Procedia of Theoretical and Applied Sciences
Volume 15 | Jan 2024
ISSN: 2795-5621 Available: http://procedia.online/index.php/applied/index

CONDUCTING A LITERATURE ANALYSIS OF ANTIBACTERIAL PROPERTIES OF OXADIAZOLE DERIVATIVES

Nargiza Rustamzhanovna Rakhimova, Valizhon O'rinovich Masharipov, Ra'no Shokhtursinovna Boltaeva
Tashkent Medical Academy, Department of Microbiology, Virology and Immunology

Annotation: Scientists are compelled by the global rise in antibiotic resistance to look for novel substances that microorganisms would be susceptible to. The 1,3,4-oxadiazole ring is present in many novel structures and has been shown to have a variety of antimicrobial properties, including antiviral, antibacterial, antitubercular, and antifungal properties. The potential of these new compounds as novel drugs is very promising, as evidenced by numerous publications showing that their activity outperforms that of known antibiotics and other antimicrobial agents. The literature from 2015 to 2021 is the basis for the review of 1,3,4-oxadiazole derivatives with active antimicrobial properties. Different research groups are constantly creating novel drug molecules against both exploited and unexplored targets due to the emergence of drug-resistant microbial strains. Derivatives of 1,3,4-Oxadiazole demonstrated notable antimicrobial activity. Antimicrobial agents that contain the 1,3,4-oxadiazole moiety can change their polarity and flexibility, which greatly enhances biological activities because of a variety of bonded and non-bonded interactions with target sites, including hydrophobic, steric, electrostatic, and hydrogen bond interactions. The current review explains the mode of action and therapeutic targets of 1,3,4-oxadiazoles in relation to microbes. 1,3,4-oxadiazole derivatives target the following enzymes: enoyl reductase (InhA), 14α-demethylase in mycobacterial cells; GlcN-6-P synthase, thymidylate synthase, peptide deformylase, RNA polymerase, dehydrosqualene synthase in bacterial strains; protein-N-myristoyltransferase, P450-14α demethylase, and ergosterol biosynthesis pathway in fungal strains; FtsZ protein, interfere with purine and functional protein synthesis in plant bacteria. The impact of various moieties and functional groups on the antimicrobial activity of 1,3,4-oxadiazole derivatives is also summarized in the current review.

***Keywords*:** 1,3,4-oxadiazole; antiviral, antimicrobial, antibacterial, antifungal, and antiprotozoal properties.

Introduction. In tropical nations, infectious diseases account for almost half of all fatalities. While the number of deaths resulting from bacterial and fungal infections has decreased in wealthy nations, these illnesses continue to pose a serious threat in developing nations [1]. Scientists are compelled by the global rise in antibiotic resistance to look for novel substances that microorganisms would be susceptible to. Antimicrobial resistance (AMR) is a primary issue in contemporary medicine. Certain germs are no longer suscepti ble to the majority of medications now in use because of inadequate infection treatment, excessive antibiotic prescriptions, and improper administration by patients. As a result, treating infections becomes increasingly challenging as the antibiotics and other antimicrobial medications that have been utilized up to this point are no longer effective [2,3,4]. AMR poses a progressively greater risk to public health and life. The expense of treating patients with drug-resistant illnesses rises in the absence of efficient antibiotic therapy, and surgical and other medical operations carry a significant risk. AMR is the result of microbes learning to withstand medications meant to destroy them. A wide range of microbial defense techniques exist [5,6]. The oxadiazole structure is one of the appealing backbones for scientists producing new therapeutic medicines. This five-

Procedia of Theoretical and Applied Sciences
Volume 15 | Jan 2024
ISSN: 2795-5621 Available: http://procedia.online/index.php/applied/index

membered heterocycle has four known isomers: 1,2,4-, 1,2,3-, 1,2,5-, and 1,3,4-oxadiazole. That being said, 1,3,4-oxadiazole's amazing biological activities make it more significant. The pharmacological actions of compounds possessing the 1,3,4-oxadiazole structure range from antibacterial to antifungal, anti-tubercular, anticonvulsant, anti-allergic, anti-inflammatory, cytotoxic, and insecticidal. For carboxylic acids, esters, and carboxyamides, this structure can be employed as a bioisoester [7-11]. The oxadiazole derivatives tiodazosin, nosapidil, and furamizole have been approved as antihypertensive and bactericidal medications, respectively. It has been demonstrated that a variety of 2,5 substituted 1,3,4-oxadiazoles are effective against a broad spectrum of gram-positive and gram-negative bacteria [12-16]. These characteristics of the 1,3,4-oxadiazole ring have led to a multitude of pharmacological uses for this molecule. The literature claims that for a long time, researchers all over the world have been creating novel compounds with the 1,3,4-oxadiazole core, which has a variety of biological activities, such as analgesic, anti-inflammatory, antidepressant, anticancer, and anti-diabetic effects. Furthermore, a large body of research has confirmed the wide-ranging antimicrobial activity of substances with the 1,3,4-oxadiazole ring in their structure. Research on compounds with a 1,3,4-oxadiazole scaffold that have antibacterial, antifungal, or antiviral properties has been done [7-21]. Owing to the broad antimicrobial activity of 1,3,4-oxadiazole derivatives, we wish to highlight the scientific accomplishments of the previous seven years in this review. The PubMed database was searched for relevant literature using the following keywords: "1,3,4-oxadiazole," "antibacterial," "antitubercular," "antifungal," "antiprotozoal," "antiviral," and "activity." The review is based on articles published between 2015 and 2021. Where possible, a division based on chemical structure was also used; otherwise, structures were categorized based on specific antimicrobial activities [22-25].

The main purpose of the study is to conduct a brief analysis of the literature on the antimicrobial activity of heterocyclic compounds with high activity.

The antibacterial properties of derivatives of 1,3,4-Oxadiazole. Scientists are now using known quinolone antibacterial medications as a foundation to change their structural makeup. Nalidixic acid was a pharmacophore moiety for structure modification according to Peraman et al. (2015). A thiosemicarbazide/acid carbarbazide chain or a thioxo-1,2,4-triazole/1,3,4-oxadiazole coupled with quinoxaline was used to substitute the carboxylic group. Compared to the reference medications (ciprofloxacin and amoxicillin), the compound containing 1,3,4-oxadiazole (1, Figure 2) demonstrated greater or comparable activity against Pseudomonas aeruginosa and Staphylococcus aureus. Furthermore, the novel derivatives exhibited antitubercular properties [26-29].

It is evident from examining the data above that quinolone antibacterial medication modifications occur in two ways. The 1,3,4-oxadiazole ring functions as a bioisosteric structure in place of the carboxylic moiety in nalidixic acid. The 1,3,4-oxadiazole molecule is introduced at the piperazine substituent in the case of fluoroquinolones (norflaxacin/ciprofloxacin), preceded by a methylene linker. The activity of the derivatives is frequently increased by halogen or methyl substituents on the aromatic ring [30–33].

The antibacterial properties of 1,3,4-Oxadiazole's aryl/heteroaryl derivatives. Antibacterial compounds are also searched for in 1,3,4-oxadiazole derivatives that are heteroaromatic or aromatic. We can identify aryl derivatives, aryl and/or heteroaryl structures, and derivatives with an aryl and/or heteroaryl bi- or tricyclic ring by dividing the new compounds based on the direct surrounding of the 1,3,4-oxadiazole ring [34, 35, 36]. Structures with a 1,3,4-oxadiazole ring that have an aryl substituent directly on top of the heterocycle exhibit antimicrobial activity.

A number of benzothiazepine and benzodiazepine derivatives of aryl-1,3,4-oxadiazole were created in 2016 by Navin et al., and their broad antimicrobial activity was evaluated. In comparison to the reference medication ampicillin, the most active derivatives, represented as a general structure 6 in

Procedia of Theoretical and Applied Sciences
Volume 15 | Jan 2024
ISSN: 2795-5621 Available: http://procedia.online/index.php/applied/index

Figure 4, proved to be more effective against strains of P. aeruginosa and S. aureus. Furthermore, the produced compounds' antitubecular and antiprotozoal properties were shown [37–40].

1,3,4-Oxadiazole's Amino Derivatives' Antibacterial Activity. Amino derivatives were among the numerous 1,3,4-oxadiazole derivatives that exhibited antibacterial activity. Many 2-amino-1,3,4-oxadiazole derivatives with quinoline rings in their structures were obtained by Ladani et al. (2015). A thorough assessment of the novel compounds' antimicrobial activity was conducted. In comparison to ampicillin, the strongest derivative 20, which also possessed a pyridine moiety, had a strong to moderate effect on strains of C. tetani, B. subtilis, S. typhi, and E. coli. Furthermore, it exhibited good to excellent antimalarial and tubeculostatic activity [41–44].

In conclusion, there are a number of conclusions that can be drawn about the structure-activity relationship. It is evident from the amino derivatives of 1,3,4-oxadiazole that the addition of a second heterocyclic ring can increase the antimicrobial activity's range. The structures with 10–12 carbon atoms in the chain exhibit the highest activity when it comes to N-alkyl derivatives. Amidine structures, as opposed to amide or imine groups, exhibited the best activity in the symmetrically substituted 2,5-diamino-1,3,4-oxadiazole derivatives. The enhanced anti-MRSA potency in the 5-(4-methyl-thiazol-5-yl)-1,3,4-oxadiazole-2-amine derivatives was caused by the hydrazine or guanidine moiety's increased polarity of the nitrogenous group [45-48].

Discussion. Novel derivatives of oxadiazole and triazole were synthesized. The targeted compounds' antioxidant and antimicrobial qualities were assessed. Compound 7b demonstrated half the antimicrobial activity of the common medication chloramphenicol against B. subtilis, while all compounds demonstrated weak antibacterial and antifungal activity. With IC50 values of 2.75 and 2.67 mg/mL, compounds 4a and 7a demonstrated exceptional antioxidant capabilities, while ascorbic acid had an IC50 value of 0.49 mg/mL. The pharmacokinetic. It is simpler and more convenient to prepare oxadiazole derivatives from N, N-diacylhydrazine intermediate in two steps as opposed to directly preparing them from carboxylic acids and acylhydrazides in one step [49-53]. A straightforward, one-step process under mild conditions was employed to create the derivative of furan-oxadiazole. N-acylhydrazone was produced in high yields by a condensation reaction involving 2-hydroxy-2-phenyl-acetohydrazide and 5-nitro-2-furaldehyde in 95% ethanol, with glacial acetic acid serving as the catalyst. Compound nitro-furan-oxadiazole is readily produced by reacting moderately yielding amounts of N-acylhydrazone with acetic anhydride. The antimicrobial results indicated that oxadiazole furan derivatives had possible antibacterial properties and that oxadiazole para-substituted phenyl derivatives had strong antifungal properties [54,55,56].

In conclusion, an easy, practical, and effective synthetic route was used to design and synthesize a series of azole derivatives based on 1,4-benzodioxane for the first time. Azole combined with 1,4-benzodioxane is a promising template for antibacterial and antifungal activities, according to the antimicrobial results [57,58,59].

The 1,3,4-oxadiazole derivatives reviewed have a high potential for antimicrobial activity. The new structures are active against a broad range of microorganisms, including viruses, bacteria, and fungi. Some of the new compounds have their probable mechanisms of action described, based on inhibiting different enzymes such as lanosterol-14α-demethylase, enoyl reductase, and DNA gyrase. The activity of many of the novel derivatives is higher than that of the well-known antimicrobial medications. Their value as novel drugs in the fight against antimicrobial resistance is confirmed by the diversity of new structures and their high activity. For in vivo safety and efficacy to be confirmed, more research is required [60-64].

Procedia of Theoretical and Applied Sciences
Volume 15 | Jan 2024
ISSN: 2795-5621 Available: http://procedia.online/index.php/applied/index

References.

1. Jafari E, Mohammadi T, Jahanian-Najafabadi A, Hassanzadeh F. Synthesis and antimicrobial evaluation of some 2,5 disubstituted 1,3,4-oxadiazole derivatives. Res Pharm Sci. 2017 Aug;12(4):330-336. doi: 10.4103/1735-5362.212051.
2. Glomb T, Świątek P. Antimicrobial Activity of 1,3,4-Oxadiazole Derivatives. Int J Mol Sci. 2021 Jun 29;22(13):6979. doi: 10.3390/ijms22136979.
3. Annunziato G. Strategies to Overcome Antimicrobial Resistance (AMR) Making Use of Non-Essential Target Inhibitors: A Review. Int. J. Mol. Sci. 2019;20:5844. doi: 10.3390/ijms20235844.
4. Duval R.E., Grare M., Demoré B. Fight against Antimicrobial Resistance: We Always Need New Antibacterials but for Right Bacteria. Molecules. 2019;24:3152. doi: 10.3390/molecules24173152.
5. Hinchliffe S., Butcher A., Rahman M.M. The AMR Problem: Demanding Economies, Biological Margins, and Co-Producing Alternative Strategies. Palgrave Commun. 2018;4:1–12. doi: 10.1057/s41599-018-0195-4.
6. Prestinaci F., Pezzotti P., Pantosti A. Antimicrobial Resistance: A Global Multifaceted Phenomenon. Pathog. Glob. Health. 2015:309–318. doi: 10.1179/2047773215Y.0000000030.
7. Sahu VKR, Singh AK, Yadav D. Review article on 1,3,4-oxadiazole derivatives and its pharmacological activities. Int J ChemTech Res. 2011;3(3):1362–1372.
8. Husain A, Ajmal M. Synthesis of novel 1, 3, 4-oxadiazole derivatives and their biological properties. Acta Pharm. 2009;59(2):223–233.
9. Singh AK, Lohani M, Parthsarthy R. Synthesis, characterization and anti-inflammatory activity of some 1,3,4-oxadiazole derivatives. Iran J Pharm Res. 2013;12(2):319–323.
10. Joshi SD, Vagdevi HM, Vaidya VP, Gadaginamath GS. Synthesis of new 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. 2008;43(9):1989–1996.
11. Redhu S, Kharb R. Recent updates on chemistry and pharmacological aspects of 1, 3, 4-oxadiazole scaffold. Int J Pharm Innov. 2013;3(1):93–110.
12. de Oliveira CS, Lira B, Barbosa-Filho JM, Lorenzo JG, de Athayde-Filho PF. Synthetic approaches and pharmacological activity of 1,3,4-Oxadiazoles: a review of the literature from 2000-2012. Molecules. 2012;17(2):10192–10231. [PMC free article] [PubMed] [Google Scholar]
13. Bhat K, Sufeera K, Chaitanya SK. Synthesis, characterization and biological activity studies of 1, 3, 4-Oxadiazole analogs . J Young Pharm. 2011;3(4):310–314.
14. Azzawi AMA, Al-Obiadi KKH. Synthesis and antimicrobial screening new bisshiff bases and their acetyl oxadiazole azetidinone derivatives from pyromelliticdiimide. Int J Res Pharm Chem. 2016;6(1):1–8.
15. Malhotra M, Sanduja M, Samad A, Deep A. New oxadiazole derivatives of isonicotinohydrazide in the search for antimicrobial agents: synthesis and in vitro evaluation. J Serb Chem Soc. 2012;77(1):9–16.
16. Singh I, Kumar A. Synthesis and antibacterial activity of 2-(substituted phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazoles. Chem Sci Trans. 2015;4(1):133–136.
17. Yar MS, Siddiqui AA, Ali MA. Synthesis and anti tuberculostatic activity of novel 1,3,4-Oxadiazole derivatives. J Chin Chem Soc. 2007;54(1):5–8.

18. Singh R, Chouhan A. Various approaches for synthesis of 1, 3, 4-Oxadiazole derivatives and their pharmacological activity. World J Pharm Pharm Sci. 2014;3(10):1474–1505.
19. Zheng X, Li Z, Wang Y, Chen W, Huang Q, Liu C, Song G. Syntheses and insecticidal activities of novel 2,5-disubstituted 1,3,4-oxadiazoles. J Fluorine Chem. 2003;123(2):163–169.
20. Kumar R, Yar MS, Rai AK, Chaturvedi S. Synthesis and biological evaluation of some novel 1, 3, 4-oxadiazoles derived from bi phenyl 4- carboxylic acid. Der Pharmacia Lettre. 2013;5(1):366–370.
21. Peraman R., Varma R.V., Reddy Y.P. Re-Engineering Nalidixic Acid's Chemical Scaffold: A Step towards the Development of Novel Anti-Tubercular and Anti-Bacterial Leads for Resistant Pathogens. Bioorg. Med. Chem. Lett. 2015;25:4314–4319. doi: 10.1016/j.bmcl.2015.07.071.
22. Omar F.A., Abelrasoul M., Sheha M.M., Hassan H.Y., Ibrahiem Y.M. Synthesis, Antibacterial Activity and Molecular Docking of Substituted Naphthyridines as Potential DNA Gyrase Inhibitors. ChemistrySelect. 2018;3:2604–2612. doi: 10.1002/slct.201800108.
23. Hofny H.A., Mohamed M.F.A., Gomaa H.A.M., Abdel-Aziz S.A., Youssif B.G.M., El-koussi N.A., Aboraia A.S. Design, Synthesis, and Antibacterial Evaluation of New Quinoline-1,3,4-Oxadiazole and Quinoline-1,2,4-Triazole Hybrids as Potential Inhibitors of DNA Gyrase and Topoisomerase IV. Bioorg. Chem. 2021;112:104920. doi: 10.1016/j.bioorg.2021.104920.
24. Guo Y., Xu T., Bao C., Liu Z., Fan J., Yang R., Qin S. Design and Synthesis of New Norfloxacin-1,3,4-Oxadiazole Hybrids as Antibacterial Agents against Methicillin-Resistant Staphylococcus Aureus (MRSA) Eur. J. Pharm. Sci. 2019;136:104966. doi: 10.1016/j.ejps.2019.104966.
25. Mermer A., Faiz O., Demirbas A., Demirbas N., Alagumuthu M., Arumugam S. Piperazine-Azole-Fluoroquinolone Hybrids: Conventional and Microwave Irradiated Synthesis, Biological Activity Screening and Molecular Docking Studies. Bioorg. Chem. 2019;85:308–318. doi: 10.1016/j.bioorg.2019.01.009.
26. Navin P., Sarvil P., Amit P., Divyesh P., Dhansukh R., Moo-Puc R., Rivera G. Synthesis and Biological Evaluation of Newer 1,3,4-Oxadiazoles Incorporated with Benzothiazepine and Benzodiazepine Moieties. Zeitschrift Naturforsch. Sect. C J. Biosci. 2017;72:133–146. doi: 10.1515/znc-2016-0129.
27. Alghamdi A.A., Alam M.M., Nazreen S. In Silico ADME Predictions and in Vitro Antibacterial Evaluation of 2-Hydroxy Benzothiazole-Based 1,3,4-Oxadiazole Derivatives. Turkish J. Chem. 2020;44:1068–1084. doi: 10.3906/kim-1912-55.
28. Dhumal S.T., Deshmukh A.R., Bhosle M.R., Khedkar V.M., Nawale L.U., Sarkar D., Mane R.A. Synthesis and Antitubercular Activity of New 1,3,4-Oxadiazoles Bearing Pyridyl and Thiazolyl Scaffolds. Bioorg. Med. Chem. Lett. 2016;26:3646–3651. doi: 10.1016/j.bmcl.2016.05.093.
29. Desai N.C., Somani H., Trivedi A., Bhatt K., Nawale L., Khedkar V.M., Jha P.C., Sarkar D. Synthesis, Biological Evaluation and Molecular Docking Study of Some Novel Indole and Pyridine Based 1,3,4-Oxadiazole Derivatives as Potential Antitubercular Agents. Bioorg. Med. Chem. Lett. 2016;26:1776–1783. doi: 10.1016/j.bmcl.2016.02.043.
30. Desai N.C., Trivedi A., Somani H., Jadeja K.A., Vaja D., Nawale L., Khedkar V.M., Sarkar D. Synthesis, Biological Evaluation, and Molecular Docking Study of Pyridine Clubbed 1,3,4-Oxadiazoles as Potential Antituberculars. Synth. Commun. 2018;48:524–540. doi: 10.1080/00397911.2017.1410892.

31. Mansoori M.H., Khatik G.L., Mishra V. Synthesis and Pharmacological Evaluation of Pyridinyl-1,3,4-Oxadiazolyl-Ethanone Derivatives as Antimicrobial, Antifungal and Antitubercular Agents. Med. Chem. Res. 2018;27:744–755. doi: 10.1007/s00044-017-2098-0.

32. 46. Shingare R.M., Patil Y.S., Sangshetti J.N., Patil R.B., Rajani D.P., Madje B.R. Synthesis, Biological Evaluation and Docking Study of Some Novel Isoxazole Clubbed 1,3,4-Oxadiazoles Derivatives. Med. Chem. Res. 2018;27:1283–1291. doi: 10.1007/s00044-018-2148-2.

33. Das R., Mehta D.K. Evaluation and Docking Study of Pyrazine Containing 1,3,4-Oxadiazoles Clubbed with Substituted Azetidin-2-One: A New Class of Potential Antimicrobial and Antitubercular. Drug Res. 2021;71:26–35. doi: 10.1055/a-1252-2378.

34. Sindhe M.A., Bodke Y.D., Kenchappa R., Telkar S., Chandrashekar A. Synthesis of a Series of Novel 2,5-Disubstituted-1,3,4-Oxadiazole Derivatives as Potential Antioxidant and Antibacterial Agents. J. Chem. Biol. 2016;9:79–90. doi: 10.1007/s12154-016-0153-9.

35. Sajja Y., Vanguru S., Vulupala H.R., Nagarapu L., Perumal Y., Sriram D., Nanubolu J.B. Design, Synthesis, and in Vitro Antituberculosis Activity of Benzo[6,7]Cyclohepta[1,2- b]Pyridine-1,3,4-Oxadiazole Derivatives. Chem. Biol. Drug Des. 2017;90:496–500. doi: 10.1111/cbdd.12969.

36. Gholap S., Tambe M., Nawale L., Sarkar D., Sangshetti J., Damale M. Design, Synthesis, and Pharmacological Evaluation of Fluorinated Azoles as Anti-Tubercular Agents. Arch. Pharm. 2018;351:1700294. doi: 10.1002/ardp.201700294.

37. Triloknadh S., Venkata Rao C., Nagaraju K., Hari Krishna N., Venkata Ramaiah C., Rajendra W., Trinath D., Suneetha Y. Design, Synthesis, Neuroprotective, Antibacterial Activities and Docking Studies of Novel Thieno[2,3-d]Pyrimidine-Alkyne Mannich Base and Oxadiazole Hybrids. Bioorg. Med. Chem. Lett. 2018;28:1663–1669. doi: 10.1016/j.bmcl.2018.03.030.

38. Paruch K., Popiołek Ł., Biernasiuk A., Hordyjewska A., Malm A., Wujec M. Novel 3-Acetyl-2,5-Disubstituted-1,3,4-Oxadiazolines: Synthesis and Biological Activity. Molecules. 2020;25:5844. doi: 10.3390/molecules25245844.

39. Ladani G.G., Patel M.P. Novel 1,3,4-Oxadiazole Motifs Bearing a Quinoline Nucleus: Synthesis, Characterization and Biological Evaluation of Their Antimicrobial, Antitubercular, Antimalarial and Cytotoxic Activities. New J. Chem. 2015;39:9848–9857. doi: 10.1039/C5NJ02566D.

40. Vosátka R., Krátký M., Švarcová M., Janoušek J., Stolaříková J., Madacki J., Huszár S., Mikušová K., Korduláková J., Trejtnar F., et al. New Lipophilic Isoniazid Derivatives and Their 1,3,4-Oxadiazole Analogues: Synthesis, Antimycobacterial Activity and Investigation of Their Mechanism of Action. Eur. J. Med. Chem. 2018;151:824–835. doi: 10.1016/j.ejmech.2018.04.017.

41. Li T., Wen G., Li J., Zhang W., Wu S. A Useful Synthesis of 2-Acylamino-1,3,4-Oxadiazoles from Acylthiosemicarbazides Using Potassium Iodate and the Discovery of New Antibacterial Compounds. Molecules. 2019;24:1490. doi: 10.3390/molecules24081490.

42. Hkiri S., Hafidh A., Cavalier J., Touil S., Samarat A. Design, Synthesis, Antimicrobial Evaluation, and Molecular Docking Studies of Novel Symmetrical 2,5-difunctionalized 1,3,4-oxadiazoles. J. Heterocycl. Chem. 2020;57:1044–1054. doi: 10.1002/jhet.3837.

43. Salama E.E. Synthesis of New 2-Amino-1,3,4-Oxadiazole Derivatives with Anti-Salmonella Typhi Activity Evaluation. BMC Chem. 2020;14:s13065. doi: 10.1186/s13065-020-00682-6.

44. Hagras M., Hegazy Y.A., Elkabbany A.H., Mohammad H., Ghiaty A., Abdelghany T.M., Seleem M.N., Mayhoub A.S. Biphenylthiazole Antibiotics with an Oxadiazole Linker: An Approach to

Improve Physicochemical Properties and Oral Bioavailability. Eur. J. Med. Chem. 2018;143:1448–1456. doi: 10.1016/j.ejmech.2017.10.048.

45. Kotb A., Abutaleb N.S., Hagras M., Bayoumi A., Moustafa M.M., Ghiaty A., Seleem M.N., Mayhoub A.S. Tert -Butylphenylthiazoles with an Oxadiazole Linker: A Novel Orally Bioavailable Class of Antibiotics Exhibiting Antibiofilm Activity. RSC Adv. 2019;9:6770–6778. doi: 10.1039/C8RA10525A.
46. Hannoun M.H., Hagras M., Kotb A., El-Attar A.A.M.M., Abulkhair H.S. Synthesis and Antibacterial Evaluation of a Novel Library of 2-(Thiazol-5-Yl)-1,3,4-Oxadiazole Derivatives against Methicillin-Resistant Staphylococcus Aureus (MRSA) Bioorg. Chem. 2020;94:103364. doi: 10.1016/j.bioorg.2019.103364.
47. Opoku-Temeng C., Naclerio G.A., Mohammad H., Dayal N., Abutaleb N.S., Seleem M.N., Sintim H.O. N-(1,3,4-Oxadiazol-2-Yl)Benzamide Analogs, Bacteriostatic Agents against Methicillin- and Vancomycin-Resistant Bacteria. Eur. J. Med. Chem. 2018;155:797–805. doi: 10.1016/j.ejmech.2018.06.023.
48. Sahu VKR, Singh AK, Yadav D. Review article on 1,3,4-oxadiazole derivatives and its pharmacological activities. Int J ChemTech Res. 2011;3(3):1362–1372.
49. Husain A, Ajmal M. Synthesis of novel 1, 3, 4-oxadiazole derivatives and their biological properties. Acta Pharm. 2009;59(2):223–233.
50. Singh AK, Lohani M, Parthsarthy R. Synthesis, characterization and anti-inflammatory activity of some 1,3,4-oxadiazole derivatives. Iran J Pharm Res. 2013;12(2):319–323.
51. Joshi SD, Vagdevi HM, Vaidya VP, Gadaginamath GS. Synthesis of new 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. 2008;43(9):1989–1996.
52. Redhu S, Kharb R. Recent updates on chemistry and pharmacological aspects of 1, 3, 4-oxadiazole scaffold. Int J Pharm Innov. 2013;3(1):93–110.
53. de Oliveira CS, Lira B, Barbosa-Filho JM, Lorenzo JG, de Athayde-Filho PF. Synthetic approaches and pharmacological activity of 1,3,4-Oxadiazoles: a review of the literature from 2000-2012. Molecules. 2012;17(2):10192–10231.
54. Bhat K, Sufeera K, Chaitanya SK. Synthesis, characterization and biological activity studies of 1, 3, 4-Oxadiazole analogs . J Young Pharm. 2011;3(4):310–314.
55. Azzawi AMA, Al-Obiadi KKH. Synthesis and antimicrobial screening new bisshiff bases and their acetyl oxadiazole azetidinone derivatives from pyromelliticdiimide. Int J Res Pharm Chem. 2016;6(1):1–8.
56. Malhotra M, Sanduja M, Samad A, Deep A. New oxadiazole derivatives of isonicotinohydrazide in the search for antimicrobial agents: synthesis and in vitro evaluation. J Serb Chem Soc. 2012;77(1):9–16.
57. Singh I, Kumar A. Synthesis and antibacterial activity of 2-(substituted phenyl)-5-(pyridin-4-yl)-1,3,4-oxadiazoles. Chem Sci Trans. 2015;4(1):133–136.
58. Yar MS, Siddiqui AA, Ali MA. Synthesis and anti tuberculostatic activity of novel 1,3,4-Oxadiazole derivatives. J Chin Chem Soc. 2007;54(1):5–8.
59. Singh R, Chouhan A. Various approaches for synthesis of 1, 3, 4-Oxadiazole derivatives and their pharmacological activity. World J Pharm Pharm Sci. 2014;3(10):1474–1505.

60. Zheng X, Li Z, Wang Y, Chen W, Huang Q, Liu C, Song G. Syntheses and insecticidal activities of novel 2,5-disubstituted 1,3,4-oxadiazoles. J Fluorine Chem. 2003;123(2):163–169.

61. Kumar R, Yar MS, Rai AK, Chaturvedi S. Synthesis and biological evaluation of some novel 1, 3, 4-oxadiazoles derived from bi phenyl 4- carboxylic acid. Der Pharmacia Lettre. 2013;5(1):366–370.

62. Salih N, Salimon J, Hameed A, Yousif E. Synthesis, characterization and antimicrobial evaluation of some 1,3,4-oxadiazole derivatives. Int J PharmTech Res. 2011;3(2):1097–1102.

63. Khan K, Rani M, Ambreen N, Muhammad A, Hussain S, Perveen S, et al. 2, 5-disubstituted-1,3,4-oxadiazoles: thymidine phosphorylase inhibitors. Med Chem Res. 2013;22:6022–6028.

64. Motamedifar M, Bazargani A, Namazi MR, Sarai E, Sedigh H. Antimicrobial activity of mandelic acid against methicillin-resistant Staphylococcus aureus: a novel finding with important practical implications. World Appl Sci J. 2014;31(5):925–929.