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Review Paper

Various Pharmacological aspects of 2, 5-Disubstituted 1,3,4-Oxadiazole Derivatives: A Review

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Abstract

Heterocyclic compounds possess diverse biological properties that have lead to intense study and research of these compounds. One of these compounds is Oxadiazole which has been found to exhibit various pharmacological activities. 1,3,4-oxadiazole having heterocyclic nucleus is a novel molecule which attract the chemist to search a new therapeutic molecule. 1,3,4-oxadizole exhibited a wide range of biological activities which includes antibacterial, anti-tubercular, anticonvulsant, hypoglycemic, anti-allergic, enzyme inhibitor, vasodialatory, antifungal, cytotoxic, anti-inflammatory, analgesic, hypolipidemic, anticancer, insecticidal, ulcerogenic activities etc. Out of the various derivative 2,5-Disubstituted-1,3,4-oxadiazole is a widely exploited for various application. A large number of drugs used clinically have oxadiazole ring as a structural building block. The capacity of 1,3,4-oxadiazole nucleus to undergo variety of chemical reactions including electrophilic substitution, nucleophilic substitution, thermal and photochemical which make it medicinal backbone on which a number of potential molecules can be constructed. This review has basic information about 2,5-disubstituted-1,3,4-oxadiazole derivatives published in various journals for further development in the field.

Keywords: 1,3,4-oxadiazoles, antibacterial, Antimicrobial, anti-tubercular, anti-inflammatory.

Introduction

The chemistry of heterocyclic compounds is an interesting field of study since a long time. Oxadiazole is a cyclic compound having one oxygen and two nitrogen atoms in a five member ring[1]. Oxadiazoles have occupied a specific place in the field of medicinal chemistry due to its wide range of activities[2]. From the existing literature we can see that 1,3,4-Oxadiazole nucleus has been possessing antimicrobial[3], antifungal[4], anti-inflammatory[5], anticonvulsant[6], antioxidant, analgesic[7], antitubercular[8] and mutagenic activity[9]. One pot synthesis of 1,3,4-oxadiazoleshas been reported by the reaction of appropriate hydrazide and carboxylic acid[10]. Derivatives of oxadiazole are used in the market such as Tiodazosin, Nosapidil, and Furamizole[11]. The present review attempts to summarize some pharmacological activities of 2,5-disubstituted 1,3,4-oxadiazole.

Antimicrobial Activity: Ajaykumar TV et al. synthesized some new 3-acetyl-5-(3-chloro-1-benzo[b]thiophen-2-yl)-2-substituted phenyl-2,3-dihydro-1,3,4-oxadiazoles and 2-(3-chloro-1-benzo[b]thiophen-2-yl)-5-substituted phenyl-1,3,4 oxadiazoles derivatives. All the newly synthesized compounds are evaluated for antimicrobial activity against *Staphylococcus aureus, Bacillus subtilis, Escherichia coli* and *Pseudomonas aeruginosa* and for antifungal activity against *Candida albicans* and *Asperigillusniger*. The compounds showed significant antibacterial and moderate antifungal activities. Compounds 4c and 4e were found to be most potent against *Staphylococcus aureus*and *Bacillus subtilis* when compared with standard drug ciprofloxacin[12].

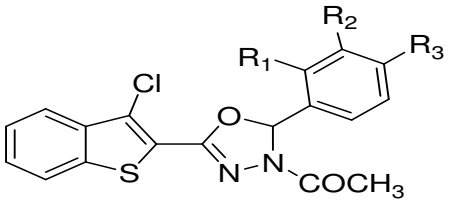
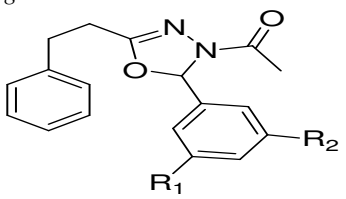


Figure-1

3-acetyl-5-(3-chloro-1-benzo[b]thiophen-2-yl)-2-substituted phenyl-2,3-dihydro-1,3,4-oxadiazoles Derivatives

S. Kumar synthesized a new series 1-(2-aryl-5-phenethyl- 1,3,4-oxadiazole-3(2H)-yl)-ethanonesand found to exhibit good antibacterial and antifungal activity. These newly synthesized compounds were shown the maximum activity against the strains of micro-organisms *Staphylococcusaureus*and *Pseudomonas aeruginosa*[13].



R_1 = H, H, OH, H, H
R_2 = $N(CH_3)_2$, Cl, OH, OH, H

Figure-2

1-(2-aryl-5-phenethyl- 1,3,4-oxadiazole-3(2H)-yl)-ethanones

1,3,4-oxadiazole derivatives were obtained from aromatic aldehyde and acetic anhydride and $POCl_3$by Glory Mathew et al. All the synthesized compounds showed significant analgesic, anti-inflammatory, anti-bacterial and anti-tubercular activities. But compound 1a and 1b was found to possess better activity then others[14].

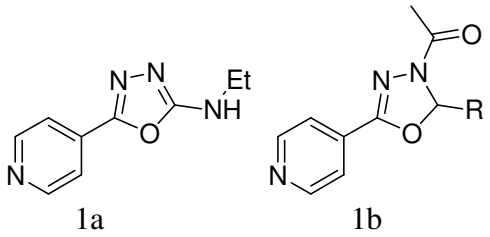


Figure-3
1,3,4-oxadiazole (1a and 1b)

A series of 2,5-disubstituted-1,3,4-oxadiazoles were prepared by Hemavathi SN et al. which contain pyridine and piperidine ring. These synthesized compounds have been found to be potent antibacterial[15].

3,5-bis(5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)azo dyes were synthesized by Palak K et. al. The newly synthesized azo dye fused with (5-(furan- 2-yl)-1,3,4-oxadiazole) were screened for their in-vitro anti-microbial activity. The antimicrobial activity of the test compounds were screened against bacterial strains belonging of *Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis* and *Escherchia coli* and fungal strains *Candida albicans* and *Candida parapsilosis* respectively. Synthesized compounds exhibit significant biological activity[16].

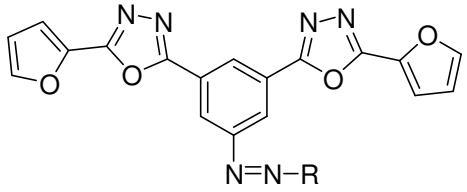


Figure-4
3,5-bis(5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)azo dyes

A series of 2-[5-(substituted sulfanyl)-1,3,4-oxadiazol-2-yl]phenol derivatives were prepared by Arun KW by condensation reaction between 2-hydroxybenzohydrazine and carbon disulfide. The in-vitro antibacterial activity of synthesized compound was tested against Gram positive bacteria viz. *Staphylococcus aureus* ATCC 9144, *Bacillus subtilis* ATCC 6633 and *Pseudomonas aeruginosa* MTCC 1688 , Gram negative bacteria viz*Escherichia coli* ATCC 25922 and antifungal activity was tested against *Candida albicans*. All the compounds showed good activity against all cultures[17].

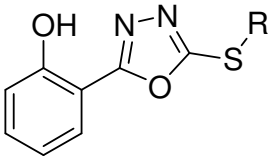


Figure-5
2-[5-(substituted sulfanyl)-1,3,4-oxadiazol-2-yl]phenol derivatives

Shridhar AH etal. synthesized a new series of 2,5-disubstituted-1,3,4-oxadiazoles by reaction of nicotinic acid hydrazide with various substituted aromatic acids in presence of $POCl_3$. Some of the synthesized compounds showed very good antifungal activity when compared to standard. Antibacterial activity was carried out against *Staphylococcus aureus, Pseudomonas aeruginosa, Escherichia coli* and *Bacillus subtilis* at a concentration of 100µgml^{-1}. The standard drug used was Ampicillin and DMF was kept as solvent control. The antifungal studies were carried out against fungus *Candida albicans* and *Aspergillusniger* using Griseofulvin as standard[18].

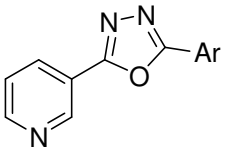


Figure-6
2, 5-disubstituted-1, 3, 4-oxadiazoles

The synthesis of 1-[(5-sustituted-1,3,4-oxadiazol-2-yl) methyl]-4-benzylpiperazines was carried out by SudhirBhardwaj et al. All the title compounds were screened for their antibacterial activity against *Staphylococcus aureus, Escherichia coli, Bacillus subtilis*and *Pseudomonas vulgaris*. One compound showed highest activity (figure-7)[19].

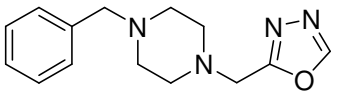


Figure-7
1-[(5-sustituted-1,3,4-oxadiazol-2-yl) methyl]-4-benzylpiperazines

Some 2-[5-(aryl)-[1,3,4]oxadiazole-2-ylsulfanyl]alkanoic acids were synthesized and screened for their antibacterial activity by Mudasir RB et al. All the compounds were studied for their in-vitro antibacterial activity against two Gram negative strains such as *Escherichia coli* and *Pseudomonas aeruginosa* and two Gram positive strains like *Bacillus subtilis* and *Staphylococcus aureus* and their minimum inhibitory concentration (MIC) were determined. Ciprofloxacin was used as a standard drug[20].

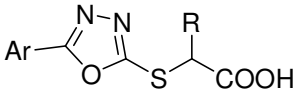


Figure-8
2-[5-(aryl)-[1,3,4]oxadiazole-2-ylsulfanyl]alkanoic acids

A series of 3-(1,3,4-oxadiazole-2-yl)-quinazolin-4(3H)-ones were synthesized by Patel NB et al. and screened for their in-vitro antimicrobial activity against Gram positive bacteria *Staphylococcus aureus*and Gram negative bacteria *Escherichia coli*. The synthesized compounds are found to be potent antibatcterial[21].

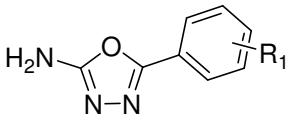


Figure-9
3-(1,3,4-oxadiazole-2-yl)-quinazolin-4(3H)-ones

RavitasDeshmukh et al. synthesized a series of new 1,3,4-oxadiazole derivatives having 6-bromonaphthalene moiety. 2-[(6-bromo-2-naphthyl)oxy] acetohydrazide was treated with various aromatic acids in presence of $POCl_3$ to give 2-{[(6-bromo-2-naphthyl)oxy]methyl}-5-aryl-1,3,4-oxadiazole and with hydrazide on treating with CS_2/KOH gave 5-{[(6- bromo-2 naphthyl)oxy]methyl}-1,3,4-oxadiazole-2(3H)-thione, which was subjected to Mannich reaction to get a series of Mannich bases and with alkyl or aryl halide to give 2-{[(6-bromo-2-naphthyl)oxy]methyl}-5-[(alkyl/aryl)thio]-1,3,4-oxadiazole.
Antimicrobial activities of these compounds were carried out and some of them have exhibited good activity[22].

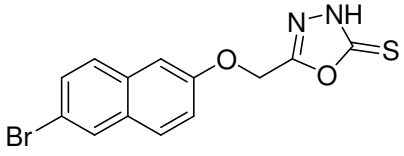


Figure-10
1,3,4-oxadiazole derivatives having 6-bromonaphthalene moiety

Anil MM et al. prepared a series of 5-(2-aminophenyl)-1,3,4-oxadiazole-2(3H)-thione derivatives by Mannich reaction. In vitro anti-microbial activity of all newly synthesized compounds was evaluated against Gram +ve organisms such as Staphylococcus aureus, Streptococcus pyogenes, Gram –ve organisms such as *Escherichia coli, Klebsiellaaerogenes* and fungus such as *Candida albicans*. Amikacin and ketoconazole (10µg/ml) were used as reference standard for antibacterial and antifungal activity respectively. Three compounds showed moderate antibacterial and antifungal activities at a concentration of 100µg/ml[23].

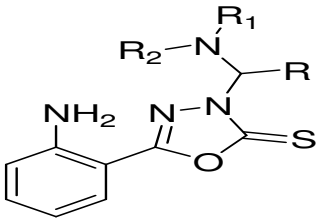


Figure-11
5-(2-aminophenyl)-1,3,4-oxadiazole-2(3H)-thione derivatives

New 5-alkyl and 3-(2,4-dimethylphenyl)-substituted-1,3,4-oxadiazole-2-thione derivativeswere synthesized by RakeshChawla et al. Mannich bases for some of these compounds were also synthesized by condensation with benzaldehyde and primary amines. All new compounds were tested for their antibacterial against *Staphylococcus aureus* using tetracycline as the standard. Some compounds were found to be most effective antibacterial[24].

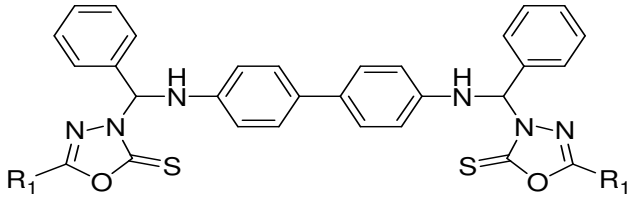


Figure-12
5-alkyl and 3-(2,4-dimethylphenyl)-substituted-1,3,4-oxadiazole-2-thione derivatives

Jha KK et al. synthesized 1,3,4-oxadiazole derivatives. All the synthesized compounds were evaluated for their antimicrobial activity against *Escherichia coli, Staphylococcus aureus*and*Staphylococcus epidermidis* and found to be most potent[25].

KanthamSrinivas et al. investigated four 1,3,4-bis-oxadiazole derivatives as potential antimicrobial agents. The compounds are: 5,5'-dimercapto-bis-[1,3,4- oxadiazol-2-yl]propane (2a), 5,5'-dimercapto-bis-[1,3,4-- oxadiazol-2-yl]butane (2b), 5,5'-dimercapto-bis-[1,3,4- oxadiazol-2-yl]octane (2c) and 5,5'-dibenzylthio-bis-[1,3,4- oxadiazol-2-yl]butane (3). The newly synthesized compounds were investigated for their antibacterial and antifungal activities. The results revealed that the compounds 2a-c exhibited both antibacterial and antifungal activities *against Staphylococcus aureus* and *Bacillus subtilis*. Compound 2a also showed activity against *Pseudomonas aeureoginosa*. All the above compounds and compound 3 exhibited activity against *Candida albicans*[26].

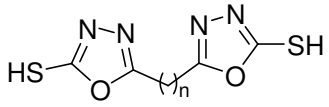


Figure-13
1,3,4-bis-oxadiazole derivatives

Various new 2-Amino-5-(substituted)phenyl-1,3,4-Oxadiazole derivatives were synthesized by Manish Srivastava et al. The synthesized compounds were evaluated for their antimicrobial properties against *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa, Candida albicans*. Norfloxacin was used for comparison with antibacterial activity[27].

Microwave assisted as well as conventional synthesis of 5-substituted-2-(2-methyl-4-nitro-1-imidazomethyl)-1,3,4-oxadiazoles containing the nitroimidazole moiety is carried out by Manish KM et al. and tested for their antibacterial and antifungal activity. Studies on the antibacterial activity of synthesized compounds proved it to be more effective against four pathogenic organisms, viz., *Staphylococcus aureus, Klebsiellapneumoniae, Escherichia coli* and *Pseudomonas aeruginosa*[28].

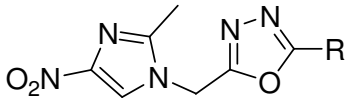


Figure-14

5-substituted-2-(2-methyl-4-nitro-1-imidazomethyl)-1,3,4-oxadiazoles containing the nitroimidazole moiety

Disubstituted 1,3,4-oxadaizoles, Mannich bases and S-alkylated derivatives have been synthesized from 2-(aryloxy-methyl)-benzoic acids through a multi-step reaction sequence by Channamata SN. All the synthesized compounds were screened for their in-vitro antibacterial and antifungal activity and some of them exhibited good activity[29].

Jumat Salimon et al. synthesized 6–Methyl–4–aryl–5-(5-phenyl-1,3,4–oxadiazol-2-yl)-1,2,3,4-tetrahydropyrimidine-2(1H)-one derivatives. Compound 3 has significant effect against *Streptococcus pneumonia* and *Escherichia coli*[30].

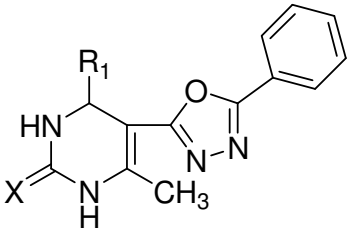


Figure-15

6–Methyl–4–aryl–5-(5-phenyl-1,3,4–oxadiazol-2-yl)-1,2,3,4-tetrahydropyrimidine-2(1H)-one derivatives

A series of 2,2'-(5-nitrobenzene-1,3-diyl)bis(5-alkyl-1,3,4-oxadiazole), 5,5'-(5-nitrobenzene-1,3-diyl)bis(1,3,4-oxadiazole-2-thiol) and 5,5'-(5-nitrobenzene-1,3- diyl)bis(4-amino-4H-1,2,4-triazole-3-thiol were obtained via reaction of 5-nitroisophthalic dihydrazide by KanthamSrinivas et al. All these newly synthesized compounds were displayed potent antibacterial activity[31].

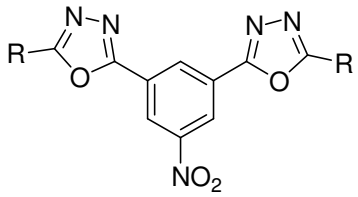


Figure-16

2,2'-(5-nitrobenzene-1,3-diyl)bis(5-alkyl-1,3,4-oxadiazole) derivatives

A series of 2-(3,4,5-trihydroxyphenyl)-5-aryl-1,3,4-oxadiazole was synthesized by Jain et al. All the synthesized compounds were subjected to antimicrobial and anti-fungal activity. Anti-microbial activity was carried out against *Escherichia coli, Pseudomonas aeruginosa*, *Klebsiellapneumoniae* and *Staphylococcus aureus* at a concentration of 100µg/ml. Streptomycin was used as standard. Anti-fungal activity was performed against *Aspergillusniger* with test compounds at a concentration of 100µg/ml. Ketaconazole was the standard drug[32].

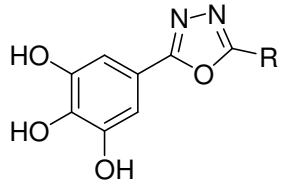


Figure-17

2-(3,4,5-trihydroxyphenyl)-5-aryl-1,3,4-oxadiazole

Arunkumar et al. synthesized a series of Mannich bases by the reaction of 5–{2–(ethylthio)–1H–benzimidazol–1–yl}–methyl–1,3,4–oxadiazole–2–thione with formaldehyde and appropriate amines by conventional and microwave techniques. The antibacterial screening against *Staphylococcus aureus, Escherichia coli* and *Pseudomonas aeruginosa* at three different concentrations revealed that one compound (figure) is significantly active[33].

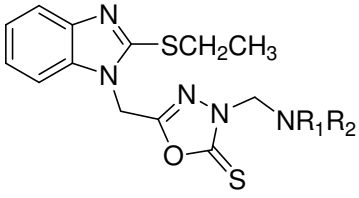


Figure-18

5–{2–(ethylthio)–1H–benzimidazol–1–yl}–methyl–1,3,4–oxadiazole–2–thione derivatives

Copper(II) complexes of chromen-2-one-3-carboxyhydrazide and 2-(chromen-3'-onyl)-5-(aryl)-1,3,4-oxadiazole derivatives have been synthesized by RakeshSaini et al. These complexes have been screened for their antimicrobial activities against some bacterial species like *Staphylococcus aureus, Escherichia*

coli and *Pseudomonas aeruginosa* and few fungal strains *Candida albicans*and *Cryptococcus neoformans* and found to be most active[34].

Neeraj KF prepared novel 5-phenyl-1,3,4-oxadiazole-2-thiol derivatives. Most of them were tested for their antibacterial activity against *Pseudomonas vulgaris, Pseudomonas aeruginosa*and *Escherichia coli* at a concentration of 50µg/ml and 100µg/ml. The standard drug used was Tetracycline and DMF was kept as control[35].

A series of novel 5-aryl-2-[N,N-di-substituted-thiocarbamoyl-thio)-calamine]-1,3,4-oxadiazole derivatives were synthesized by R. Saini et al. and screened for their antimicrobial activity against various micro-organism such as *Staphylococcus aureus*, *Staphylococcus epidermidis*. The synthesized compound possesses high antimicrobial activity[36].

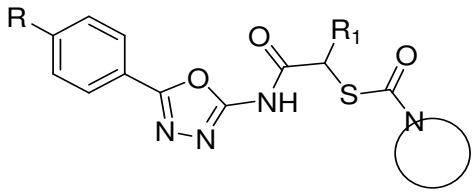


Figure-19
5-phenyl-1,3,4-oxadiazole-2-thiol derivatives

A series of 2-(Phenyl substituted)-5-indole-1,3,4-oxadizole derivatives were prepared by NitiBhardwaj et al. Three compounds were found effective against bacterial strains at a much higher concentration and none of the synthesized compound was found effective against fungal strain. Norfloxacin and Fluconazole were used as standard drugs for antibacterial and anti fungal activities respectively[37].

Mojahidul Islam et al. studied anti-bacterial and anti-fungal activity of a series of five new 1-(2-aryl-5-phenethyl-1,3,4-oxadiazol-3-(2H)-yl)ethanones. Among the newly synthesized compounds, 1-(2-(4-(dimethylamino)phenyl)-5-phenethyl-1,3,4-oxadiazol-3(2H)-yl)ethanone and 1-(2-(4-chlorophenyl)-5-phenethyl-1,3,4-oxadiazol-3(2H)-yl) ethanone were found to possess maximum activity against the tested strains of *Staphylococcus aureus* and *Pseudomonas aeruginosa*[38].

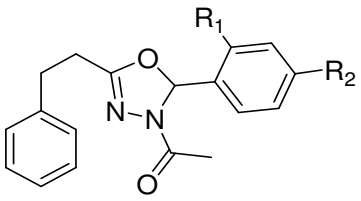


Figure-20
1-(2-aryl-5-phenethyl-1,3,4-oxadiazol-3-(2H)-yl)ethanones derivatives

ZuhairMuhi-eldeen et al. synthesized a series of N-(substituted-aryl-1,3,4-oxadiazole-2 yl) methyl-N- (4H-1,2,4–triazol-4yl) benzamide derivatives. Antimicrobial and antifungal activities of the final compounds have been evaluated and all the compounds have shown significant inhibition of bacterial and fungal growth[39].

ShaharYar M et al. Synthesized (ethyl-2-(1H) Benzo[d] [1,2,3]triazole–1-yl]acetate) and (2H–benzo[d][1,2,3] triazole–1–yl-acetohydrazine) derivatives. The antimicrobial activity of the synthesized compounds was evaluated, on *Staphylococcus aureus* and *Escherichia coli*. Ofloxacin was used as standard in a concentration of 30µg/disc. One compound (figure) showed maximum activity was found in against Staphylococcus aureus[40].

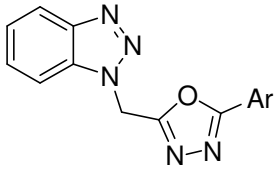


Figure-21
(2H–benzo[d][1,2,3]triazole–1–yl-acetohydrazine) derivatives

Alkyl, alkenyl, sulfonyl, thiocarbamates and Mannich derivatives were synthesized Priya VF et al. The most promising compound as antibacterial agent was 5-(pyridyl)-1,3,4-oxadiazole-2-benzylthiocarbamates[41].

The series of several new 5-[4ʿ-(5-phenyl-1,3,4-oxadiazole-2-yl-sulfonylmethyl)-biphenyl-2-yl]-tetrazole derivatives were synthesized by Chao Jun-Shu et al. and these compound screened for their antimicrobial activity against *Bacillus subtilis*and *Escherichia coli* at the concentration of 100µg/mL. These compounds showed a better inhibitory of this bacterial growth[42].

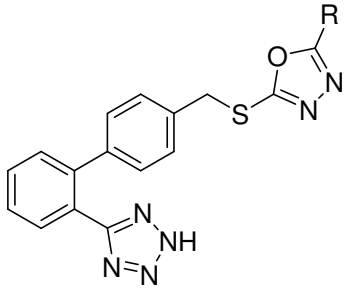


Figure-22
New 5-[4ʿ-(5-phenyl-1,3,4-oxadiazole-2-yl-sulfonylmethyl)-biphenyl-2-yl]-tetrazole derivatives

FerayAydogan synthesized a series of novel 2,5-disubstituted-1,3,4-oxadiazole derivatives were synthesized and tested for their in vitro antimycobacterial activity. Some compounds

showed interesting activity of greater than 90% inhibition against a strain of *Mycobacterium tuberculosis* H37Rv[43].

Ahmed OM et al prepared a series of 5-{3'-oxo-6'-(substituted-aryl)-2',3',4',5'- tetrahydropyridazini-2-ylmethyl}-2-substituted -1,3,4-oxadiazole. All the final compounds were screened for antibacterial and antifungal activity. All the compounds are evaluated for their antibacterial activity against *Escherichia coli, Staphylococcus aureus, Micrococcus luteus* and *Klebsiella pneumonia* and antifungal activity against *Candida albicans* and *C. neoformans* at 100µg/mL concentration. The zone of inhibition of each compound was determined and compared with standard drug fluconazole[44].

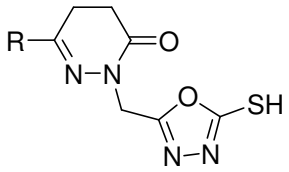


Figure-23
5-{3'-oxo-6'-(substituted-aryl)-2',3',4',5'-tetrahydropyridazini-2-ylmethyl}-2-substituted-1,3,4-oxadiazole derivatives

A novel series of 5-[substituted–(1,1-biphenyl)-3-yl]-1,3,4-oxadiazole-2(3H)-thiones and its 5-alkyl derivatives were synthesized by Aatesh OE et al. All the synthesized compounds were screened for their antimicrobial activity against various bacterial strains namely *Staphylococcus aureus* and *Pseudomonas aeruginosa*. The compounds exhibited good antimicrobial activity[45].

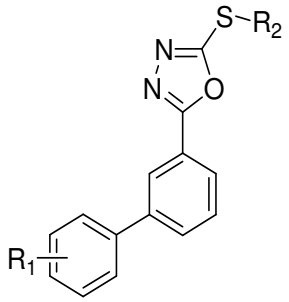


Figure-24
5-[substituted–(1,1-biphenyl)-3-yl]-1,3,4-oxadiazole-2(3H)-thiones and its 5-alkyl derivatives

Anti-Inflammatory Activity: Singh AK synthesized a new series of 1-(2ʿ,4ʿ-chloroacridine-9ʿyl)-3-(5ʿ-pyridine-4-yl)-(1,3,4-oxadiazole-2-yl-thiomethyl)-pyrazole-5-one derivatives. The all new synthesized compounds were evaluated for their anti-inflammatory activity. The reference drugs used was phenylbutazoneand aspirin. The compounds possess high activity as compared with standard[46].

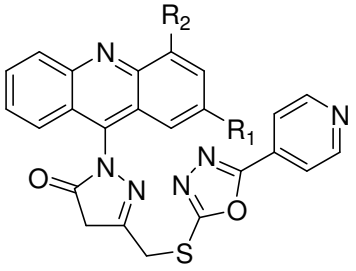
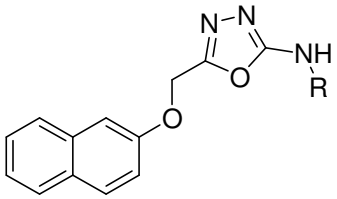


Figure-25
1-(2ʿ,4ʿ-chloroacridine-9ʿyl)-3-(5ʿ-pyridine-4-yl)-(1,3,4-oxadiazole-2-yl-thiomethyl)-pyrazole-5-one derivatives

A novelseries of 2-(2-napthyloxymethyl)-5-substitutedamino-1,3,4-oxadiazole derivatives has been synthesized by Chandra T et al. and found to possess considerable anti-inflammatory property as compared with standard[47].



R = Me, Et, ph, $-CH_2-CH=CH_2$

Figure-26
2-(2-napthyloxymethyl)-5-substitutedamino-1,3,4-oxadiazole derivatives

Burbuliene MM prepared a 1,3,4-oxadiazole derivatives belonging to a series of 5-[(2-disubstituted-amino-6-methyl-pyrimidine-4-yl)-sulfonylmethyl]-3H-1,3,4-oxadiazole-2-thiones. The synthesized compound was tested for their anti-inflammatory activity by using the method of carrageenan andbentonite induced paw oedema in rats. These compounds were found to be much more potent than ibuprofen. One compound (figure) showed moderate anti- inflammatory activity[48].

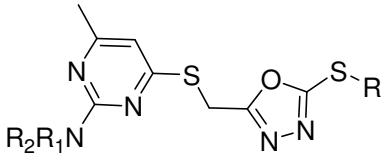


Figure-27
5-[(2-disubstituted-amino-6-methyl-pyrimidine-4-yl)-sulfonylmethyl]-3H-1,3,4-oxadiazole-2-thiones derivatives

Another series of 1,3,4-oxadiazole derivatives of biphenyl-4-yloxy acetic acid were synthesized by Mymoona et al. and screened them for their potent anti-inflammatory activity. The lead compound having much more anti-inflammatory activity (81.81%) than the reference drug flurbiprofen (79.54%)[49].

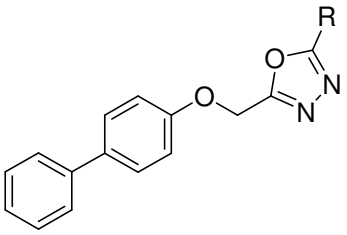


Figure-28
1,3,4-oxadiazole derivatives of biphenyl-4-yloxy acetic acid

Kumar H et al. synthesized a new series of 2-[3-(4-bromophenyl)-propane-3-ones]-5-(substituted phenyl)-1,3,4-oxadiazoles derivatives. All new synthesized compounds were screened for their anti-inflammatory activity. The results were compared with standard drug indomethacin. The compounds showed a potent anti-inflammatory activity[50].

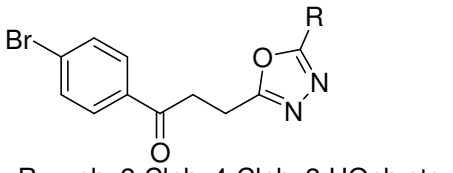


Figure-29
2-[3-(4-bromophenyl)-propane-3-ones]-5-(substituted phenyl)-1,3,4-oxadiazoles derivatives

A. Mohammed et al. synthesized some new 2-substituted-aryl-5-(2,4,6-trichloro-phenoxy-methyl)-1,3,4-oxadiazole derivatives and tested for their in-vitro anti-inflammatory activity by using carrageenan induced rat paw oedema method[51].

Potent anti-inflammatory activity has been reported in 2,5-disubstituted-1,3,4-oxadiazoles derivatives based on aryl propionic acid by Erhan P et al. These synthesized compounds showed anti-inflammatory activity 81.46% and 81.48% respectively against to the standard drug ibuprofen[52].

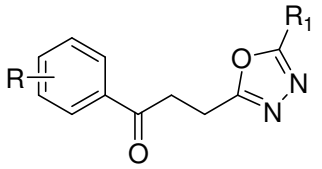


Figure-30
2,5-disubstituted-1,3,4-oxadiazoles derivatives

Analgesic Activity: A series of 5-(2-aminophenyl)-1,3,4-oxadiazole-2(3H)-thione derivatives have been synthesized by K. Selvakumar et al. Among the newly synthesized 1,3,4-oxadiazoles, **four** compounds showed highly significant ($p<0.001$) analgesic activity, Pentazocine (5mg/ml, IP) was used as reference standard[53].

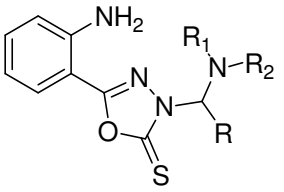


Figure-31
5-(2-aminophenyl)-1,3,4-oxadiazole-2(3H)-thione derivatives

Jayashankar B et al. synthesized a series of novel ether-linked bis-(heterocycles) via [3+2]-cycloaddition reaction of nitric oxide with allyl alcohol followed by intramolecular 1,3-diploar cycloaddition reaction of nitrile imine with carbonyl group. All the newly synthesized compounds were screened for their anti-inflammatory and analgesic activities. Among all synthesized four compounds exhibited excellent activity comparable to ibuprofen and aspirin at the similar dosages[54].

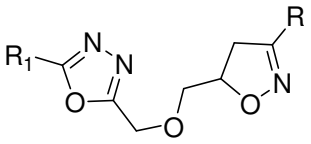


Figure-32
ether-linked bis-(heterocycles) derivatives

Anticonvulsant Activity: Y. Mohammad et al. synthesized some new derivatives of 2-(4-chlorophenyl)-amino-5-(4-pyridyl)-1,3,4-oxadiazole. The newly synthesized compounds were tested for their anticonvulsant activity. The range of all compounds showed activity in 33-100%. Compound (a) showed maximal activity and compound (b) showed good activity (Figure)[55].

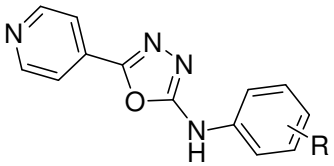


Figure-33
2-(4-chlorophenyl)-amino-5-(4-pyridyl)-1,3,4-oxadiazole derivatives

A. Zarghi et al. synthesized some new series of 2-substituted-5-{2-[(2-halobenzyl)-thio)-phenyl}-1,3,4-oxadiazoles derivatives and evaluated for their anticonvulsant activity. The synthesized compounds containg main essentials pharmacophore for binding to the benzodiazepine receptor and possess good anticonvulsant activity[56].

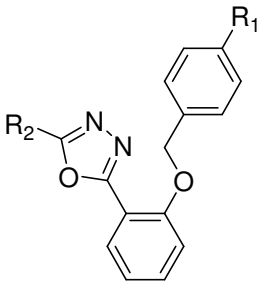


Figure-34
2-substituted-5-{2-[(2-halobenzyl)-thio)-phenyl}-1,3,4-oxadiazoles derivatives

Anti-Tubercular Activity: F. Macaev et al. synthesized a new series of 5-aryl-2-thio-1,3,4-oxadiazole derivatives. All the synthesized compounds were screened for their anti-mycobacterial activities against Mycobacterium tuberculosis H37Rv. The synthesized compounds appeared to be the most active derivatives exhibiting more than 90% inhibition of mycobacterial growth at12.5µg/mL[57].

Pathan SR et al. prepared some novel 1,3,4-oxadiazole derivatives and pyrazole derivatives and evaluated for their antitubercular activity against H37Rv strain as compare to the standard drug streptomycin. One Compound have shown promising activity and two compound have shown moderate activity (Figure)[58].

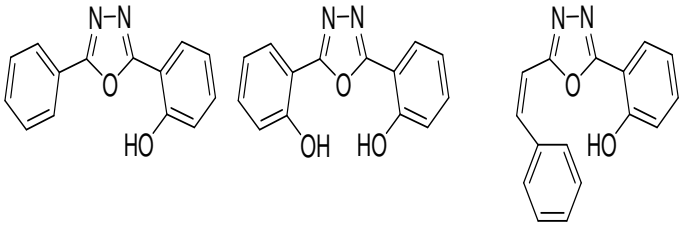


Figure-35
1,3,4-oxadiazole derivatives and pyrazole derivatives

Some novel series of 2,5-di-subsitituted-1,3,4-oxadiazoles were synthesized by Yarshahar M. et al. and the newly synthesized compound have been found to exhibit good anti- tubercular activity when compared with standard drug[59].

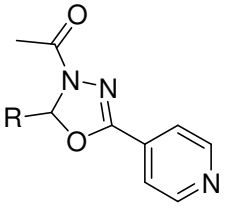


Figure 36
2,5-di-subsitituted-1,3,4-oxadiazoles derivatives

Conclusion

This review highlights the pharmacological properties of the 2,5-disubstituted 1,3,4-oxadiazole derivatives. Thus this paper proves to be significant for further research work on the bioactive oxadiazole ring containing compounds.

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