Current Trends in Technology and Science
ISSN: 2279-0535. Volume: V, Issue: IV

Oxadiazoles and Their Pharmacological Potentials: A Review

Anuj Singhai[*a], M.K. Gupta[b]

[a]Research Scholar, Oriental College of Pharmacy and Research, Oriental University, Indore (MP), India

[b]Dean, Oriental College of Pharmacy and Research, Oriental University, Indore (MP), India

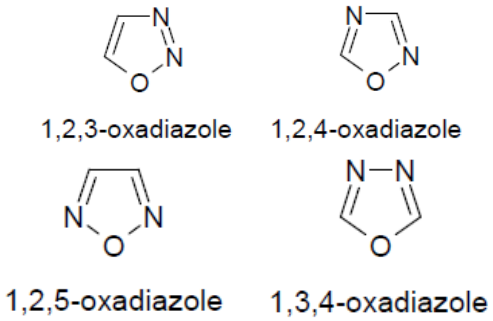
anujsinghai1989@gmail.com

Abstract:- **Oxadiazole is a five member heterocyclic ring which is a versatile lead compound for designing potent bioactive agents. The presence of heterocyclic structures in different types of compounds is increasing their pharmacological effect. oxadiazole nucleus has emerged as one of the potential pharmacophore responsible for diverse pharmacological properties. This interesting group of compound has diverse biological activities such as antimicrobial, anti-inflammatory, antitubercular, anticonvulsant, anticancer, anti-HIV, hypogycemic and genotoxic.**

Keywords:- **Oxadiazole, Antimicrobial, Anti-inflammatory, Anticonvulsant, Anticancer.**

INTRODUCTION

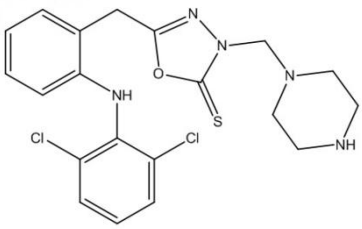
Compounds having a five member ring containing one oxygen and two nitrogen atoms are called oxadiazoles or in the older literature furadiazoles. Four types of oxadiazole are known namely 1,2,3-, 1,2,4-, 1,2,5- and 1,3,4-oxadiazoles. Out of these 1,3,4-oxadiazoles are found to be most potent biologically. The compounds containing oxadiazole ring are exhibit different pharmacological activities.



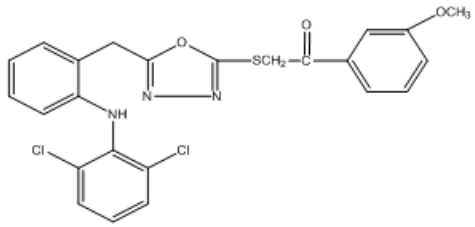
ANTI-INFLAMMATORY ACTIVITY

Non-steroidal anti-inflammatory drugs (NSAIDs) are the most preferred class of drugs in use for the treatment of various pathological conditions such as pain, fever, inflammatory diseases and rheumatoid arthritis.[1] The pharmacological activity of NSAIDs is related to the suppression of prostaglandin biosynthesis from arachidonic acid by inhibiting the enzyme Cyclooxygenases (COXs) and tromboxane synthase with a varying degree of selectivity.[2] It is well known that COX exists in two isoforms, COX-1 and COX-2, which are regulated differently. COX-1 provides cytoprotection in the gastrointestinal (GI) tract whereas inducible COX-2 mediates inflammation.[3] COX-2 is an attractive target for medicinal chemists as it is expressed only in few normal tissues and is greatly upregulated in inflamed tissues as well as many premalignant and malignant tumors. Since, most of the NSAIDs in the market show greater selectivity for COX-1 than COX-2 [4] chronic use of NSAIDs, including Diclofenac may elicit appreciable gastro-intestinal (GI) irritation, bleeding and ulceration.[5] The GI damage from NSAIDs is generally attributed to two factors, local irritation by the carboxylic acid moiety, common to most NSAIDs and (topical effect) decreased tissue prostaglandin production, which undermines the physiological role of cytoprotective prostaglandins in maintaining the GI health and homeostasis.[6] Inflammation is known not only as a symptom of great deal of common diseases but also as an early phase of some serious diseases such as cancer, cardiac vascular diseases and Alzheimer's dementia. Therefore, the challenge still exists for the pharmaceutical industry to develop, effective anti-inflammatory agents with enhanced safety profile. It has been reported in literature that certain compounds bearing oxadiazole nucleus possess significant anti-inflammatory activity with reduced ulcerogenic effect.[7-9]

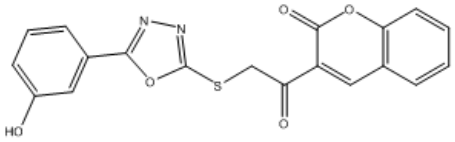
Mahesh B Palker, Anuj Singhai et al., reported synthesis, pharmacological screening and in silico studies of new class of diclofenac analogues as a promising anti-inflammatory agents. Among the series different compounds exhibited good anti inflammatory activity and less side effect as compared to diclofenac.[10]



Bhandari SV et al., synthesized novel 3-substituted phenacyl-1,3,4-oxadiazol-2-thiol and schiff bases of diclofenac as nonulcerogenic derivatives and evaluated them for anti-inflammatory, analgesic and ulcerogenic activity in the carrageenin induced rat paw edema model. Among the series diffrent compounds exhibited very significant anti-inflammatory activity.[11]

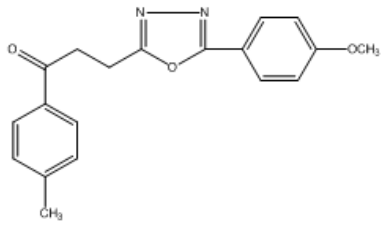


Ingale N et al., reported synthesis and evaluation of anti-inflammatory and analgesic activity of 3-[(5substituted-1,3,4-oxadiazole-2yl-thio)acetyl]-2H-chromen-2-ones. Among the series some compounds was shown good anti inflammatory activity by carrageenan induced rat paw edema method.[12]

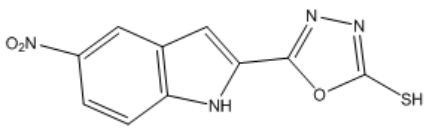


Mohammad A et al., reported the synthesis of 1,3,4-oxadiazole derivatives of aryl acetic acid and screened for their anti inflammatory and analgesic activities. Among the series following compound exhibited good anti inflammatory activity in carrageenan induced rat paw edema method.[13]

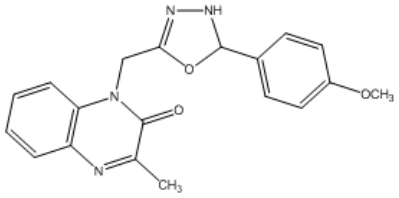
Akhter M et al., reported the synthesis of 2,5-disubstituted-1,3,4 oxadiazoles from aroylpropionic acid and screened for their anti-inflammatory and analgesic activities. Among the series following compound exhibited good anti inflammatory activity in carrageenan induced rat paw edema method.[14]



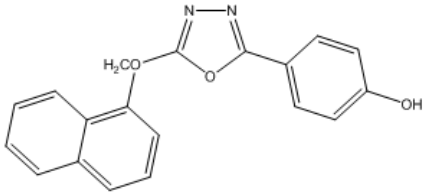
Narayana B et al., reported synthesis of heterocycles derived from substituted indole-2-carbohydrazides and screened for their anti inflammatory activity. Among the series following compound exhibited good anti inflammatory activity in carrageenan induced rat paw edema method.[15]



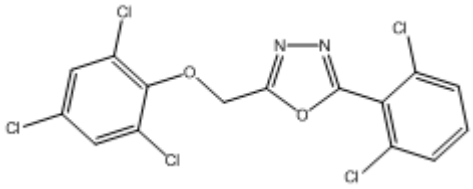
Wagle S et at., reported synthesis of some new 2-(3-methyl-7-substituted-2-oxoquinoxalinyl)-5-(aryl)-1,3,4-oxadiazole as potential non-steroidal anti-inflammatory and analgesic agent. Among the series following compound exhibited good anti inflammatory and analgesic activity in carrageenan induced rat paw edema method and hot plate method respectively.[16]



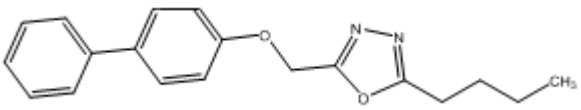
Rajak H et al., reported synthesis of some novel oxadiazole and oxadiazoline analogues for their anti-inflammatory activity. Among the series following compound exhibited good anti inflammatory activity in carrageenan induced rat paw edema method.[17]



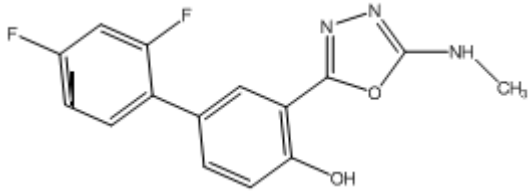
Mohd A et al., reported synthesis of some 1,3,4-oxadiazole derivatives as potential anti-inflammatory agent. Among the series following compound exhibited good anti inflammatory activity in carrageenan induced rat paw edema method.[18]



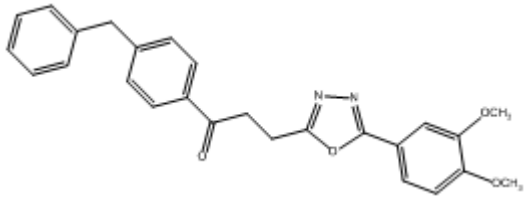
Kumar H et al., reported synthesis of 1,3,4-oxadiazole derivatives and screened for their anti-inflammatory and analgesic activities. Among the series following compound exhibited good anti inflammatory activity in carrageenan induced rat paw edema method.[19]



Kucukguzel SG et al., reported synthesis of some novel heterocyclic compounds derived from diflunisal hydrazide as potential anti-infective and anti-inflammatory agents. Among the series following compound exhibited good anti inflammatory activity.[20]

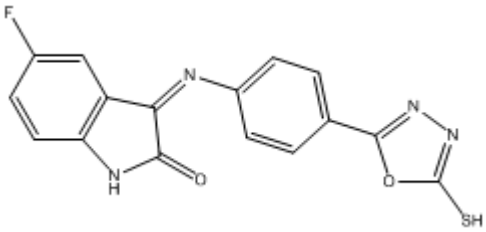


Husain A et al., reported synthesis and biological evaluation of β- aroyl propionic acid based 1,3,4-oxadiazoles and tested for anti-inflammatory, analgesic, lipid peroxadation, ulcerogenic and antibacterial activity. The compound has shown very good anti-inflammatory activity.[21]

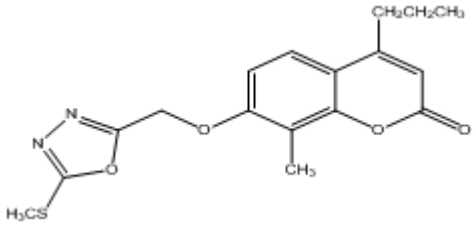


ANTICANCER ACTIVITY

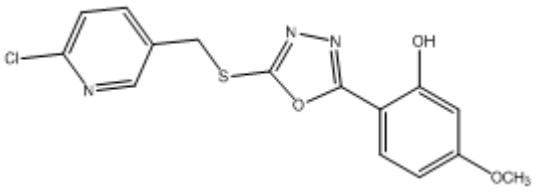
Gudipati R et al., reported synthesis, characterization and anticancer activity of certain 3{4-(-mercapto-1,3,4-oxadiazole-2-yl)phenylimino}indolin-2-one derivatives. The anticancer activity of all the synthesized compounds was evaluated against HeLa, IMR-32, MCF-7 cancer cell lines using MTT method. Among the series following compound showed good anticancer activity.[22]



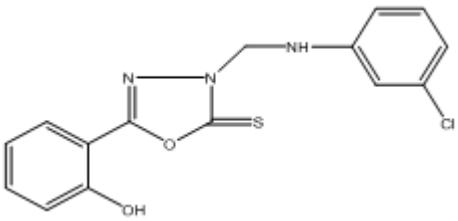
Magda MF et al., reported synthesis and docking studies of novel benzopyran-2-ones as promising anticancer agents. Among the series following compound exhibited good anticancer activity.[23]



Zheng QZ et al., reported synthesis, biological evaluation and molecular docking studies of 2-chloropyridine derivatives possessing 1,3,4-oxadiazole moiety as potential antitumor agents. All the synthesized derivatives were evaluated for their ability to antiproliferative activity against gastric cell SGC-7901 and showed good antiproliferative activity. Among the series following compound showed good antiproliferative activity.[24]



Aboraia AS et al., reported novel 5-(2-hydroxyphenyl)-3-substituted-2,3-dihydro-1,3,4 oxadiazole-2-thione derivatives as promising anticancer agents. Among the series following compound exhibited good anticancer activity.[25]

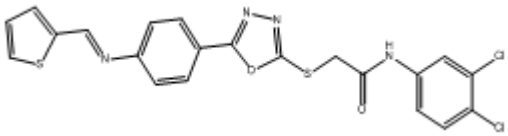


ANTIMICROBIAL ACTIVITY

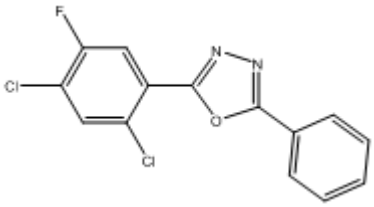
Infectious diseases are remaining a serious threat to public health, rapid resistance development by the microorganisms is recognized from the beginning. The resistance development among major pathogens makes antimicrobials more and more ineffective. The resistance is developed by bacteria due to bacterial enzymes, transfer of genetic material, acquired resistance and poor prescribing and utilization of antimicrobial in practice [26,27]. The incidence of multidrug-resistant pathogenic bacteria is increasing. One additional reason for developing new antibiotics is related to their own toxicity. As with other therapeutic agents, the use of antibiotics may also cause side effects in patients. These include mild reactions such as upset stomach, vomiting, and diarrhoea (cephalosporins, macrolides, penicillins and tetracyclines), rash, other mild and severe allergic reactions (cephalosporins and penicillins), sensitivity to sunlight (tetracyclines), nervousness, tremors and seizures (quinolones). Some side effects are more severe and depending on the antibiotic, may disrupt the hearing function (aminoglycosides), kidneys (aminoglycosides and polypeptides) or liver (rifampin). To counteract the resistance produced by microbes there is a need to invent new drugs, which are more safe and effective [28-29]. A large number of medicines which have been discovered belong to a major class of heterocycles containing nitrogen, oxygen and sulphur. Biological activities of these hetrocycles has helped the medicinal chemist to plan, organize and implement newer approaches towards the discovery of new drugs.[30-31]

Desai NC et at reported synthesis and antimicrobial screening of 1,3,4-oxadiazole and clubbed thiophene derivatives. All the synthesized compounds were

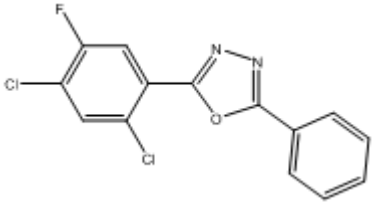
evaluated for antibacterial and antifungal activities. Among the synthesized compounds, the following compound showed good antibacterial and antifungal activity.[32]



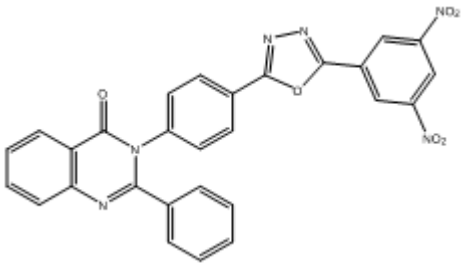
Jha KK et al., reported synthesis and biological evaluation of 1,3,4-oxadiazoles. The newly synthesized compounds were screened for their antibacterial activity against Escherichia coli (MTCC 443), Staphylococcus epidermidis (ATCC12228) and Staphylococcus aureus (ATCC25923) bacterial strains by disc diffusion method. Among the synthesized compounds, the following compound showed good antibacterial activity.[33]



Sah P et al., reported synthesis and in vitro biological evaluation of some quinazolin substituted pyrazoles, pyrazolones and 1,3,4-oxadiazoles. The antibacterial activity of compounds was evaluated by disc diffusion method. Among the synthesized compounds, the following compound showed good antibacterial activity.[34]

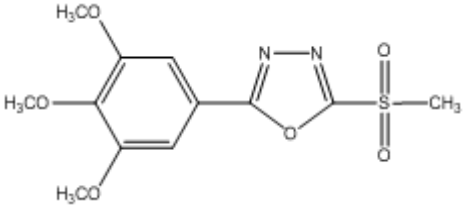


Salimon J et al., reported synthesis and pharmacological evaluation of 9(10H)-acridone bearing 1,3,4-oxadiazole derivatives as antimicrobial agent.

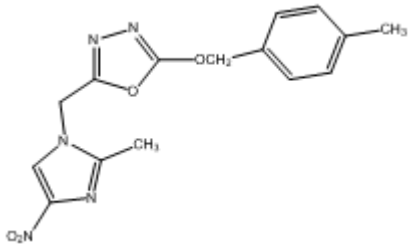


All the newly synthesized compounds were evaluated for their in vitro antibacterial activity against Staphylococcus aureus, Streptcoccus viridans and Escherichia coli. by disc diffusion method. Among the synthesized compounds, the following compound has shown good antibacterial activity.[35]

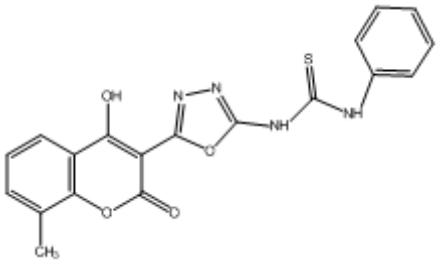
Cai-Jun Chen et al., reported synthesis and antifungal activity of 1,3,4-oxadiazole derivatives. All the newly synthesized compounds were evaluated for their *in vitro* antifungal activity. Among the series following compound exhibited good antifungal activity.[36]



Frank PV et al., reported solvent-free microwave-assisted synthesis of oxadiazole containing imidazole moiety. All the synthesized compounds were evaluated for antibacterial and antifungal activities. Among the synthesized compounds, the following compound showed good antibacterial and antifungal activity.[37]

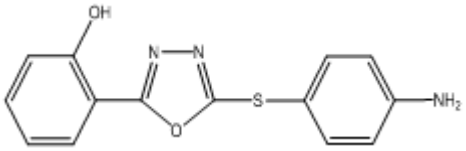


Mulwad VV et al., reported synthesis and antibacterial activity of 2,5 disubstituted-1,3,4-oxadiazole derivatives. All the newly synthesized compounds were evaluated for their *in vitro* antibacterial activity. Among the synthesized compounds, the following compound showed good antibacterial and antifungal activity.[38]

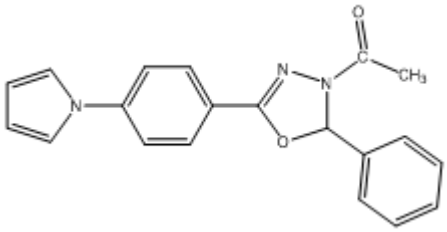


ANTITUBERCULAR ACTIVITY

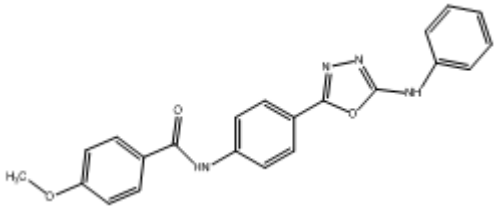
Pattan SR et al., reported synthesis and evaluation of some novel substituted 1,3,4-oxadiazole and pyrazole derivatives for antitubercular activity. Among the series compound exhibited good antitubercular activity by middle brook 7H9 agar medium against $H_{37}Rv$ strain.[39]



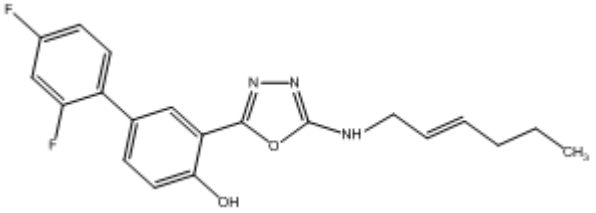
Joshi SD et al., reported synthesis of some new 1,3,4-oxadiazole derivatives and screened them for their antitubercular activity. Among the series following compound showed good antitubercular activity.[40]



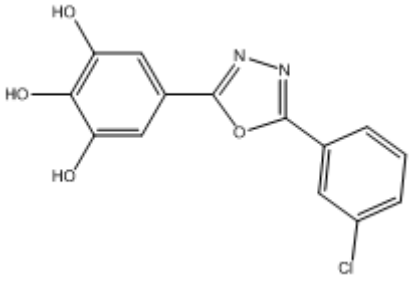
Kucukguzel SG et al., reported synthesis, characterization and biological activity of novel 4-thiazolidinones, 1,3,4-oxadiazoles and some related compounds. The synthesized compounds were screened for antitubercular activity. Among the series following compound showed good antitubercular activity.[41]



Kucukguzel G et al., reported synthesis and biological activity of 4-thiazolidinones, thiosemicarbazides derived from diflunisal hydrazide. These compounds screened for anti-TB activity against *Mycobacterium tuberculosis* H37Rv. The following compound showed good antitubercular activity.[42]

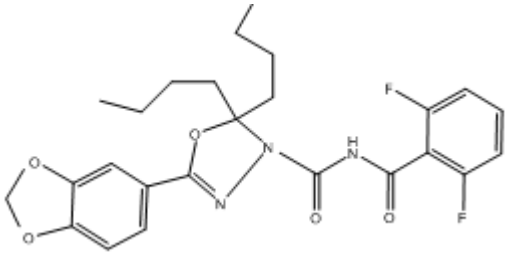


Arunkumar S et al., reported synthesis characterization and biological evaluation of some novel 2,5 disubstituted-1,3,4-oxadiazole derivatives of gallic acid. All synthesized compounds were subjected to antimicrobial, anti-fungal and anti-tubercular activity. The antitubercular activity was observed at concentrations 100µg/ml on Mycobacterium tuberculosis. Among the synthesized compounds the following compound showed good antitubercular activity.[43]

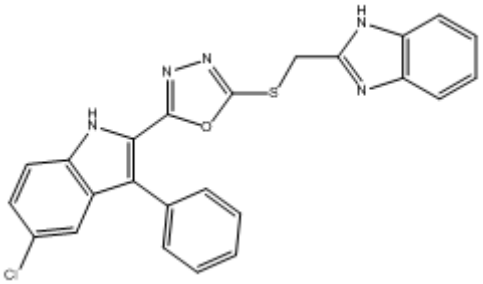


MISCELLANEOUS ACTIVITIES

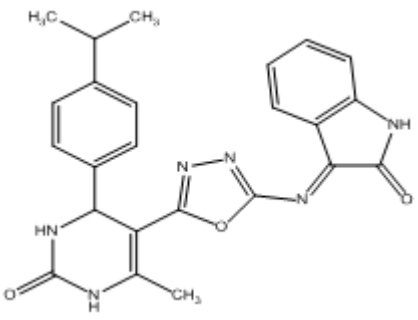
Shaoyong K et al., reported synthesis of 1,3,4-oxadiazole derivative. The newly synthesized compounds were evaluated for their MAO inhibitory activity by kynuramine fluorimetric assay method. The following compound was most potent of the series.[44]



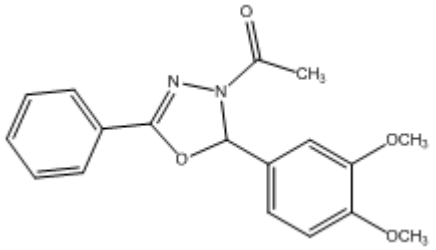
Manjunath SY et al., reported synthesis and anthelmintic activity of trihetrocycles:[5-(5"substituted-3"-phenylidol-2"yl)-1,3,4-oxadiazol-2'-yl thiomethyl] benzimidazoles. Among the series following compound showed good anthelminitic activity.[45]



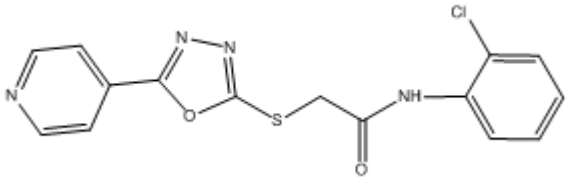
Georeg S et al., reported synthesis and biological evaluation of some 1,3,4-oxadiazole derivatives. Among the series following compound showed the good free radical scavenging activity.[46]



Aanandhi MV et al., reported synthesis and In-vitro antioxidant activity of substituted-1,3,4-oxadiazole derivatives. Among the synthesized compounds the following compound showed good antioxidant activity.[47]



Rajasekaran S et al., reported microwave assisted synthesis of some 5-pyridyl-2-[(N-substitutedphenyl) thioacetamido]-1,3,4-oxadiazoles as antibacterial and antioxidant agents. Among the synthesized compounds the following compound showed good antioxidant activity.[48]



CONCLUSION

Abovementioned research work confirms the potential of oxadiazole as lead for development of novel and better compounds possessing excellent biological activities. Oxadiazole moiety and its various derivatives studied frequently in the past time and found potent in various pharmacological and Biological conditions. This article mainly focused on the various derivatives of oxadiazole showed different important pharmacological activities.

ACKNOWLEDGEMENT

I express my humble thanks to Dr S. P. Chaturvedi and Dr S. Bindaiya for their co-operation and guidance in searching various articles and journals for completing this review. I would like to express my sincere regards to my wife Palak and entire family.

REFERENCES

1. Praveen M, Tanya M, Textbook of Pathology, Jaypee Brothers Medical publishers New Delhi, 4th edition, 2000.
2. Husain A, Ahmad A, Alam MM, Ajmal M, Ahuja P, Fenbufen based 3-[5-(substituted aryl)-1,3,4-oxadiazol-2-yl]-1-(biphenyl-4-yl)propan-1-ones as safer antiinflammatory and analgesic agents, Eur J Med Chem.,44, 3798-804, 2009.
3. Sujith KV, Rao JN, Shetty P, Kalluraya B., Regioselective reaction: synthesis and pharmacological study of mannich bases containing ibuprofen moiety, Eur J Med Chem., 44, 3697-702, 2009.
4. Kujubu DA, Fletcher BS, Varnum BC, Lim RW, Herschman HR, TIS10, a phorbol ester tumor promoter-inducible mRNA from swiss 3T3 cells, encodes a novel prostaglandin synthase/cyclooxygenase homologue, J Biol Chem., 266, 12866-72, 1991.
5. Marnett LJ, Cyclooxygenase mechanisms, Curr Opin Chem Biol, 4, 545-52, 2004.
6. Talley JJ, Bertenshaw SR, Brown DL, Carter JS, Graneto MJ, Kellogg MS, et al., N-[[(5-methyl-3-phenylisoxazol-4-yl)- phenyl]sulfonyl]propanamide, sodium salt, parecoxib sodium: A potent and selective inhibitor of COX-2 for parenteral administration, J Med Chem, 43, 1661-3, 2000.
7. Prakash O, Kumar M, Kumar R, Sharma C, Aneja KR., Hypervalent iodine(III) mediated synthesis of novel unsymmetrical 2,5-disubstituted 1,3,4-oxadiazoles as antibacterial and antifungal agents, Eur J Med Chem, 45, 4252-7, 2010.
8. Fuloria NK, Singh V, Mohammad S, Mohammad A., Synthesis and antimicrobial evaluation of some new oxadiazoles derived from phenylpropionohydrazides, Molecules, 14, 1898-903, 2009.
9. Desai NC, Bhavsar AM, Shah MD, Saxena AK, Synthesis and QSAR studies of thiosemicarbazides, 1,2,4-triazoles, 1,3,4-thiadiazoles and 1,3,4-oxadiazoles derivatives as potential antibacterial agents, Ind J Chem, 47B, 579-89, 2008.
10. Palkar M B, Singhai A, Synthesis, pharmacological screening and in silico studies of new class of Diclofenac analogues as a promising anti-inflammatory agents, Bioorg Med Chem, 22, 2855-66, 2014.
11. Bhandari SV, Bothara KG, Raut MK, Patil AA, Sarkate AP, Mokale VJ., Design, synthesis and evaluation of anti inflammatory, analgesic and ulcerogenicity studies of novel S-substituted phenacyl-1,3,4-oxadiazole-2-thiol and schiff bases of diclofenac acid as nonulcerogenic derivatives, Bioorg Med Chem,16, 1822-31, 2008.
12. Ingale N, Maddi V, Palkar M, Ronad P, Mamledesai S, Vishwanathswamy AHM, et al. Synthesis and evaluation of anti-inflammatory and analgesic activity of 3-[(5 substituted-1,3,4-oxadiazol-2-yl-thio)acetyl]-2H-chromen-2-ones, Med Chem Res., 21, 16-26, 2012.
13. Mohammad A, Saifullah K, Akhter W, Design, synthesis and pharmacological evaluation of 1,3,4-oxadiazole derivative of aryl acetic acid as anti-inflammatory and analgesic agent, Ind J Chem, 50B, 1107-11, 2011.
14. Akhter M, Husain A, Azad B, Ajmal M, Aroylpropionic acid based 2,5-disubstituted-1,3,4-oxadiazoles: synthesis and their anti-inflammatory and analgesic activities, Eur J Med Chem, 44, 2372-8,2009.

15. Narayana B, Ashalatha BV, Vijaya Raj KK, Sarojini BK, Synthesis and studies on antimicrobial, antiinflammatory and antiproliferative activities of heterocycles derived from 4-/5-/6-/7-nitro/5-fluoro/chloro/bromoindole-2-carbohydrazides, Ind J Chem, 48B, 1794-805, 2009.
16. Wagle S, Adhikari AV, Kumari NS, Synthesis of some new 2-(3-methyl-7-substituted-2-oxoquinoxalinyl)-5-(aryl)-1,3,4-oxadiazole as potential non-steroidal anti-inflammatory and analgesic agent, Ind J Chem, 47B, 437-48, 2008.
17. Rajak H, Kharya MD, Mishra P, Synthesis of some novel oxadiazole and oxadiazoline analogues for their anti-infammatory activity, Yakugaku Zasshi, 127(10), 1757-64, 2007.
18. Mohd A, Javed SA, Kumar H, Synthesis of 1, 3, 4-oxadiazole derivatives as potential anti-inflammatory agent, Ind J Chem, 46B, 1014-9, 2007.
19. Kumar H, Sadique AJ, Khan SA, Mohammad A, 1,3,4-Oxadiazole/thiadiazole and 1,2,4-triazole derivatives of biphenyl-4-yloxy acetic acid: Synthesis and preliminary evaluation of biological properties, Eur J Med Chem, 43, 2688-98, 2008.
20. Kucukguzel SG, Kucukguzel I, Tatar E, Rollas S, Sanin F, Gulluce M, Clercq ED, Kabasakal L, Synthesis of some novel heterocyclic compounds derived from diflunisal hyrazide as potential anti-infective and anti-inflammatory agents, Eur J Med Chem, 42, 893-901, 2007.
21. Husain A, Ahuja P, Sarafroz, Synthesis and biological evaluation of β- aroylpropionic acid based 1,3,4-Oxadiazoles, Ind J Pharm Sci, 7, 62-3, 2009.
22. Gudipati R, Reddy RM, Manda S, Synthesis, characterization and anticancer activity of certain 3-{4-(5-mercapto-1,3,4-oxadiazole-2-yl)phenylimino}indolin-2-one derivatives, Saudi Pharm J, 19, 153-8, 2011.
23. Magda MF, Heba SR, Hussein MM, Synthesis and docking studies of novel benzopyran-2-ones with anticancer activity, Eur J Med Chem, 45, 3950-9, 2010.
24. Zheng QZ, Zhang X, Ying Xu, Kui Cheng, Qing-Cai J, Hai-Liang Z, Synthesis, biological evaluation, and molecular docking studies of 2-chloropyridine derivatives possessing 1,3,4-oxadiazole moiety as potential antitumor agents, Bioorg Med Chem, 18, 7836-41, 2010.
25. Aboraia AS, Abdel-Rahman HM, Mahfouz NM, EL-Gendy MA, Novel 5-(2-hydroxyphenyl)-3-substituted-2,3-dihydro-1,3,4-oxadiazole-2-thione derivatives: promising anticancer agents, Bioorg Med Chem, 14, 1236–46, 2006.
26. Tripathi, K.D., Essentials of Medical Pharmacology, Jaypee Brothers Medical Publishers Ltd., 6th ed., 739-741, 2006.
27. Tomas LL, David AW, Foye's Principles of Medicinal Chemistry, Wolterskluwer Pvt. Ltd., 6th ed.,1139-1140, 2012.
28. Burmudez, L.E, Interlied C.B, Young L.S, Curr C, In Topics Infect Dis, 12, 257, 1992.
29. Siddiqui N, Ahuja P, Ahsan W, Pandeya S.N, Alam M.S, Progress report on Biological Activities, J. Che Phar Res,1, 19-30, 2009.
30. Sharma, S.D, Bandari S, Synthesis of 2-azetidinones and their heterocycles from N-(3-hydroxy propyl)imines, Indian J Hetero Chem, 11, 221-24, 2012.
31. Martin, Y.C, Drug research: path to better and safer drugs, 2008.
32. Desai NC, Dodiya AM, Rajpara KM, Rupala YM, Synthesis and antimicrobial screening of 1,3,4-oxadiazole and clubbed thiophene derivatives, J Saudi Chem Soci, 4, 1020-29, 2011.
33. Jha KK, Samad A, Kumar Y, Shaharyar M, Khosa RL, Jain J, et al., Design, synthesis and biological evaluation of 1,3,4-oxadiazole derivatives, Eur J Med Chem, 45, 4963-7, 2010.
34. Sah P, Kaul V, synthesis and in-vitro biological evaluation of some quinazolin substituted pyrazoles, pyrazolones and 1, 3, 4-oxadiazole, Ind J Chem, 49B, 1406-12, 2010.
35. Salimon J, Salih N, Emad Y, Ayad H, Ayad K, Synthesis and pharmacological evaluation of 9(10H)-acridone bearing 1,3,4-oxadiazole derivatives as antimicrobial agents, Arab J Chem, 3, 205-10, 2010.
36. Cai-Jun Chen, Bao-An Song, Song Yang, Guang-Fang Xu, Pinaki S. Bhadury, Lin-Hong Jin, et al., Synthesis and antifungal activities of 5-(3,4,5-trimethoxyphenyl)-2-sulfonyl-1,3,4-thiadiazole and 5- (3,4,5 trimethoxyphenyl)-2-sulfonyl-1,3,4-oxadiazole derivatives, Bioorg Med Chem, 15, 3981–9, 2007.
37. Frank PV, Girish KS, Kalluraya B, Solvent-free microwave-assisted synthesis of oxadiazole containing imidazole moiety, J Chem Sci,119, 41-6, 2007
38. Mulwad VV, Chaskar AC, Synthesis and antibacterial activity of oxadiazolo 1, 3, 4-triazine, 1, 2, 4-triazolo and thiadiazolo 1, 3, 4-oxadiazole derivatives, Ind J Chem, 45B, 1710-15, 2006.
39. Pattan SR, Bukitagar PA, Wakale VS and Musmade DS, Synthesis and evaluation of some novel substituted 1, 3, 4-oxadiazole and pyrazole derivatives for tuberculosis activity, Ind J Chem, 48B, 1453-6, 2009.
40. Joshi SD, Vagdevi HM, Vaidya VP, Gadaginamath GS, Synthesis of 4-pyrrol-1-yl benzoic acid hydrazide analogs and some derived oxadiazole, triazole and pyrrole ring systems: A novel class of potential antibacterial and antitubercular agents, Eur J Med Chem, 43, 1989-6, 2009.
41. Kucukguzel SG, Oruc EE, Rollas S, Sahin F, Ozbek A, Synthesis, characterization and biological activity of novel 4-thiazolidinones, 1,3,4-oxadiazoles and some related compounds, Eur J Med Chem, 37, 197-206, 2002.

42. Kucukguzel G, Kocatepe A, Clercq ED, F Sahin, M Gulluce, Synthesis and biological activity of 4-thiazolidinones, thiosemicarbazides derived from diflunisal hyrazide. Eur J Med Chem, 41, 353-9, 2006.
43. Arunkumar S, Kiang K, Manikandan RS, Sudha M, Ramalakshmi N, Synthesis and characterization and biological evaluation of some novel 2,5-disubstituted-1,3,4-oxadiazole derivatives of gallic acid. Int J Chem Tech Res,1, 1094-9, 2009.
44. Shaoyong K, Zhong L, Xuhong Q, 1,3,4-Oxadiazole-3(2H)-carboxamide derivatives as potential novel class of monoamine oxidase (MAO) inhibitors: synthesis, evaluation, and role of urea moiety. Bioorg Med Chem, 16, 7565-72, 2008.
45. Manjunath SY, Biradar R, Basawaraj, Synthesis and anthelminitic activity of triheterocycles: [5(5-substituted-3-phenylindol-2-yl)1,3,4-oxadiazole-2-yl thiomethyl] benzimidazols. Ind J Het Chem, 18, 321-4, 2009.
46. Georeg S, Parameswaran MK, Chakaraborty AR, Ravi TK, Synthesis and evaluation of biological activities of some 3-{[5-(6-methyl-4-aryl-2-oxo-1,2,3,4-tetrahydropyrinidin-3yl)-1,3,4-oxadiazole-2-yl-imino}-1,3-dihydro-2H-indo]-2-one derivatives. Acta Pharm, 58, 119-29, 2008.
47. Aanandhi MV, Mohammed HM, Shanmugapriya S, George S, Synthesis and In- vitro antioxidant activity of substituted pyridinyl 1, 3, 4-oxadiazole derivatives, Res J Pharm Bio Chem Sci, 1(4), 1083-90, 2010.
48. Rajasekaran S, Rao GP, Pai S P, Vedavathy J, Microwave assisted synthesis of some 5-pyridyl-2-[(N-substituted phenyl) thioacetamido]-1,3,4-oxadiazoles as antibacterial and antioxidant agents, J Chem Pharm Res, 2(2), 101-6, 2010.