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A comprehensive review on Oxadiazoles: Synthesis, properties, and medicinal applications

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Abstract
Oxadiazoles are an important group of heterocyclic compounds that have become highly valuable in medicinal chemistry. Their ring contains both nitrogen and oxygen atoms, which give them special chemical and biological properties. These atoms help oxadiazoles form strong interactions with targets inside the body, making them useful in the design of many new drug molecules. Oxadiazoles are also known for their good stability, lipophilicity, and ability to act as bioisosteres, which means they can replace certain functional groups in drug structures without losing activity. Because they are easy to modify, different substituents can be added to the ring to improve their pharmacological behaviour. Over the years, many researchers have focused on the synthesis, structural features, and general medicinal value of oxadiazole derivatives. Their wide applications in drug discovery show that they are attractive scaffolds for developing molecules with better selectivity and improved therapeutic potential. This review explains the overall importance of oxadiazoles, highlights recent progress in their development, and provides a clear understanding of why they continue to be an essential class of compounds in modern pharmaceutical research.

Keywords: Oxadiazole, anti-microbial activity, anti-cancer activity, anti-convulsant activity, anti-tubercular activity, analgesics, anti-inflammatory activity

Introduction

Oxadiazoles are an important class of five-membered heterocyclic compounds containing oxygen and nitrogen atoms in the ring structure [1]. These scaffolds have gained significant attention in medicinal chemistry due to their versatile biological properties and favourable pharmacokinetic characteristics such as good lipophilicity, metabolic stability, and hydrogen-bonding capacity [2]. The presence of heteroatoms within the ring enhances their ability to interact with various biological targets, making them valuable candidates for drug discovery and development [3].

Various biological activities have been reported for oxadiazole derivatives, including antimicrobial, anti-inflammatory, anticancer, antitubercular, analgesic, anticonvulsant, and especially antiviral activity [4]. Among the different Regioisomers, 1,2,4- and 1,3,4-oxadiazoles are the most commonly explored in drug research due to their synthetic accessibility and biological significance. Their ability to act as bioisosteres of amides and esters further enhances their medicinal value [5].

Several oxadiazole-containing compounds have reached the pharmaceutical market or are under clinical trials. For example, Raltegravir, a 1,3,4-oxadiazole derivative, is a clinically approved HIV integrase inhibitor used in the treatment of HIV/AIDS [6]. Similarly, Zibotentan, containing an oxadiazole moiety, has shown promise in the treatment of prostate cancer. These examples clearly indicate that oxadiazoles can be structurally optimised to develop potent and selective therapeutic agents [7].

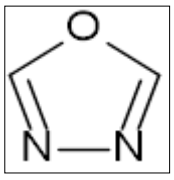


Fig 1: Oxadiazole

Structurally, oxadiazoles possess a conjugated system that allows electron delocalisation, which contributes to their chemical stability and reactivity [8]. The incorporation of different substituents at the 2- and 5-positions of the oxadiazole ring provides opportunities to tune their biological properties. The nitrogen and oxygen atoms in the ring can form strong hydrogen bonds with enzyme active sites or receptor pockets, which play a crucial role in drug-target interactions [9, 10].

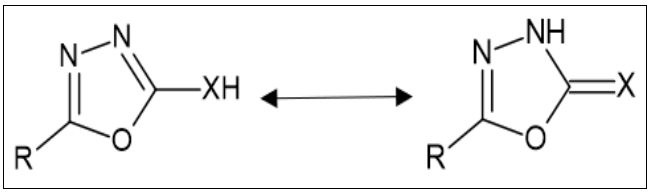
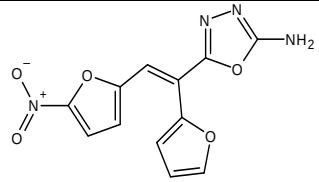
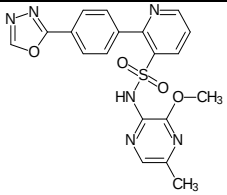
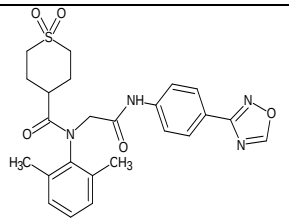
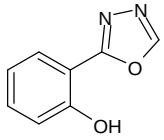
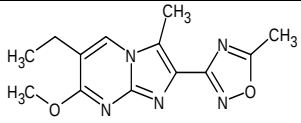
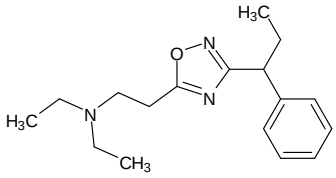
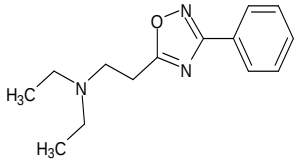
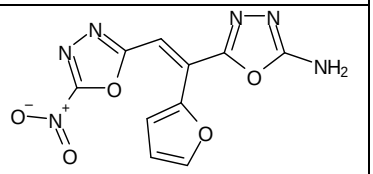
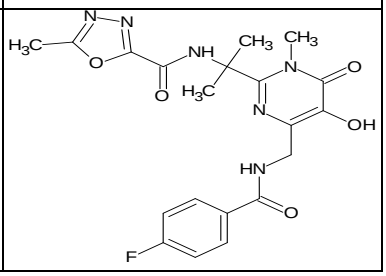


Fig 1: Oxadiazole possessing Tautomerism [11]

Table 1: Commercially available drugs

Sl No.	Drug name	Structure
1	Furamizole	
2	Zibotentan	

3	Amenamevir	
4	Fenadiazole	
5	Fasiplon	
6	Proxazole	
7	Oxolamine	
8	Nesapidil	
9	Raltegravir	

Pharmacological activities of Oxadiazole derivatives

1. Kahdr Alatawi [12] *et al*., 2024 presented the synthesis of a new series of 1,3,4-oxadiazole functionalized pyrano [2,3-f] chromene derivatives starting from Diethyl 2-(((4-methyl-2-oxo-2H-chromen-7-yl) oxy) methylene) malonate and sugar-based hydrazones. The compounds were characterised and evaluated for anti-bacterial activity against (B. subtilis, S. aureus, E. coli & P. aeruginosa). The Compounds 1a & 1b exhibited the highest activity compared to Chloramphenicol as a standard drug. Fig.2
2. Adeeb Salim [13] *et al*., 2024 reported the alkylation of 5-(((4-bromophenyl) (3,4,5-trimethoxybenzyl) amino) methyl)-1,3,4 oxadiazole-2(3H)-thione using six alkyl halides in K_2CO_3 (anhydrous) medium. The resulting compounds were characterised and evaluated for anti-bacterial activity against S. aureus and E. coli, showing significant inhibition. Compound 2a and 2b show the most activity compared to amoxicillin as a reference drug. Molecular docking supported their potential binding to PPARα receptors, indicating promising activity. Fig.2
3. Farghaly [14] *et al*., 2024 investigated nicotinoyl-based azoles for antimicrobial potential. Strong inhibition was observed with compound 23, Compound 16 displayed notable activity against gram-positive and gram-negative bacteria. Pyrimidine derivative compound 24 produced moderate effect on Candida and bacterial strains. Hydrazone 4a showed mild activity on gram-negative organisms. Minimal inhibition appeared for compound 2 so overall, the compound 3 was the most effective antimicrobial compared with streptomycin as a standard drug. Fig.3
4. Eeduri Ramya Devi [15] *et al*., 2024 developed new amide compounds containing of 1,3,4-oxadiazole-isoxazol-pyridine-benzimidazole rings. They analysed the structures using NMR & Mass spectrometry. The compounds were tested on PC3 (prostate), A549 (lung), MCF-7 (breast) and DU-145 (prostate) cancer cell lines. Some molecules, especially 24f, 24g, 24h, & 24j showed significant anti-cancer activity. Among that Compound 4 exhibited more promising activity with IC50 values of 0.11 ± 0.07 µM, 0.26 ± 0.08 µM, 0.55 ± 0.06 µM, and 0.87 ± 0.09 µM than the standard drug Etoposide. Fig.3
5. Marwa Serag I [16] *et al*., 2024 reported two new series of oxadiazole and pyrazoline derivatives were designed and synthesized as promising EGFR-TK inhibitors. They synthesized and evaluated for *in-vitro* anti-cancer activity was studied against three human cancer cell lines namely, HCT116, HepG-2 & MCF7 using MTT assay. Compound 5 showed the most potent anticancer activity against all cancer cell lines, with IC_{50} range of 1.82 to 5.55 µM, while proving safe towards normal cells WI-38 (IC_{50} = 41.17Mm) compared to the reference drug Doxorubicin (IC_{50} = 6.72Mm). Fig.3
6. Manjunath R [17] *et al.*, 2025 reported the synthesis of 2-butyl-4-chloroimidazole-based 1,3,4-oxadiazoles through a multistep procedure using substituted aromatic precursors. The obtained derivatives were examined for ACE inhibition, anticancer response, and antitubercular activity by standard *in-vitro* assays. Compound 5c exhibited strong ACE blocking potential when compared with lisinopril. Compound 6 produced high growth suppression against MDA-MB-231 and Caco-2 cells in the MTS assay, similar to cisplatin. Compounds 5b and 5e showed good MIC values toward the H37Rv strain, indicating useful anti-TB action. The study suggested that electron-withdrawing groups improved overall biological performance. Fig.3
7. Tulika Anthwal [18] *et al*., 2025 reported the design and synthesis of new 1,3,4- thiadiazole derivatives for anti-convulsant activity. The compounds were characterized and tested for carbonic anhydrase (CA-II & CA-IX) inhibition. They also evaluated seizure protection using MES & sc-PTZ animal models. Among all derivatives, two compounds, 6d and 7d showed the highest activity. In that, compound 7 performed better than standard drugs like sodium valproate and acetazolamide. Fig.3
8. Anagha Balachandra [19] *et al*., 2024 synthesised a new set of 1,3,4-oxadiazole derivatives and confirmed their use using spectroscopic data. Molecular docking showed strong interactions between these compounds and the target protein. *In-vivo* studies revealed that compound 8 significantly reduced stages in MES & PTZ models. When compared to phenytoin as a standard drug. Fig.3

9. Aenkatala Chenakeshwari [20] *et al*., (2024) introduced newly designed oxadiazole-based molecules for biological assessment. Among the series, 3c showed the strongest seizure-blocking response compared with the reference drug Phenytoin. Another molecule, 3d produced marked antibacterial action compared with Ciprofloxacin. Each structure exhibited distinct behaviour due to variations in aromatic substitution. The investigation identified Compound 9 as the best anticonvulsant while 3d displayed notable bacterial suppression. Fig.3
10. Saritha Keerthi [21] *et al*., 2025 synthesized pyrazole-linked 1,3,4-oxadiazole hybrids for anti-tubercular activity. All synthesized molecules were checked against Mycobacterium tuberculosis(H37Rv). Among them, Compound 10a & Compound 10b showed the strongest activity with (MIC ¼ 1.56mg/mL) when compared to the ethambutol as a reference drug. Fig.4
11. S. P. Jisha [22] *et al*., 2025 carried out the preparation of isoniazid-embedded 1,3,4-oxadiazole hybrids using a simple synthetic route. The new molecules for examined for anti-tuberculosis, anti-oxidant, & COX-inhibitory properties. The structures were verified by various spectroscopic methods. Compounds 3d, 3f, & 3h demonstrated strong antioxidant potential at 10µg/ml concentration. Compounds 3e, 3f, & 3h exhibited notable COX-1 inhibitory activity with lower IC50 values than aspirin. Among all, Compound 11 showed excellent anti-TB activity when compared to Isoniazid as a standard drug. Fig.4
12. Daniele Zampieri [23] *et al*., 2022 designed new 1,3,4-oxadiazole hydrazide derivatives for antitubercular evaluation. The series showed varied action, and compound 12a exhibited the highest effect with a MIC of 8 µg/mL against the H37Rv strain. Similarly, compound 12b also produced strong inhibition with MIC 8 µg/mL and notable activity on pyrazinamide-resistant strains (MIC 4 µg/mL). The activity was compared with the standard drug isoniazid (INH), which showed MIC 0.25 µg/mL. Both active compounds displayed good selectivity, low toxicity, and favourable InhA interaction. Fig.4
13. Ayca Erdogan [24] *et al*., 2024 designed a new set of 1,3,4-oxadiazole & 1,2,4-triazole derivatives for evaluating their anti-inflammatory and analgesic activity. The synthesized molecules were tested for nitric oxide (NO) and prostaglandin E2 (PGE2), and interleukin (IL-6) inhibition in a dose-dependent manner. Among all the derivatives, Compound 13 showed the highest inhibitory activity at 1 µM concentration. The activity of the new derivatives was compared with the standard drug indomethacin (100 µM), indicating its significant anti-inflammatory potential. Fig.4
14. Amrita Pathak [25] *et al.,* 2024 presented the synthesis of a new series of 1,3,4-oxadiazole derivatives by reacting 2-furoic carbohydrazide / thiophenyl carbohydrazide with different substituted carboxylic acid chlorides. The prepared compounds were assessed for analgesic and anti-inflammatory activity through standard pharmacological models. Among all the tested molecules, Compound Oxa-14 displayed the strongest effect, showing superior activity compared to the standard drug tramadol. Fig.4
15. Medarametla Venkatesh [26] *et al*., 2024 synthesized indole-based 1,3,4-oxadiazole derivatives for biological evaluation. The molecules were prepared as 1-(1H-indol-5-yl)-2-substituted-1,3,4-oxadiazol-3(2H)-yl) ethenone compounds. All compounds were tested for antibacterial, antifungal, and anti-inflammatory activities. Among those, Compound 6k showed maximum antibacterial effect against Pseudomonas aeruginosa with MIC 6.25 µg/mL. Several analogues (6a–6j) demonstrated moderate antifungal activity with MIC values of 6.25–50 µg/mL. Anti-inflammatory activity of 15a-15b was lower than Diclofenac (85.5% inhibition) as a standard drug. Fig.4

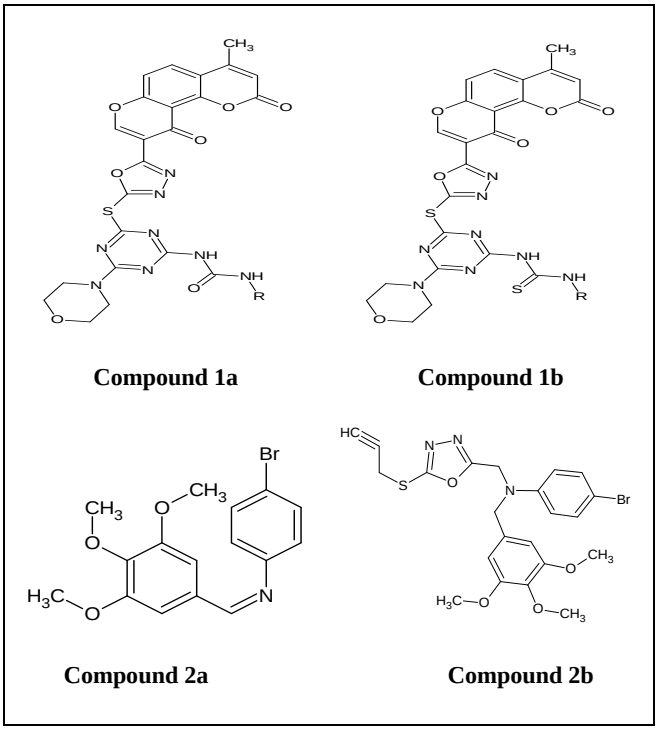
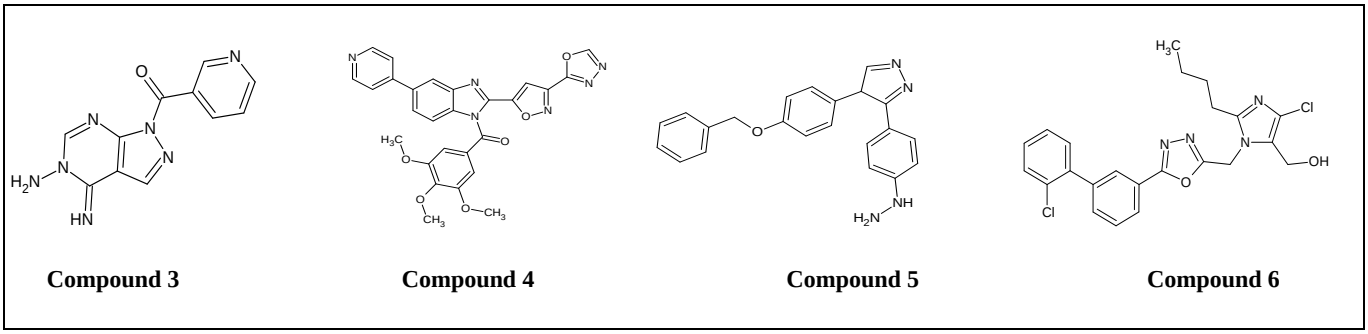
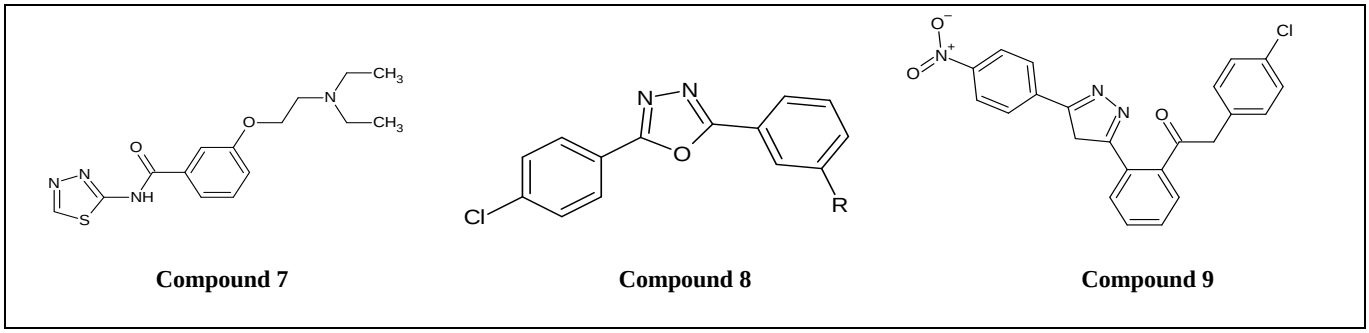


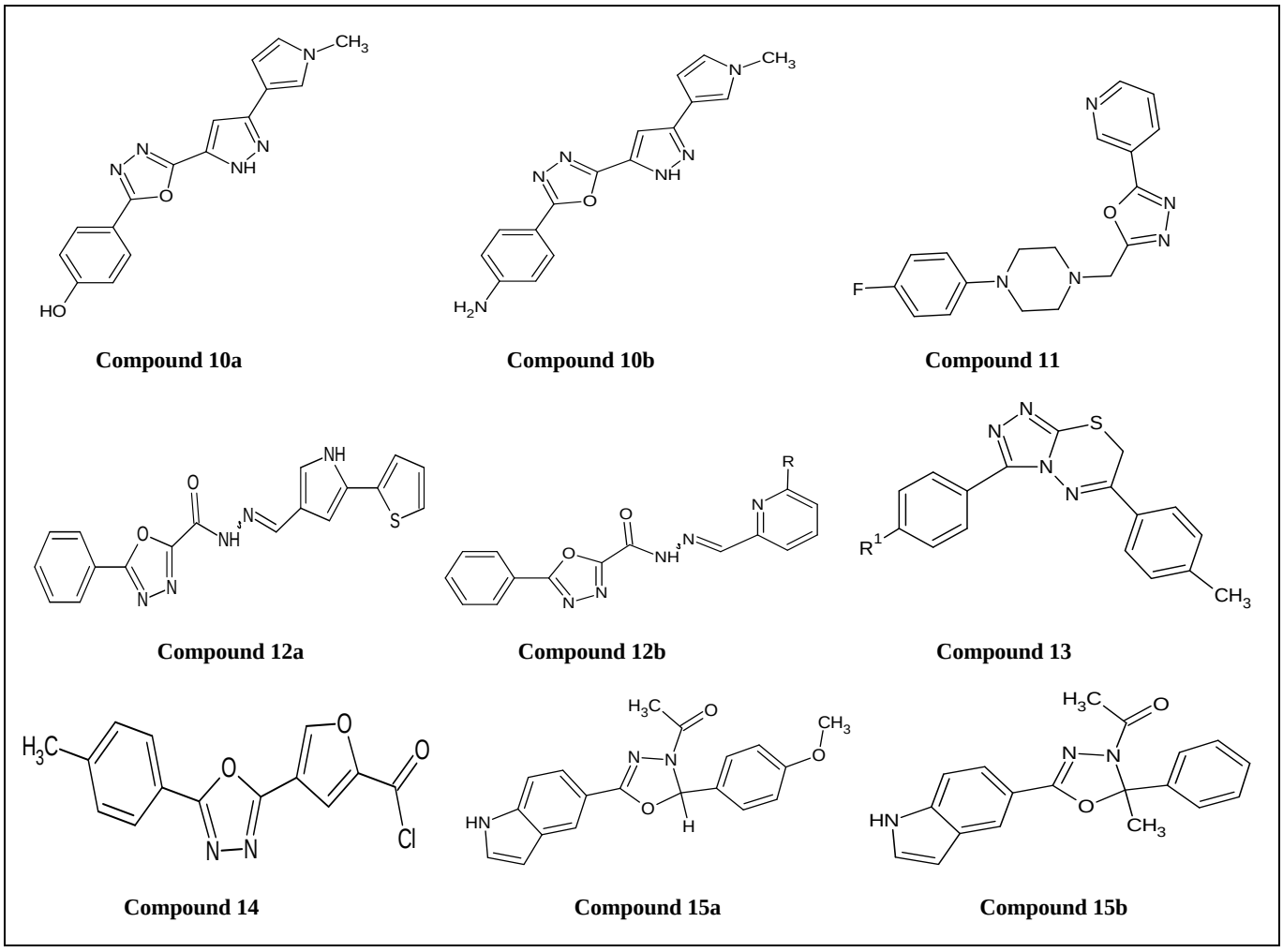
Fig 2: Pharmacological activities of Oxadiazole derivatives





Compound 7 **Compound 8** **Compound 9**

Fig 3: Pharmacological activities of Oxadiazole derivatives



Compound 10a **Compound 10b** **Compound 11**

Compound 12a **Compound 12b** **Compound 13**

Compound 14 **Compound 15a** **Compound 15b**

Fig 4: Pharmacological activities of Oxadiazole derivatives

Conclusion

Oxadiazoles remain a highly promising class of compounds in medicinal chemistry due to their adaptable structure and favourable properties. Their heterocyclic ring allows easy modification, which helps researchers design molecules with improved biological performance. The presence of nitrogen and oxygen atoms increases their ability to interact with different biological systems, supporting their use in various therapeutic areas. Numerous studies have demonstrated that oxadiazoles can be effectively utilised as core structures for new drug candidates, and ongoing research has further enhanced their significance. Overall, the findings suggest that oxadiazole derivatives will continue to play an important role in the discovery of safer, more effective, and more selective drugs. Future work in this area will help identify new molecules, improve synthetic strategies, and contribute to the development of better treatments for different diseases.

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