: As potent anti-diabetic agents. *Bioorganic Chemistry*. 2018;81:253-263.
 28. Ramesh SG, Avinash KK, Timanagouda K. Raghuvver, 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
 29. Wagle S, Adhikari AV, Kumari NS. Synthesis of some new 2-(3-methyl-7-substituted-2-oxoquinoxaliny)-5-(aryl)-1,3,4-oxadiazoles as potential non-steroidal anti-inflammatory and analgesic agents. *Indian Journal of Chemistry-Section B*. 2008;47B(03):439-448.
 30. Mohd Amir, Javed SA, 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.
31. Ravindra KC, Vagdevi HM, Vaidya VP, Padmashali B. Synthesis, antimicrobial and antiinflammatory activities of 1,3,4-oxadiazoles linked to naphtha [2,1-b] furan. *Indian Journal of Chemistry-Section B.* 2006;45B(11):2506-2511.
 32. Mohd Amir, Saifullah Khalid, Wasim Akhter. Design, synthesis and pharmacological evaluation of 1,3,4-oxadiazole derivatives of aryl acetic acid as anti-inflammatory and analgesic agents. *Indian Journal of Chemistry-Section B.* 2011;50B(08):1107-1111.
 33. Kittur BS, Sastry BS, Pattan SR, Parag Rabara. Synthesis and Antiinflammatory activity of some novel 1,3,4- Oxadiazole and pyrazole derivatives. *Indian Drugs.* 2009;46(5):404-408.
 34. Somani RR, Bhanushali UV. Synthesis 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.
 35. Banerjee AG, Nirupam das, Shengule SA, 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.
 36. Glomb T, Wiatrak B, Gebczak K, Gebarowski T. New 1,3,4-Oxadiazole Derivatives of Pyridothiazine 1,1-Dioxide with Anti-Inflammatory Activity. *International Journal of Molecular Sciences.* 2020;21(23):9122
 37. Ilango K, Valentina p, Umarani N, Kumar T. Synthesis and Characterization of 2, 5-Disubstituted- 1, 3, 4-oxadiazoles as Potential Anti-inflammatory Agents. *Journal of Young Pharmacists.* 2009;1(1):72-76.
 38. Desai NC, Bhavsar AM, Shah MD, 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.
 39. Desai D, 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.
 40. Khan MSY, Khan RM, Drabu S. Anticonvulsant and antibacterial activity of some new 1,3,4-oxadiazole derivatives. *Indian Journal of Heterocyclic Chemistry.* 2001;11(2):119-122.
 41. Rai NP, Narayanswamy VK, Shashikanth S, 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 Journal of Medicinal Chemistry.* 2009;44(11):4522-4527.
 42. Piccionello AP, Masumeci R, Cocuzza CE, Fortuna CG. Synthesis and preliminary antibacterial evaluation of Linezolid-like 1,2,4-oxadiazole derivatives. *European Journal of Medicinal Chemistry.* 2012;50:441-448.
 43. Wang L, Zhou X, Hui L, Mu X. Synthesis and Antibacterial Evaluation of Novel 1,3,4-Oxadiazole Derivatives Containing Sulfonate/Carboxylate Moiety. *Molecules.* 2020;25(7).
 44. Pattan SR, Pattan JS, Gadhave PP, 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.
 45. Desai NC, Bhatt NB, Somani HC, 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.
 46. Desai JM, 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 Chemistry.* 1999;8:329-334.
 47. Saundane AR, kalpana R, 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.
 48. Godhani DR, Dobariya PB, Sanghani AM. Synthesis and antimicrobial evaluation of some new 1,3,4- Oxadiazoles. *Indian*

- Journal of Heterocyclic Chemistry. 2012;21(3):259-262.
49. Mahajan N, Dhavale SC, Jawarkar R, Manikrao AM. Synthesis and antimicrobial evaluation of 2-amino-6-[(5-(2-chlorophenyl)-1,3,4-oxadiazole-2-ylthio) methyl]-13 4-aryl nicotinonitriles. Indian Journal of Heterocyclic Chemistry. 2012;22(1):13-16.
 50. Desai SR, Laddi U, Bennur RS, 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.
 51. Patil SG, Girisha M, Badiger J, Kudari SM. Synthesis and anticonvulsant, antimicrobial activity of some bis -1,3,4-oxadiazole and bis-1,2,4-triazole derivatives from sebacic acid. Indian Journal of Heterocyclic Chemistry. 2007;17(1):37-40.
 52. Basavaraja BM, Vagdevi HM, Srikrishna LP, Shubha BS. Synthesis and antimicrobial activity of 1,3,4-oxadiazole incorporated benzoxazoles. Indian Journal of Heterocyclic Chemistry. 2008;18(1):05-08.
 53. Jia-chun liu, Chang-ji zheng, Meng-xiao wang, 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.
 54. Shyma PC, Kalluraya balakrishna, Peethambar SK, 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.
 55. Gaonkar SL, Rai KML, 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.
 56. Chandrakantha B, Shetty Prakash, Nambiyar vijesh, 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.
 57. Kinga paruch, Popiolek Lukasz, Biernasiuk anna, Hordyjewska anna. Novel 3-Acetyl-2,5-disubstituted-1,3,4-oxadiazolines: Synthesis and Biological Activity. Molecules. 2020;25(24):5844.
 58. Shah HP, Shah B, Bhatt JJ, Desai NC. Synthesis of 2,5-disubstituted 1, 3, 4-oxadiazoles as potential antimicrobial, anticancer and anti-HIV agnets. Cheminform. 2010;29(39):58.
 59. Shiben Wang, Hui Liu, Wang X, 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.
 60. Xiang Yu, You-Fang Zhao, Guo-Juan Huang, 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.
 61. Liang Ma, Yu Xiao, Cong li, 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.
 62. Kotaiah Y, Harikrishna N, Nagaraju K, 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.
 63. Biju CR, Ilango K, Manju Prathap, Rekha K. Design and Microwave-assisted Synthesis of 1,3,4-Oxadiazole derivatives for analgesic and Anti-inflammatory activity. Journal of Young Pharmacists. 2012;4(1):33-37.
 64. Ilango K, Valetina P, Gajendra Kumar, Dushyant Dixit. Design, Synthesis and QSAR Studies on a Series of 2, 5-Disubstituted 1,3,4-oxadiazole derivatives of diclofenac and naproxen for analgesic and anti-inflammatory activity. Medicinal Chemistry. 2015;11(8):753-763.
 65. Rajnish K, Ashwani K, Jain S, 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.
 66. Rane R, Banglore PV, Borhade SD, 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.
67. Shah VR, Vadodaria M, 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.
68. Laddi UV, Talawar MB, 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.
69. Desai SR, Laddi U, Bennur RS, 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.
70. Padmavathi V, Reddy GS, Padmaja A, 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.
71. Sravya G, Yamini G, Padmavathi V, 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.
72. Pattan SR, Chavan PA, Muluk RA, 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.
73. Nadagouda SG, Atul khochage, MR pradeep kumar, Karot haresh. Synthesis, antibacterial and antifungal activities of 2,5-disubstituted -1,3,4-oxadiazoles. *Indian Journal of Heterocyclic Chemistry*. 2006;41(7):841-846.
74. Gaurav Grover, 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 Chemistry*. 2003;12(3):289-290.
75. Arunkumar S, Ilango K, Manikandan RS, Sudha M, Ramalakshmi N. Synthesis, Characterisation and Biological Evaluation of some novel 2,5-Disubstituted 1,3,4-oxadiazole derivatives of Gallic acid. *International Journal of Pharm. Tech Research*. 1(4);1094-1099.
76. Gangapuram M, 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 Chemistry*. 2009;46(2):309-316.
77. Pathiyapurayil P, Poojary B, Chikkanna C, 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.
78. Bajaj S, Asati V, Jagdish singh, 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.
79. Peraman R, Varma RV, 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.
80. Mohd Albaratty, Karam AES, 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.

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