

A Solo and Duet Performance of Oxadiazole and Benzotriazoles: A Review

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Abstract:

The pharmacological impact of Oxadiazoles and Benzotriazoles are found active against number of pathogenic agents, individually. Number of biological activities has been awarded to the credit of these moieties. The combination of these two moieties also possesses pharmacological active characteristic. In this review, the biological impact of Oxadiazoles and Benzotriazoles derivatives are studied in details along with the combined impact of derivatives having these two moieties together. The findings of this review articles revealed that the solo and duet performance of Oxadiazole and Benzotriazole derivatives have been remarkable.

Introduction:

World population is increasing day by day. With increasing population, the challenges for health and quality life of people due to number of diseases, bacteria, viruses etc. from known and unknown sources are also increasing. In such scenario, these growing health and life issues catalyse research and development activities, research innovations, discoveries of new biological activities etc. so as to fix these challenges. In chemistry, Heterocyclic aromatic compounds have always been proved to be one of the most important and versatile compounds in Pharmaceuticals. Literature review suggests that compounds having either oxadiazole or benzotriazole or both have been found showing remarkable biological characteristic. Therefore, efforts are done through this article to make a comprehensive study for exploring biological characteristic of oxadiazole and benzotriazole moieties for their activities.

Biological characteristic of Oxadiazoles derivatives:

Oxadiazole from the azole family bearing the molecular formula C_2N_2O is a significant five membered aromatic compound. However, in the structure of Oxadiazole, the position of the hetero atoms varies providing us the four possible isomers and they are named as 1, 2, 5-oxadiazole, 1, 2, 4-oxadiazole, 1, 2, 3-oxadiazole and 1, 3, 4-oxadiazole, as shown in fig. 1 [1].

1,2,3-oxadiazole 1,3,4-oxadiazole 1,2,5-oxadiazole 1,2,4-oxadiazole

Fig. 1: Structures of Oxadiazoles

Among the all four possible isomers of Oxadiazole, 1, 3, 4-oxadiazole and 1, 2, 4-oxadiazole are the most common due to their diverse applications in drug synthesis while less work has been reported on 1, 2, 3-oxadiazole and 1, 2, 5-oxadiazole. Also 1,2,3-oxadiazole is unstable in its ring cyclic form due to which its uses in drugs industries are limited [2]. 1, 3, 4-oxadiazoles are most popular compounds due to their hydrogen bonding participation capacity and unique structure which has invited good amount of interest [3]. On the other hand, due to esters and bioisosteres of amides nature of 1, 2, 4-oxadiazole, the physiochemical and bioavailability properties of compounds gets enhanced bearing this moiety [4].

Almost all the Oxadiazole derivatives are known to be highly biologically active as it shows various activities like anti-allergic[5], anti-HIV [6], antiviral [7], antidiabetic[8], antiproliferative [9], anticonvulsant [10], anti-thrombotic activity [11], Hypoglycaemic activity [12] antioxidant [13] antifungal[14] antibacterial activity [15], antiurease activity[16], anticancer [17], anti-inflammatory [18], and antituberculosic[19]. The metal complexes of oxadiazole like Copper have also been synthesized and proved to have better antibacterial and antifungal activity as compared to their respective oxadiazoles [20]. It has been also found that the Nitro group provides an improved inhibition efficiency compared to the other pharma chores in Oxadiazoles [21]. Oxadiazole derivatives have drawn the attention of many biochemists due to its wide spectrum of pharmacological activities and hence research on new derivatives of oxadiazole is still going on.

Although a number of biological activity derivatives of Oxadiazoles are synthesized every year but due to their side effects, they are avoided to be used as medicines [22]. Therefore, new research and new derivatives synthesis with more potency is the need of hour. With literature survey it revealed that Oxadiazoles have wide range of activities. In addition to that few other activities are mentioned in table-1

Table 1: Biological activities of compounds bearing oxadiazole moiety

Compound	Structure	Activity	Against	Ref.
5-Bromo-3-[3-(5chloro-1-methyl-1H-indol-3yl)-1,2,4-oxadiazol-5-yl]- 1H-pyrrolo[2,3-b]pyridine		Antipoliferative	MCF-7, HCT-116, HeLa and CaCo ₂	[23]
2-[(5-(4-5(6)-Fluoro-1H-benzimidazole-2-yl)phenyl)-1,3,4-oxadiazol-2-yl]thio]-3,4-dihydroxyphenyl)ethan-1-one		Antifungal	C. Albicans, C. Krusei, C. Parapsilopsis	[24]

1-(5-(2-(4-(tert-Butyl)phenyl)-4-methylthiazol-5-yl)-1,3,4-oxadiazol-2-yl)azetidine-3-ol	Antibiofilm	Staphylococci	[25]
3-methoxy-4-((5-phenyl-1,3,4-oxadiazol-2-yl)methoxy)benzonitrile	Anticancer	MDA-MB-453, MCF-7 and Breast Cancer cell lines	[26]
Norfloxain-1,3,4 oxadiazole hybrid	Antibacterial	S. aureus and MRSA	[27]
N-[5'-chloro-ursa-12-en-(2,3)-quinoline-28-oyl]-acetohydrazide	Cytotoxic	HeLa, MDA-MB-231 and SMMC-7721,	[28]
2-((5-(4-(1H-Benzimidazol-2-yl)phenyl)-1,3,4-oxadiazole-2-yl)thio)-1-phenylethan-1 one	Anticancer	HepG2 (cell line of human liver cancer) and A549 (adenocarcinoma of human lung)	[29]
3-((4-fluorophenyl)sulfonamide)-N-(1-((5-mercapto-1,3,4-oxadiazol-2-yl)methyl)-1H-tetrazol-5-yl)-2,2-dimethyl propanamide	Antioxidant		[30]
(1-(4-bromophenyl)-2-((5-(pyridine-4-yl)-1,3,4-oxadiazol-2-yl)thio)ethylidene)hydrazine carbothioamide	Anti-tubercular	Mycobacterim strain	[31]

5[(4-decylpiperazin-1-yl)methyl]-3-phenyl-1,2,4-oxadiazole	Anti-cancer	4T1 cell line	[32]
3(2-((5-((4-chlorophenoxy)methyl)-1,3,4-oxadiazol-2-yl)thio)ethyl)8-methylquinazolin-4(3H)-one	Antifungal	Rhizoctonia Solani and Fusarium graminearum	[33]
6-chloro-2-(2-(5-(4-chlorophenyl)-1,3,4-oxadiazol-2-yl)ethyl)-1H-benzo[d]imidazole	Antibacterial	B. Subtilis	[34]

R1=8-Me
R2=4-CIPhOCH2

Biological characteristic of Benzotriazole derivatives:

Also, the microbes have been evolving themselves in order to resist the activities against them. Therefore, for the complete inhibition of the growth of microbes, chemists have been synthesizing various new compound derivatives using different moieties to come out with a biologically diverse compound with no side effects. In the light of this fact, literature survey was done for another active moiety benzotriazole for biological activity. Like Oxadiazole, Benzotriazole is also an aromatic heterocyclic compound consisting of three nitrogen atoms in different positions with the chemical formula $C_6H_5N_3$ as shown in fig. 2.

Fig. 2: Structures of Benzotriazole

It is well known that almost all the aromatic heterocycles have significant roles in pharmaceuticals and holds many physiochemical properties as well. It is inexpensive and easily available in large quantities in market. Benzotriazole, having properties like excellent ability of leaving group, electron withdrawing and electron donating character, stabilization of radicals and alpha-negative charges makes it a versatile nucleus for antimicrobial activities [35]. Most of the compounds bearing Benzotriazole nucleus shows antibacterial [36], antifungal [37], antioxidant [38], Cytotoxic [39], anticonvulsant [40], antiviral [41], antitumor [42], anti-tubular [43], and anti-inflammatory [44] activities.

Along with its drugs applications it has also been employed as a corrosion inhibitor for Copper and Stainless steel in acidic environment. Moreover, it has the ability to decrease the

corrosion rate of the Carbon steel in NaCl solution containing H₂S at different concentrations [45]. Also there are many reports on Benzotriazole and Benzoimidazole based dicationic Sulphonanes against the human pathogens. The Benzotriazole based dicationic sulphonanes have performed as both antifungal and antibacterial agents remarkably [46]. The biological activities of benzotriazole derivatives have been reported in table-2.

Table: 2 Biological activities of compounds bearing benzotriazole moiety

Compound	Structure	Activity	Against	Ref.
1-[(2,5-Dimethyl)-1H-1,3-benzimidazole-1-yl)methyl]-1-H-1,2,3-benzotriazole		Antifungal	B. Cinera, C. Albicans, A. Niger, and T. Nebreum	[47]
1-(1H-benzo[d][1,2,3]triazole-1-carbonyl)-5-(4-nitrophenyl)-3-phenylformazan		Anthelmintic	Pheretima POsthumia	[48]
1,1-(3-Phenyl-4H-(1,2,4)-triazole-5,yl methyl)-1H-benzotriazole		Antibacterial and Antifungal	Gram +ve: Staphylococcus aureus, Staphylococcus epidermis Gram -ve : E. Coli, Pseudomonas Aeruginosa Fungi- Aspergillus Niger, Aspergillus Fumigates, Aspergillus Flavus	[49]
1,1-(3-Phenyl-4H-(1,2,4)-triazole-5,yl methyl)-1H-benzotriazole		Antioxidant		[50]
1-Undecyl-1H-benzo[d]imidazole		Antifungal	C. Neoformans	[51]

<p>3-(5-((1Hbenzo[d][1,2,3]triazole-1-yl)methyl)-1,3,4-thiadiazole-2-yl)-1-ethyl-4-phenyl-1,3-dihydro-2H-imidazole-2-thione</p>		Anxiolytic	[52]
<p>N-[2-(1H-Benzo[d][1,2,3]triazol-1-yl)quinolin-3-yl)methylene]-4-chlorobenzohydrazide</p>		Vitro cytotoxic	[53]
<p>5-(2-(1S-Hbenzo[d][1,2,3]triazol-1-yl)ethyl)-1H-tetrazol-1-yl))4-aminophenyl)methanone</p>	<p>R-4Cl-C₆H₄</p>	Anti-nociceptic activity	[54]
<p>3-(5-Chloro-1H-benzo[d][1,2,3]triazol-1-yl)-5,5-dimethylcyclohex-2-enone</p>		Antipsychotic	[55]
<p>1-[5,6,7,8-Tetrahydro-[1,2,4]triazolo[1,5-a]pyridine-2-yl(methylene)-1H-benzotriazole</p>		Antitumor	Human tumour cells (colon, prostate, leukaemiaetc.) [56]

5,6-Dichloro-2-[4-hydroxyphenyl]benzotriazole

Antiviral

CVB-5, RSV, BVDV, Sb-1

[57]

4-995-991H-benzo[d][1,2,3]triazol-1-yl)methyl)-1,3,4-oxadiazole-2-ylthio)methyl)-6-methoxy-@H-chromen-2-one

Anti-TB

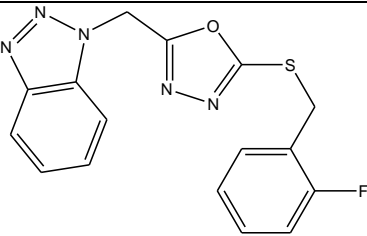
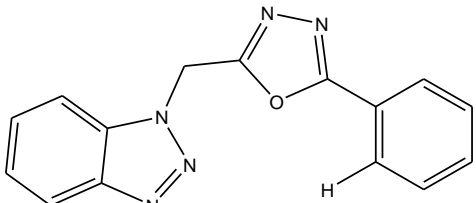
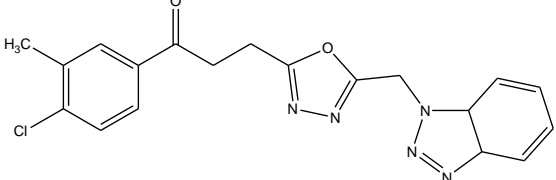
Mtb. H37Pv Strain

[58]

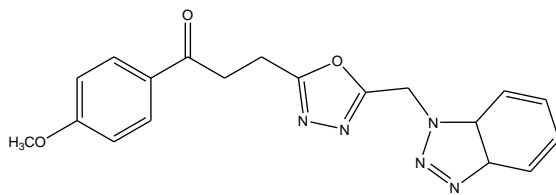
Biological characteristic of Oxadiazoles and Benzotriazole derivatives:

The compounds having both benzotriazole and oxadiazoles moieties reported remarkable biological characteristics such as anticancer, antibacterial, antifungal etc. It gives information that the impact of benzotriazole and oxadiazoles does not vanish if imparted in novel derivatives. Few of the derivatives are shown in table 3.

Table 3: Biological activities of compounds bearing Oxadiazoles and benzotriazole moiety

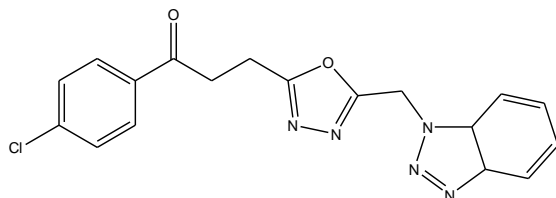
Compound	Structure	Activity	Against	Ref.
1-((5-(2-fluorobenzylthio)-1,3,4-oxadiazol-2-yl)methyl)-1H-benzo[d][1,2,3]triazole		Anticancer	MCF-7 (human breast cancer) and HT29 (human colorectal cancer) cell lines	[59]
1-((5-phenyl-1,3,4-oxadiazol-2-yl)methyl)-1H-benzo[d][1,2,3]triazole		antifungal activity	<i>C. albicans</i> , <i>A. niger</i> and <i>A. flavus</i>	[60]
3-(5-Benzotriazole-1-ylmethyl-[1,3,4]-oxadiazole-2-yl)-1-(4-chloro-3-methyl-phenyl)propan-1-one (C1)		Antibacterial activity	<i>B. subtilis</i> and <i>E. coli</i>	[61]

3-(5-Benzotriazole-1-ylmethyl-[1,3,4]-oxadiazole-2-yl)-1-(4-methoxy-phenyl)-propan-1-one



Antifungal activity *A. niger* *C.albicans* [61]

3-(5-Benzotriazole-1-ylmethyl-[1,3,4]-oxadiazole-2-yl)-1-(4-chloro-phenyl)-propan-1-one



Anticonvulsant and neurotoxicity MES screen Toxicity screen [61]

Conclusion:

The biological activities of oxadiazoles and benzotriazoles have been reported in details. The major activities of both the moieties are antibacterial, antifungal, anticancer, antioxidant, antiviral, anti-inflammatory, anti-tumour and anticonvulsant. Literature review have revealed that both moieties when substituted together in any compound, shows characteristic pharmacological activities on microorganisms and can be helpful to future researchers to come up with more interesting discoveries in the field of Pharmacology. Thus, oxadiazole and benzotriazole moieties are well justified with its solo and duet performance in medicinal field.

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Conflict of Interest:

Authors declare no conflict of interest.

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