These compounds were evaluated for their antimicrobial activity. The chemistry of heterocyclic compounds has been an interesting field of study for a long time. Oxadiazole is a cyclic compound containing one oxygen and two nitrogen atoms in a five member ring. Oxadiazoles have occupied a unique place in the field of medicinal chemistry due to its wide range of activities. From the literature survey 1,3,4-oxadiazole nucleus has been found to possess antimicrobial, antifungal, antiinflammatory, anticancer, insecticidal, ulcerogenic activities etc. The 1,3,4-Oxadiazole have shown significant antimicrobial activity against a wide variety of microorganisms like fungi, Gram +ve strains such as Staphylococcus aureus, Bacillus subtilis and Bacillus lichenus and Gram -ve strains such as Escherichia coli, Vibrio cholera and Pseudomonas aeruginosa. Oxadiazole derivatives and investigation of their chemical and biological behavior have gained more importance in recent decades for biological, medical and agricultural reasons. A large number of drugs used clinically have oxadiazole ring as a structural building block. The capacity of 1,3,4-oxadiazole nucleus to undergo variety of chemical reactions including electrophillic substitution, nucleophilic substitution, thermal and photochemical which make it medicinal backbone on which a number of potential molecules can be constructed. Present review is flooded with reports of antimicrobial activity of 1,3,4-oxadiazole derivatives published in various journals.

**Keywords:** 1,3,4-oxadiazoles, Antimicrobial Activity,

**INTRODUCTION**

The chemistry of heterocyclic compounds has been an interesting field of study for a long time. Oxadiazole is a five membered heterocyclic ring which is a versatile lead compound for designing potent bioactive agents. It exists in four isomeric forms. Out of its four isomers 1, 3, 4-oxadiazole exhibited a wide range of biological activities which includes antibacterial, antitubercular, anticonvulsant, hypoglycemic, antiallergic, enzyme inhibitor, vasodilatory, antifungal, cytotoxic, antinflammatory, analgesic, hypolipidemic, anticancer, insecticidal, ulcerogenic activities etc. The 1,3,4-Oxadiazole have shown significant antimicrobial activity against a wide variety of microorganisms like fungi, Gram +ve strains such as Staphylococcus aureus, Bacillus subtilis and Bacillus lichenus and Gram -ve strains such as Escherichia coli, Vibrio cholera and Pseudomonas aeruginosa. Oxadiazole derivatives and investigation of their chemical and biological behavior have gained more importance in recent decades for biological, medical and agricultural reasons. A large number of drugs used clinically have oxadiazole ring as a structural building block. The capacity of 1,3,4-oxadiazole nucleus to undergo variety of chemical reactions including electrophillic substitution, nucleophilic substitution, thermal and photochemical which make it medicinal backbone on which a number of potential molecules can be constructed. Present review is flooded with reports of antimicrobial activity of 1,3,4-oxadiazole derivatives published in various journals.

**Keywords:** 1,3,4-oxadiazoles, Antimicrobial Activity,

**ABSTRACT**

Heterocyclic compounds possess diverse biological properties that have lead to intense study and research of these compounds. One of these compounds is oxadiazole which has been found to exhibit various pharmacological activities. Oxadiazole is a five membered heterocyclic ring which is a versatile lead compound for designing potent bioactive agents. It exists in four isomeric forms. Out of its four isomers 1, 3, 4-oxadiazole exhibited a wide range of biological activities which includes antibacterial, antitubercular, anticonvulsant, hypoglycemic, antiallergic, enzyme inhibitor, vasodilatory, antifungal, cytotoxic, antinflammatory, analgesic, hypolipidemic, anticancer, insecticidal, ulcerogenic activities etc. The 1,3,4-Oxadiazole have shown significant antimicrobial activity against a wide variety of microorganisms like fungi, Gram +ve strains such as Staphylococcus aureus, Bacillus subtilis and Bacillus lichenus and Gram -ve strains such as Escherichia coli, Vibrio cholera and Pseudomonas aeruginosa. Oxadiazole derivatives and investigation of their chemical and biological behavior have gained more importance in recent decades for biological, medical and agricultural reasons. A large number of drugs used clinically have oxadiazole ring as a structural building block. The capacity of 1,3,4-oxadiazole nucleus to undergo variety of chemical reactions including electrophillic substitution, nucleophilic substitution, thermal and photochemical which make it medicinal backbone on which a number of potential molecules can be constructed. Present review is flooded with reports of antimicrobial activity of 1,3,4-oxadiazole derivatives published in various journals.

**Keywords:** 1,3,4-oxadiazoles, Antimicrobial Activity,
Synthesized compounds were subjected to antimicrobial, anti-fungal and anti-tubercular activity. Anti-microbial activity was carried out against *Escherichia coli*, *Pseudomonas aeruginosa*, *Klebsiella pneumoniae* and *Staphylococcus aureus* at a concentration of 100 μg/ml. Streptomycin was used as standard. Anti-fungal activity was performed against *Aspergillus niger*, with test compounds at a concentration of 100μg/ml. Ketocanazole was the standard drug employed. Finally anti-tubercular activity was observed at concentrations 100μg/ml on *Mycobacterium tuberculosis* using Rifampicin as standard.15

A series of 5-(2-aminophenyl)-1,3,4-oxadiazole-2(3H)-thione derivatives have been synthesized by manich reaction. The reaction progress of the synthesized compounds was checked by TLC. The different in melting points of the synthesized compounds indicated the formation of new chemical analogues. The structures of the newly synthesized compounds were confirmed by IR and 1H NMR spectral data. Most of them were tested for their antibacterial and antifungal activities at a concentration of 100 μg/ml.16

A series of Mannich bases 5a-5h were synthesized by the reaction of 5-[(2-ethylthio)-1H- benzimidazol–1-yl]-methyl–1,3,4–oxadiazole–2-thione 4 with formaldehyde and appropriate amines by conventional and microwave techniques. The reaction rate and yields were enhanced under microwave irradiation technique rather than conventional technique. Structures were characterized by means of spectral data and elemental analyses. The antibacterial screening against *S. aureus*, *E. coli* and *P. aeruginosa* at three different concentrations revealed that compound 5f is significantly active.17

Some new 3-acetyl-5-(3-chloro-1-benzo[b]thiophen-2-yl)-2-substituted phenyl-2,3-dihydro-1,3,4-oxadiazoles and 2-(3-chloro-1-benzo[b]thiophen-2-yl)-5-substituted phenyl-1,3,4 oxadiazoles have been synthesized and evaluated for antimicrobial activity. The structures of newly synthesized compounds (4a-h) and (5a-h) have been confirmed by spectroscopic techniques such as IR, 1H NMR and elemental analysis. All the compounds were screened for their antibacterial activities against *Staphylococcus aureus*, *Bacillus subtilis*, *Escherichia coli* and *Pseudomonas aeruginosa* and for antifungal activity against *Candida albicans* and *Aspergillus niger*. The compounds exhibited significant antibacterial and moderate antifungal activities. Compounds 4c and 4e were found to be most potent with activities, even better than standard drug ciprofloxacin against *S. aureus* and *B. subtilis*.18

New 5-alkyl and 3-(2,4-dimethylphenyl) substituted 1,3,4-oxadiazole-2-thione derivatives were synthesized by the ring closure reactions of various acylhydrazides with carbon disulphide. Mannich bases for some of these compounds were also synthesized by condensation with benzaldehyde and primary amines. All new compounds were characterized by spectral data. Most of them were tested for their antibacterial and antituberculostatic activity. The in vitro tuberculostatic activity of 1,3,4-oxadiazole-2-thione derivatives was studied against *Mycobacterium tuberculosis* using Lowenstein Jensen’s egg medium by serial twofold dilution and the retardation of the growth rate studied for six weeks at 37°C. The tuberculostatic concentration was 0.03 g/ml. The antibacterial activity of the compounds was tested by agar plate diffusion against *Staphylococcus aureus* using tetracycline as the standard.19

A series of novel 2,5-disubstituted 1,3,4-oxadiazole derivatives were synthesized and tested for their in vitro antimycobacterial activity. Some compounds showed interesting activity against a strain of *Mycobacterium tuberculosis* H37Rv. The result of the antimycobacterial activity tests revealed that 2-(2-naphthoxy)methyl)-5-phenoxyethyl-1,3,4-oxadiazole (IVd) exhibited >90% inhibition at MIC ~6.25. Our results indicate that the oxadiazole derivatives having a β-naphthoxy methyl group at the C-2 position and a phenoxy methyl group at the C-5 position enhances the anti-tubercular activity of the synthesized compounds.20
Copper(II) complexes of chromen-2-one-3-carboxyhydrazide and 2-(chromen-3-onyl)-5-(aryl)-1,3,4-oxadiazole derivatives have been synthesized. The structural features have been determined from their microanalytical, magnetic susceptibility, molar conductance, IR, UV VIS, 1H NMR and ESR spectral data. Distorted octahedral geometry for all the Cu(II) complexes is proposed. Molecular modeling studies have been made for the rapid structure building, geometry optimization and molecular display. These complexes show the conductance values, supporting their non-electrolytic nature. The monomeric nature of the complexes was confirmed from their magnetic susceptibility values. These complexes have been screened for their antimicrobial activities against some bacterial species like S.aureus, E.coli, Pseudomonas aeruginosa and few fungal strains C.albicans and Cryptococcus neoformans.\\n
The synthesis of 1-{(5-sustituted-1,3,4-oxadiazol-2-yl) methyl}-4-propylpiperazines VIa-l was carried out by refluxing the 1-propylpiperazine II with ethylchloroacetate III in dry acetone in the presence of potassium carbonate and subsequent hydrazinolysis with hydrazine hydrate. Finally 2-(4-propylpiperazin-1-yl)aceto- hydrazide V was treated with appropriate carboxylic acids in the presence of phosphorous oxy chloride to produce title compounds. The newly synthesized compounds were tested for its antibacterial, antifungal and antihelmintic activity. Compound Vlg exhibited potent antihelmintic activity against earthworms Eudrilus species, Megascoplex konkanensis and Pontocotex corethrus at a dose of 2 mg/mL. The structures of newly synthesized compounds were established on the basis of elemental analysis, IR, 1H NMR and mass spectral data.\\n
In the present investigation, four 1,3,4-bis-oxadiazole derivatives were synthesized as potential antimicrobial agents. The compounds are: 5,5′-dimercapto-bis-[1,3,4-oxadiazol-2-yl]propane (2a), 5,5′-dimercapto-bis-[1,3,4- oxadiazol-2-yl]butane (2b), 5,5′-dimercapto-bis-[1,3,4- oxadiazol-2-yl]octane (2c) and 5,5′-dibenzylthio-bis-[1,3,4- oxadiazol-2-yl]butane (3). The above newly synthesized compounds were investigated for their antibacterial, antifungal and mutagenic activities. The results of the biological activities revealed that the compounds 2a-c exhibited both antibacterial and antifungal activities against S. aureus and B. subtilis. Compound 2a also showed activity against P. aeruginosa. All the above compounds and compound 3 exhibited activity against C. albicans. Genotoxic studies showed that compound 2a had a weak base pair substitution mutagenicity but none of them exhibited a frameshift mutagenic action using Ames test.\\n
A series of 5-{3′-oxy-6′-(substituted aryl)-2′,3′,4′,5′- tetrahydropyridazin-2i-ylmethyl}-2-substituted 1,3,4- oxadiazole has been synthesized. All the final compounds were structurally elucidated on the basis of IR, 1H-NMR, MS data and elemental analysis and screened for antibacterial, antifungal and antitubercular activity. All the compounds are evaluated for their antibacterial activity against E.coli, S. aureus, Micrococcus luteus and Klebsiella pneumoniae by using cup plate technique in the nutrient agar at 100 µg/mL concentration. Antitubercular activity was determined using...
the BACTEC 460 system. All the synthesized compounds were screened at 6.25 μg/mL against M. tuberculosis H37 Rv comparable with that of standard rifampicin and isoniazid. All the final compounds were evaluated for antifungal activity against C. albicans and C. neoformans by using cup-plate method in the Sabouraud agar media. The zone of inhibition (mm) of each compound was determined and compared with standard drug fluconazole.26

In this study a series of new 1-(2-aryl-5-phenethyl-1,3,4-oxadiazol-3(2H)-yl)ethanones 2a-e was synthesized by the cyclization of imines 1a-e using acetic anhydride. The products were evaluated for anti-bacterial and anti-fungal activity. Among the newly synthesized compounds, 1-(2-(4-(dimethylamino)phenyl)-5-phenethyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (2a) and 1-(2-(4-chlorophenyl)-5-phenethyl-1,3,4-oxadiazol-3(2H)-yl)ethanone (2b) were found to possess maximum activity against the tested strains of S. aureus and P. aeruginosa. It was concluded that para-substitution enhances the activity of synthesized oxadiazoles.27

New 5-phenyl-1,3,4-oxadiazole-2-thiol derivative was synthesized by the ring closure reactions of benzohydrazides with carbon disulphide in presence of ethanolic KOH followed by substitution with secondary amines at the 2nd position. All the newly synthesized compounds were characterized by IR, NMR and LC-MASS spectral data. Most of them were tested for their anti-inflammatory and antibacterial activity. Antibacterial activity was carried out against P. vulgaris, P. aeruginosa, E. coli by the cup plate method at a conc. of 50μg/ml and 100μg/ml. The standard drug used was Tetracycline and DMF was kept as control.28

A series of 2-(Phenyl substituted)-5-indole-1,3,4-oxadizole derivatives were prepared. In this study, it was planned to incorporate the oxadiazole ring system into indole ring. Synthesis of derivatives of 1,3,4-oxadiazoles from different benzaldehydes. Characterization of the synthesized compounds along with their antimicrobial activity on different strains. Standard drugs used (Norfloxacin and Fluconazole) were taken. Out of these 4 compounds, only three were found effective against bacterial strains and none of the synthesized compound was found effective against fungal strain. The compounds which were active against bacterial strains were effective at a much higher concentration as compared to the standard drug norfloxacin.29

A survey of literature revealed that a slight modification in the structure can result in qualitative as well as quantitative changes in the activity, which prompted us to undertake the synthesis of various new 2-Amino-5-(substituted)phenyl-1,3,4-Oxadiazole derivatives with the aim of having improved activity and lesser toxicity. The synthesized compounds were evaluated their antimicrobial properties against Staphylococcus aureus, Escherichia coli, and Pseudomonas aeruginosa, Candida albicans, and using microbroth dilution method. Standard antibiotics namely Norfloxacin was used for comparison with antibacterial activity.30

3,5-bis(5-(furan-2-yl)-1,3,4-oxadiazol-2-yl)azo dyes were synthesized by multistep reaction sequences, which is diazotized and coupled with different naphthols and quinoline. Structure of newly synthesized compounds were characterized and confirmed by IR, NMR and Mass spectral studies. The newly synthesized azo dye fused with (5-(furane-2-yl)-1,3,4-oxadiazole) were screened for their acute toxicity and gross behavioral studies and in-vitro anti-microbial activity. Synthesized compounds exhibit significant biological activity and can certainly be considered in discovering safer biologically active molecules. The antimicrobial activity of the test compounds (5a-g) were screened by agar well radial diffusion method against bacterial strains belonging to Staphylococcus aureus, Pseudomonas aeruginosa, Bacillus subtilis and Escherichia coli and fungal strains Candida albicans and Candida parapsilosis respectively.31

A series of 2-[5-(substituted sulfanyl)-1,3,4-oxadizol-2-yl]phenol derivatives were prepared. 1, 3, 4 oxadiazole was synthesized by condensation reaction between 2-hydroxybenzohydrazine and carbon disulfide. This derivative on treatment with different aromatic halides produced the
desired final products. The in-vitro antibacterial activity of synthesized compound was tested against Gram-positive and Gram-negative microorganisms (Staphylococcus aureus ATCC 9144, Bacillus subtilis ATCC 6633, Pseudomonas aeruginosa MTCC No. 1688, Gram negative: Escherichia coli ATCC 25922) by filter paper disc method. The in-vitro antifungal activity was tested against Candida albicans by filter paper disc method. All the compounds showed good activity against all cultures. A series of N-(substituted aryl -1,3,4-oxadiazole -2 yl) methyl-N-(4H-1,2,4 –triazol-4 yl) benzamide derivative was synthesized by condensation of 4 amino triazole and benzoyl chloride. The identification and characterization of the synthesized compounds were carried out by Elemental analysis, melting point, Thin Layer Chromatography, FT-IR, and NMR data to ascertain that all synthesized compounds were of different chemical nature than the respective parent compound. Antimicrobial and antifungal activities of the final compounds have been evaluated and all the compounds have shown significant inhibition of bacterial and fungal growth. 

Alkyl, alkenyl, sulfonil, thiocarbamates and Mannich derivatives were synthesized and characterized through IR, NMR, and Elemental analysis. It is of interest to report the isomerization rearrangement of propynyl to allene group in Mannich reaction under basic condition. The most promising compound as antibacterial agent was 5-(pyridyl)-1, 3, 4-oxadiazole-2-benzylthiocarbamates. The MIC for the synthesized compounds indicates that the conversion of sulfhydryl group in 1,3,4-oxadizole into alkyl 3, allene 8, sulfonil 13 derivatives and manniich product 19 showed a weak antimicrobial activity. However, thiocarbamates 16 and 17 were effective against Gram positive and Gram negative bacteria with less activity against fungi. These results promote our interest to investigate further the thiocarbamate series.

Microwave-assisted as well as conventional synthesis of 5-substituted-2-(2-methyl-4-nitroimidazolyl)-1,3,4-oxadiazoles containing the nitroimidazole moiety is carried out and their antibacterial, antifungal and anti-inflammatory activity is reported. Studies on the antibacterial activity of synthesized compounds 7 have been carried out against four pathogenic organisms, viz., Staphylococcus aureus (G+), Klebsiella pneumoniae (G–), Escherichia coli (G–) and Pseudomonas aeruginosa (G–). The antibacterial activity of the newly synthesized compounds in the present investigation was assessed by the cup-plate method.

In the present study, a new 1,3,4-oxadizole and 1,3,4-thiadiazole derivatives were synthesized. Benzol hydrazine (2) was prepared by the hydrazinolysis of methyl benzoate (1) with hydrazine hydrate in abs. ethanol. Condensation of (2) with chloroacetic acid in phosphorus oxychloride results in the formation of 2-phenyl-5-chloromethyl-1,3,4-oxadiazole (3), which on reaction with 2,5-dimercapto-1,3,4-thiadiazole in pyridine affords 2,5-di-[5-phenyl-1,3,4-oxadiazole-2-thiomethyl]-1,3,4-thiadiazole (5). The newly synthesized compounds were characterized by CHNS elemental analysis, IR and NMR spectral data. The newly synthesized compounds were screened for their in vitro antibacterial activity. The prepared compounds manifested promising biological activity.

A new series of 2, 5-disubstituted-1, 3, 4-oxadiazoles were prepared by reaction of nicotinic acid hydrazide with various substituted aromatic acids in presence of POCl₃, as potential biological active agents. The newly synthesized compounds were confirmed from IR, MASS and 1H NMR spectral data. Some of the synthesized compounds showed very good antifungal activity when compared to antibacterial activity. Ten compounds from the series were screened for their antibacterial and antifungal activity. Antibacterial activity was carried out against S.aureus, P. aeruginosa, E.coli and B.subtilis by the cup plate method at a conc. of 100 µg/ml. The standard drug used was Ampicillin and DMF was kept as solvent control. The antifungal studies were carried out against fungus C.albicans and A.niger using Griseofulvin as standard.
A series of 2,2′-(5-nitrobenzene-1, 3-diyl) bis (5-alkyl-1, 3, 4-oxadiazole) (2a-e) 5,5′-(5-nitrobenzene-1,3-diyl)bis(1,3,4-oxadiazole-2-thiol) (3) and 5,5′-(5-nitrobenzene-1,3-diy)bis(4-amino-4H-1,2,4-triazole-3-thiol(5) were obtained via reaction of 5-nitro iso-phthalic dihydrazide (1). All these newly synthesized compounds were characterized by IR, NMR and Mass, spectral studies. Newly synthesized compound displayed potent antibacterial and antiinociceptive activity. Antibacterial activities were determined by the well-diffusion method.

The synthesis of 1-[(5-sustituted-1,3,4-oxadiazol-2-y1) methyl]-4-benzylpiperazines Vla-j was carried out by refluxing the 1-benzylpiperazine II with ethylchloroacetate III in dry acetone in the presence of potassium carbonate and subsequent hydrazinolysis with hydrazine hydrate. Finally 2-(4-benzylpiperazin-1-y1)aceto- hydrazide V was treated with appropriate carbboxylic acids in the presence of phosphorous oxy chloride to produce title compounds. All the title compounds (Vla-j) were screened for anticancer activity using HBL-100 cell lines by MTT method and antibacterial activity against B. subtilis, S. aureus, E.coli and P. vulgaris.

The structures of newly synthesized compounds were established on the basis of elemental analysis, IR, 1H NMR and mass spectral data.

Reaction of isonicotinohydrazide with different aromatic aldehydes under the microwave irradiation gives Schiff’s bases. These Schiff’s bases were converted into 1, 3, 4-oxadiazole derivatives by treating with acetic anhydride under the microwave irradiation. The structures of the compounds were confirmed by elemental analysis, IR, 1HNMR and Mass spectral data’s. The synthesized compounds were screened for antimicrobial, analgesic and anti-inflammatory activities. The antibacterial activity of all the synthesized compounds (2a-m) were examined against Gram-positive (S.aureus) and Gram-negative (E.coli) organisms by measuring zone of inhibition. The antibacterial activity was performed by Agar diffusion method [27,28] at the concentration level 200,100,50 μg/mL ciprofloxacin was used as standard drug at concentration of 50 μg /ml.

CONCLUSION

This literature review reveals that 1, 3, 4 Oxadiazole have diverse biological activity, and very simple synthetic process too. It has shown the good anti-microbial activities. By the present scenario it can be concluded that 1, 3, 4 Oxadiazole have remarkable anti-microbial activity.

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