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Review Article **Open Access**

Various Biological Activity of 1, 3, 4-Oxadiazole Derivatives: A Review

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A B S T R A C T

Oxadiazole a heterocyclic nucleus has attracted a wide attention for the researchers in search for the new therapeutic molecules. Among them, 1,3,4-oxadiazoles have exhibited a wide range of biological properties. The first mono-substituted 1,3,4-oxadiazoles were reported in 1955 by two independent laboratories.1,3,4-oxadiazole considered as simple five membered Heterocyclic molecule possessing one oxygen and two nitrogen atoms at C-1, C-3 and C-4 respectively. 1,3,4-oxadizole exhibited a wide range of biological activities which includes antimicrobial, anti-tubercular, anticonvulsant, hypoglycemic, anti-allergic, vasodilator, anti-inflammatory, analgesic, anthelmintic, anticancer, antiviral, antioxidant, hemolytic, antiprolifrative activities etc. The purpose of this review is to collect the literature work reported by researchers on 1,3,4-oxadiazole derivatives for their various pharmacological activities and also efforts made on this moiety.

Keywords: antimicrobial, anticonvulsant, anti-inflammatory, antioxidant activities.

A R T I C L EI N F O

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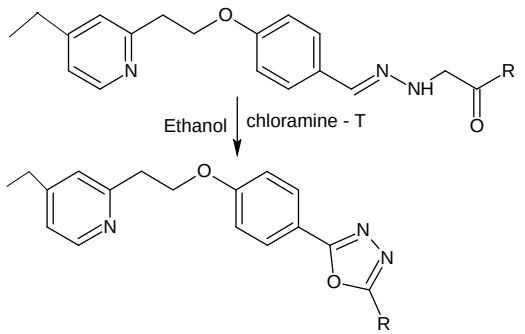
1. Introduction

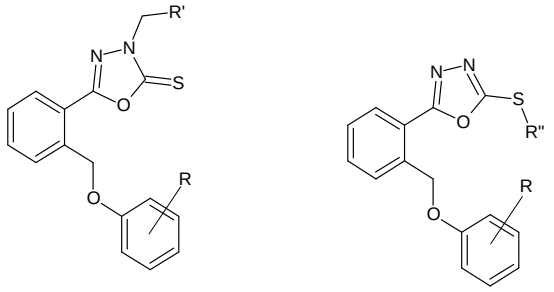
1,3,4-Oxadiazoles are unicyclic ring system which found to have diverse chemical reactivity and broad spectrum of biological activity. 1,3,4-oxadiazole considered as simple five membered Heterocyclic molecule possessing one oxygen and two nitrogen atoms at C-1, C-3 and C-4 respectively. Although they have been known from long ago to be biologically active, their varied biological features are still of great scientific interest. 1,3,4-oxadizole exhibited a wide range of biological activities which includes antimicrobial, anti-tubercular, anti-allergic, anticonvulsant, hypoglycemic, vasodilator, anti-inflammatory, analgesic, anthelmintic, anticancer, antiviral, antioxidant, hemolytic, anti-proliferative activities etc. The 1,3,4-oxadiazole undergoes number of reactions including electrophilic substitution, nucleophilic substitution, thermal and photochemical reactions.In drug discovery and development, a number of compounds containing an oxadiazole moietyare in late stage clinical trials, including Zibotentan as an anticancer agent and Ataluren for the treatment of cystic fibrosis. So far, one oxadiazole containing compound, Raltegravir, an antiretroviral drug for the treatment of HIV infection, has been launched onto the marketplace. Given below is a brief account of various alterations conducted on 1,3,4-oxadiazole ring and their associated biological activities [1-15].

Antimicrobial Activity

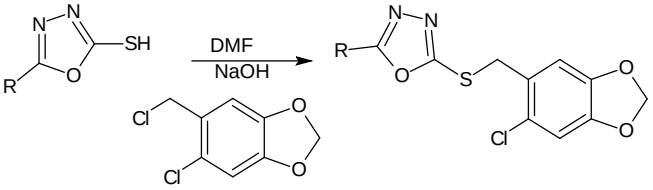
1,3,4-oxadiazole show a wide spectrum of antimicrobial activity and a considerable amount of work has been done on the synthesis of new potent antibacterial and antifungal 1,3,4-oxadiazoles.S.L. Gaonkar et al. Synthesis and antimicrobial studies of a new seriesof 2-{4-[2-(5-ethylpyridin-2-yl)ethoxy] phenyl} -5-substituted-1,3,4-oxadiazoles.Five bacteria and six fungal species were used as the antimicrobialtest. The bacterial strains were maintained on the LB agar medium and the filamentous fungi were maintained on Potato dextrose agar (PDA) medium at 28 °C. The agar disk diffusion method was used to test antimicrobial activity using potato dextrose agar medium. Nystatin was used as positive control for fungiand streptomycin and tetracycline for bacteria [16].



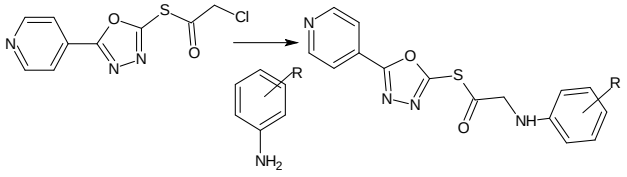
C.S. Naveena et al. Synthesis, characterization and antimicrobial activity of some di-substituted1,3,4-oxadiazoles carrying 2-(aryloxymethyl)phenyl moietyAll the newly synthesized oxadiazoles were screened for their invitro antibacterial and antifungal activity. Both microbial studies were assessed by Minimum InhibitoryConcentration (MIC) by serial dilution method [17].



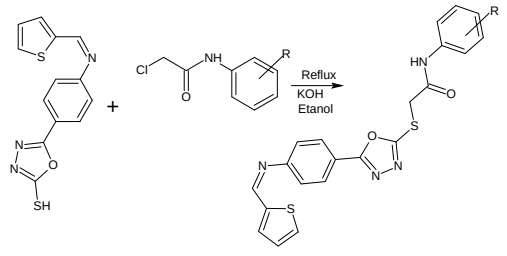
Aziz-ur-Rehman et al. synthesis of some new 5-substituted-2-((6-chloro-3,4-methylenedioxyphenyl)methylthio)-1,3,4-oxadiazole derivatives as suitable antibacterialinhibitors. The percentage inhibition and minimuminhibitory concentration results of in vitro antibacterial activity of the synthesized molecules against bacterial strains ofGram-bacteria are depicted. The most active moleculeamong the whole series was 6j which exhibited good inhibitoryaction against all the strains. The prominent activity of this molecule owes to the presence of the 4-chlorophenoxygroup in the molecule [18].



J.P. Raval et al. synthesis and in vitro antibacterial activity of newoxoethylthio-1, 3, 4-oxadiazole derivatives. The primary screening was conducted at (6.25 lg/ml) concentration against M. tuberculosis H37Rv (ATCC27294) in BACTEC12B medium using the BACTEC 460 radiometric system. Compounds demonstrating at least 90% inhibition in the primary screenwere re-examined at lower concentration (MIC) in broth micro-dilution assay with Alamar Blue [19].

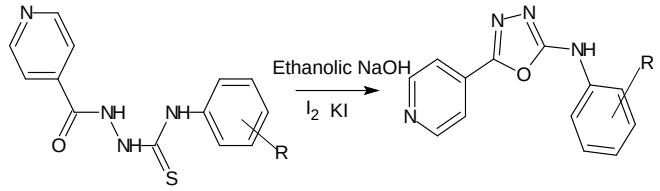


N.C. Desai et al. Synthesis and antimicrobial screening of1,3,4-oxadiazole and clubbed thiophene derivatives.The results of antimicrobial studies of newly synthesized compoundsreveal that the compounds possess significant antibacterialand antifungal activities [20].

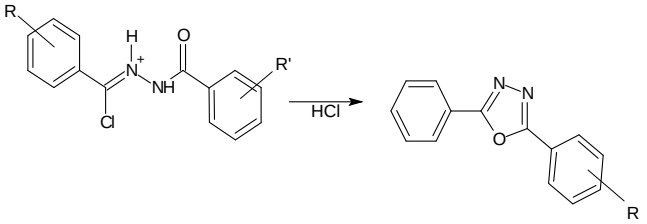


2. Anticonvulsant Activity

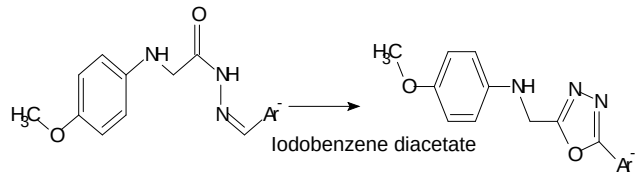
1,3,4-oxadiazole show a wide spectrum of anticonvulsant activity and a considerable amount of work has been done on the synthesis of new potent anticonvulsant 1,3,4-oxadiazoles.M. S. Yar et al. Synthesis and anticonvulsant activity of substituted Oxadiazole and thiadiazole derivatives. All the newly synthesized compounds were evaluated for their anticonvulsant activity by maximum electric shock Method. All the compounds showed activity inthe range of 33-100 % in comparison to phenytoinwhich completely inhibited the convulsions produced by electro convulse meter in albino mice [21].



Singh et al. Synthesis and evaluation of substituted diphenyl-1,3,4-oxadiazole derivatives for central nervous system depressant activity. Among the compounds synthesized (XIII-XXII), few Compounds were selected (XIII-XVII) and evaluated for CNS depressant activities such as antidepressant, anticonvulsant, antianxiety, and neurotoxicity activity. The pharmacological data indicated that among all the compounds being screened [22].

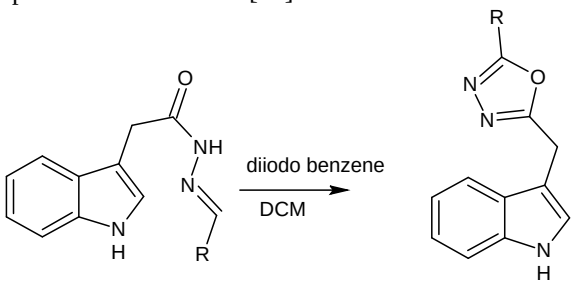


B. N. Prasanna Kumar et al. Synthesis of *N*-[{5-Aryl-1,3,4-oxadiazole-2-yl}methyl]-4-methoxyaniline Derivatives and Their Anticonvulsant Activity. Compounds possessing a chloro group had good anticonvulsant activityin the by maximum electric shock method [23].

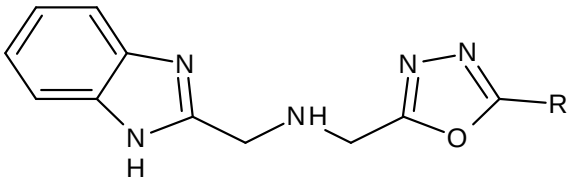


3. Anti-Inflammatory Activity

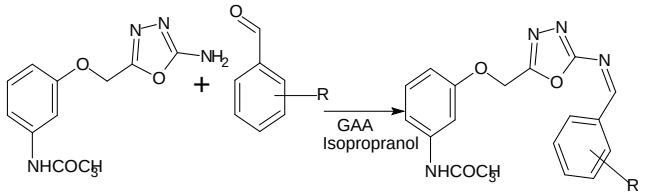
1,3,4-oxadiazole show a wide spectrum of anti-inflammatory activity and a considerable amount of work has been done on the synthesis of new potent anti-inflammatory1,3,4-oxadiazoles.S. Rapolu et al. Synthesis and biological screening of 5-(alkyl (1H-indol-3-yl))-2-(substituted) 1,3,4-oxadiazoles as anti-proliferative and anti-inflammatory Agents. Majority of the compounds showed goodinhibition of paw edema and cancer cell line growth. Compoundhaving 4-chlorophenyl substitution at C-2 position of the oxadiazolering exhibited better inhibition of inflammation than that ofthe standard reference Ibuprofen, whereas the anti-inflammatoryactivity comparable with standard [24].



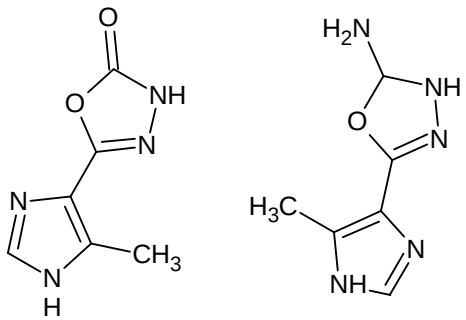
B. Vishwanathan et al. In vitro antioxidant and in vivo anti-inflammatory activity of 1,3,4 Oxadiazole derivatives. The in vivo anti-inflammatoryactivity was evaluated by carrageenan induced paw edema method at a dose of 25 mg/ kgand the results were encouraging. The anti-inflammatory activity data indicated that the 1,3,4-oxadizole derivatives were could be considered as possible hit as therapeutic agents [25].



Satyendra deka et al. Syntheses and characterization of some novel Oxadiazoles for in-vitro anti-inflammatory activity. Anti-inflammatory activity was carried outusing bovine serum albumin de-naturation method. All the title compounds were screened for anti-inflammatory activity[26].



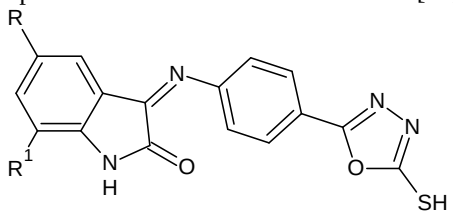
Almasirad et al. Synthesis, analgesic and anti-inflammatory activitiesof new methyl-imidazolyl-1,3,4-oxadiazoles and 1,2,4-triazoles. Effective compounds in analgesic test were screened for their anti-inflammatory activities using carrageenan induced paw edema on Wister male rats [27].



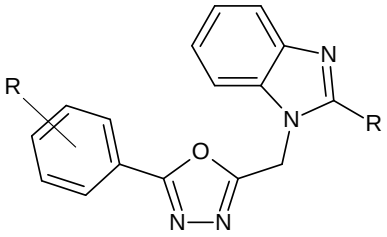
4. Anti-Cancer Activity

1,3,4-oxadiazole show a wide spectrum of anti-cancer activity and a considerable amount of work has been done on the synthesis of new potent anti-cancer 1,3,4-oxadiazoles.

R. Gudipati et al. Synthesis, characterization and anticancer activityof certain 3-{4-(5-mercapto-1,3,4-oxadiazole-2-yl) phenyl imino}indolin-2-one derivatives. The anticancer activity of all the synthesized compounds was evaluated against HeLa, IMR-32 & MCF-7 cancer cell to all the tested compounds than IMR-32 & MCF-7 cells [28].



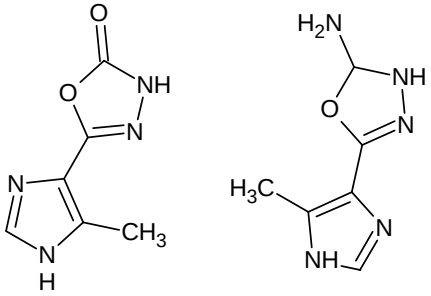
Salahuddin et al. Synthesis, characterization and anticancerevaluation of 2-(naphthalen-1-ylmethyl/naphthalen- 2-yloxymethyl)-1-[5-(substituted phenyl) - [1,3,4]oxadiazol-2-ylmethyl]-1H-benzimidazole. The in vitro anticancer studies reveal that the compound with para substituent like p-NO2 showed a prominent activity against MDA-MB-468 (Breast cancer)and SK-MEL-28 (Melanoma) (GP = 36.23 and 47.56, respectively)probably because of more electron withdrawing power of the other substituents. While the other compounds showed moderate activity against selected cancer cell line [29].



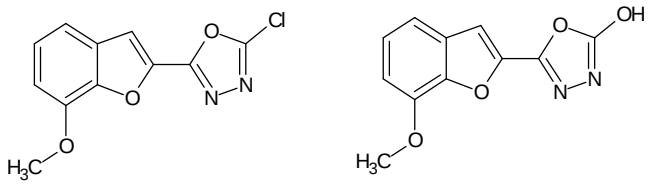
5. Analgesic Activity

1,3,4-oxadiazole show a wide spectrum of analgesic activity and a considerable amount of work has been done on the synthesis of new potent analgesic 1,3,4-oxadiazoles.

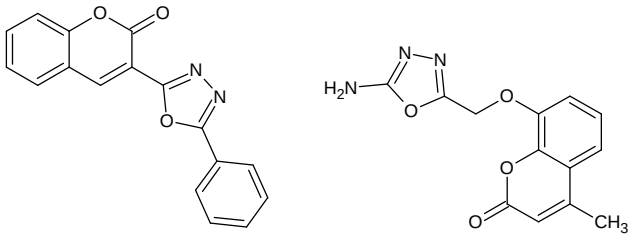
Almasirad et al. Synthesis, analgesic and anti-inflammatory activities of new methyl-imidazolyl-1,3,4-oxadiazoles and 1,2,4-triazoles. Acetic acid writhing test was performed on mice and indomethacin was used as standard drug.



K. M. Basavaraja et al. Synthesis and biological evaluation of some new oxadiazole and pyrazolederivatives incorporating benzofuran moiety. The analgesic activity was carried out by Tail-flick and writhing methods [30].



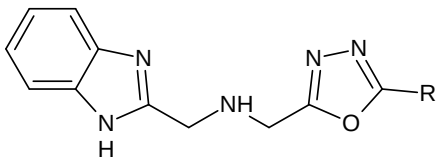
Khan et al. synthesis of some new 2,5-di-substituted 1,3,4-oxadiazole derivatives and their biological activity. The activity was carried out on wister mice weighing between 20-30gm using tail flick method [31].



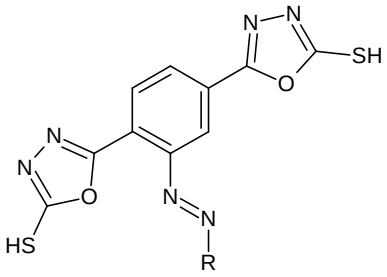
6. Antioxidant Activity

1,3,4-oxadiazole show a wide spectrum of antioxidant activity and a considerable amount of work has been done on the synthesis of new potent antioxidant 1,3,4-oxadiazoles.

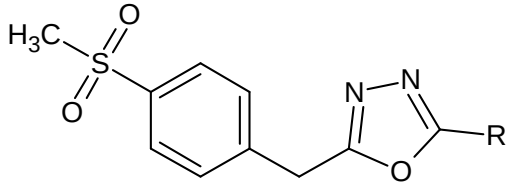
B. Vishwanathan et al. In vitro antioxidant and in vivo anti-inflammatory activity of 1,3,4 Oxadiazole derivatives. The 1,3,4-oxadiazole derivatives were evaluated for their free radical scavenging activity by DPPH (1,1-Di-phenyl-2-picrylhydrazyl) radical assay method using ascorbic acid as standard.



Keshavayya et al. synthesis of 1,3,4-oxadiazole incorporated azo dye derivatives as a potentbiological activity molecules. The free radical scavenging activity of test samples wasmeasured by DPPH (1, 1-Diphenyl-2-picrylhydrazyl) method [32].



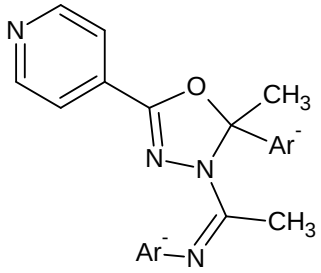
Boja Poojary et al. Synthesis, characterization and antioxidant activity of some 1,3,4-oxadiazoles carrying 4-(methylsulfonyl)benzyl moiety. The antioxidant activity of the compounds and the standard (Rutin) were assessed on thebasis of radical scavenging effect of the stable DPPH (1,1-Diphenyl-2-picrylhydrazyl) freeradical, with minor modification of the method [33].



7. Vasodialatory Activity

1,3,4-oxadiazole show a wide spectrum of vasodialatory activity and a considerable amount of work has been done on the synthesis of new potent vasodilator 1,3,4-oxadiazoles.

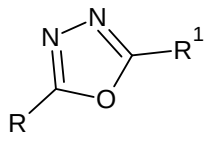
Pramod kumar J. Shirote et al. Synthesis and goat pulmonary vasodilatory activity of some novel 1,3,4-oxadiazoles. All the synthesized compounds were screened for their pulmonary vein relaxation activity using goat pulmonary vein [34].

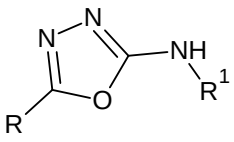


8. Anti-tubercular Activity

1,3,4-oxadiazole show a wide spectrum of antitubercular activity and a considerable amount of work has been done on the synthesis of new potent antitubercular 1,3,4-oxadiazoles.

Shahar Yar et al. Synthesis and Anti Tuberculostatic Activity of Novel 1,3,4-Oxadiazole derivatives. New oxadiazole derivativeswere synthesized andscreened for their anti-mycobacterial activity against Mycobacterium tuberculosis H37RV using the BACTEC-460radiometric system [35].





9. Conclusion

The present review highlights that the 1,3,4-oxadiazole moiety as a template for the development of newer therapeutic agents. Modified 1,3,4-oxadiazole moiety displayed the valuable biological activities. The 1,3,4-oxadiazole derivatives showed significant anticonvulsant, anti-inflammatory, anti-cancer, antioxidant and anti-microbial activities while compared with other activities. They may be used for the development of new drugs for the treatment of cancer, inflammation, central nervous system depressant, bacterial and fungal diseases by researcher for developing new, innovative drugs [36-85].

10. Acknowledgments

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