STM JOURNALS

Journal of
Modern Chemistry &
Chemical Technology

ISSN: 2229-6999 (Online)
ISSN: 2321-5208 (Print)
Volume 15, Issue 1, 2024
January–April
DOI (Journal): 10.37591/JoMCCT

http://sciencejournals.stmjournals.in/index.php/JoMCCT/index

Research JoMCCT

# Oxadiazole Derivatives Recent Progress in Synthesis and Bioactivity

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***Abstract***

*Over the past few decades, significant advancements have been made in the development of heterocyclic derivatives, leading to the production of numerous novel agents, both synthetic and natural in origin. Because of its numerous biological properties, including antibacterial, antiviral, and antifungal properties, thiazole is a special five-membered heterocyclic motif among heterocyclic compounds. It is utilized as a fundamental building block in many pharmaceutically significant compounds. To the best of our knowledge, there are currently over 90 derivatives containing thiazoles that are being studied clinically, and several thiazole analogs have been given the go-ahead to treat a range of illnesses. Thiazole derivatives can be further thoroughly investigated as the possibly privileged scaffolds in an effort to find novel medications with enhanced therapeutic efficacy and comparable biological targets. In order to help medical researchers rationally create more potent thiazole-containing therapeutic candidates, this article attempts to summarize the uses and synthetic pathways of a few typical thiazole-containing medications that have been approved for use in clinical settings. Numerous significant and powerful pharmaceutical products, such as raltegravir, butalamine, fasiplon, oxolamine, and pleconaril, contain stable isomeric forms of oxadiazoles. Many oxadiazole derivatives are widely used as possible medicinal agents and are quite well-liked. Nonetheless, utilizing biological and in-silico models, several researchers are working and have tried to discover additional synthetic analogues for anticancer, antifungal, and anti-HIV medicines. An effort has been made to highlight the pharmacology and chemistry related to oxadiazole and its derivatives.*

**Keywords:** Oxadiazole, Biological activities, analgesic activity, anti-bacterial activity, anti- convulsant activity, anti-tubercular activity

## INTRODUCTION

Green chemistry has gained a lot of attention recently because of its potential to reduce waste, minimize dangers to individuals, ameliorate chemical hazards, and reduce environmental pollution. A catalyst is required in organic synthesis in order to accelerate the reaction and produce a large amount of the target product. The creation of heterogeneous catalytic systems for liquid-phase chemical and biological transformations is an important subject of study because of its straightforward catalyst separation, recovery, and recycling. The creation of more effective and clean processes depends on this. Polysaccharide-based natural biopolymer chitosan has garnered significant attention in the scientific and technical fields. The "green" accessibility of chitosan-based catalysts may be advantageous for organic catalysis [1].

According to data from the International Diabetes Foundation (IDF), 629 million people worldwide

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Received Date: March 12, 2024
Accepted Date: May 10, 2024
Published Date: June 12, 2024

**Citation:** J Neha Sahu, Rizwan Arif. Oxadiazole Derivatives Recent Progress in Synthesis and Bioactivity. Journal of Modern Chemistry & Chemical Technology. 2024; 15(1): 62–67p.

 

may have diabetes by 2045. Emergent elements that contribute to the spread of Type II diabetes among the 352 million individuals at risk include eating habits, a sedentary lifestyle, and a progressing technology culture. Diabetes mellitus is a metabolic disease marked by persistent hyperglycemia brought on by high-calorie diets high in fats, carbs, and proteins. It is brought on by insufficient insulin secretion. Type II diabetes is associated with obesity, hypertension, dyslipidemia, cardiovascular disease, and other conditions. It could cause tissue or vascular damage, which could result in major diabetes consequences such nephropathy, neuropathy, and retinopathy. α-glucosidase and α-amylase are the two main enzymes that aid in lowering the postprandial hyperglycemia linked to Type II diabetes mellitus (DM2). Through its ability to prevent the body from absorbing starch from diet, α-amylase lowers blood glucose levels in the body. α-amylase inhibitors can be broadly classified into two groups: (i) proteinaceous inhibitors and (ii) non-proteinaceous inhibitors [2].

Potential anti-diabetic medications include chalcones, flavones, benzo-thiazoles, and other non-proteinaceous inhibitors. In contrast, the rise of bacterial resistance in harmful microbes is one of the most urgent global public health issues. Antibiotic resistance may have an effect on the veterinary and agricultural industries, the healthcare system, and people at any stage of life [3].

## LITERATURE

### 1,3,4-oxadiazole and Napecotic Acid Hybrids

Singh et al. created a set of 15 hybrids based on 1,3,4-oxadiazole and nipecotic acid. When compared to traditional tiagabine, compound and exhibited the greatest antiepileptic activity among all the produced compounds, providing a percentage of protection. These compounds were also found to possess potent antidepressant qualities. None of the drugs were neurotoxic, and they were all safe for the liver and kidneys [4].

Many novel 1,2,4-oxadiazole compounds were designed and synthesized by Wang et al. using the multi-target guided ligand approach. The compounds were evaluated for their anti-neurin-inflammatory, neuroprotective, and impacts on cell glucose consumption properties in addition to their capacity to inhibit glycogen synthase kinase. The outcomes showed the compound's inhibition and anti-neuro-inflammatory potency [4].

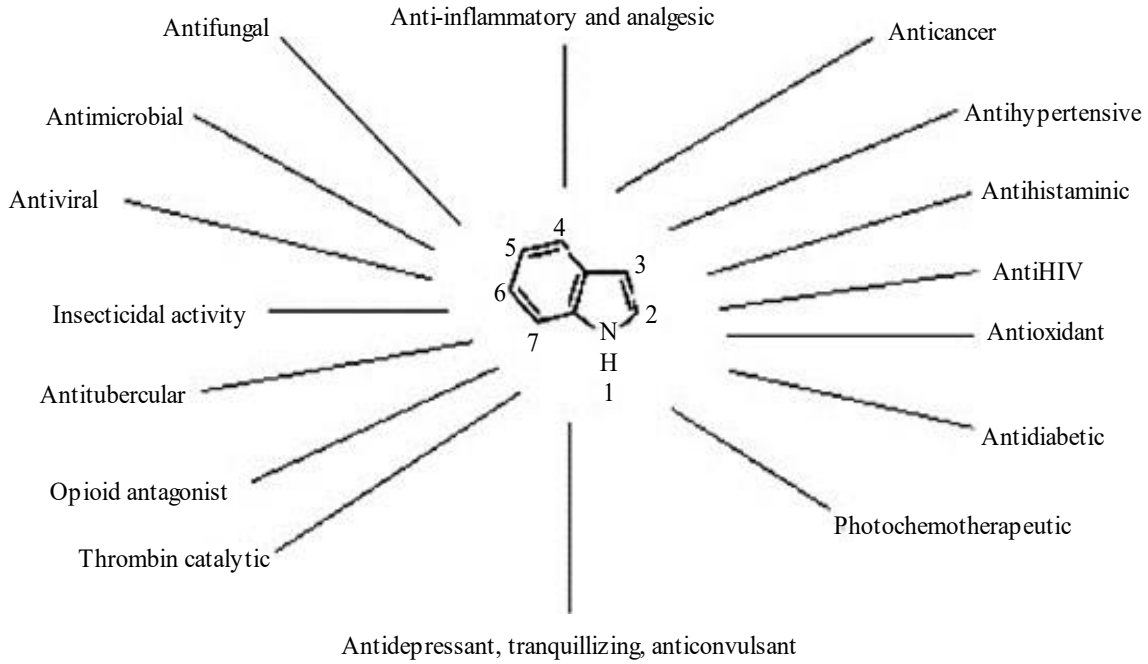


**Figure 1.** Shown: Biological significance in different areas.

 

When it came to glucose consumption, the chemical outperformed the drug Metformin. Compound significantly reduced the induced hyperphosphorylation of Tau, inhibiting it at the cellular level. It's interesting to note that the substance effectively inhibited intracellular production. Furthermore, these drugs can traverse the blood-brain barrier and are safe at concentrations. Finally, in vivo studies demonstrated that the chemical attenuated the cognitive damage generated in the mouse model by scopolamine [5].

**Antifungal Properties**

Organisms classified as fungi are separate from the kingdoms of plants and animals. They are present in humans, animals, plants, soil, moisture, air, and decomposing organic materials. In our ecosystem, fungi and bacteria work together to break down organic matter into simpler forms that plants can use. They consist of molds, fungi, mushrooms, and domestic yeast, among many more. The most common types of fungi include Aspergillus, Mucormycetes, Histoplasma, Candida, Pneumocystis, and Cryptococcus [6].

Numerous types of fungi generally do not infect people, but opportunistic infections—which afflict those with weakened immune systems—can result in disease. Figure 1 shown: Biological significance in different areas. A number of illnesses can lower our immunity, including diabetes, blood cancers, iron overload, trauma, steroid medication side effects, malnourishment, etc [7].

Mucormycosis, often known as black fungus, is a rare and fatal fungal disease that is brought on by a type of mold called micromycetes. This infection usually affects a small number of subgroups, such as Rhizomucor, Mucor, and Rhizopus. These fungi are angioinvasive, meaning they cause tissue necrosis and death by entering the surrounding blood vessels and inflicting harm. Because of how severe these illnesses are, most people would not survive if they were left untreated. The death rate linked to it ranges from 25% to 90%. There is a significant chance of dying if the infection spreads to the brain. Early detection and treatment are therefore highly valued [8].

A black fungus infection can cause pain, redness around the nose and/or eyes, coughing, fever, chest pain, shortness of breath, headaches, altered mental status, bloody vomits, toothaches, double vision, and painfully loosened teeth [9].

**Recent Findings on the Biological Significance of the Indole Nucleus**

The human body uses inflammation as a defense mechanism against stimuli or foreign particles that could harm or injure its cells. The main indicators of inflammation in any tissue are pain, heat feeling, swelling, and redness, which eventually changes the tissue's function. Numerous microcirculatory processes, including the formation of white blood cells, changes in vascular permeability, and is necessary for the creation of cytokines such as not type in sera, even while inoculating mice with poly I:C causes the production of cytokines as well as type in mice (Kato et al., 2006) [10].

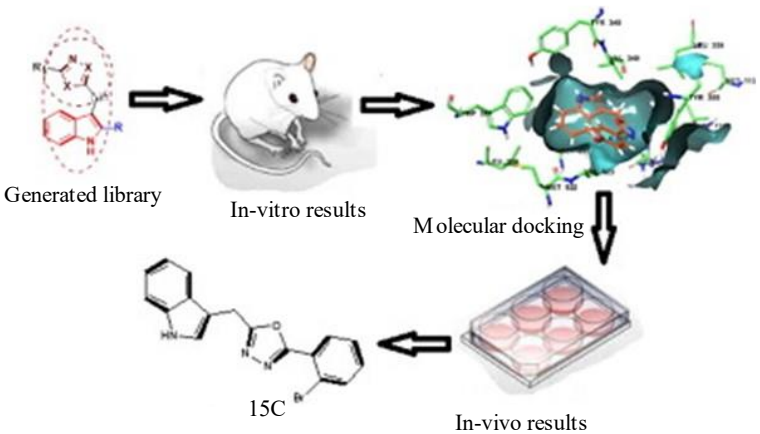


**Figure 2.** Shown: The biological significance of the indole nucleus.

 

The crystal structure of coupled to dsRNA showed that two molecules are dimerized by dsRNA's binding to the N- and C-terminal regions of TLR3 LRRs.

Mediated microbial identification plays a critical role in protecting hosts against infections. Conversely, excessive ligand-induced reactions result in fatal septic shock syndrome. Figure 2 shown: The biological significance of the indole nucleus. These findings suggest that proper activation is essential for eliminating invasive infections without endangering the host [11].

A growing body of research highlights how crucial location is for ligand detection within the cell (Barton and Kagan, 2009). It is still unclear how nucleotide-recognizing are drawn from the ER into the endolysosome compartment [12].

## Approach

### *Antimicrobial Agents*

To far, about 1400 different types of microorganisms have been identified in literature, including fungi, viruses, bacteria, protozoa, and helminthes. These microorganisms can infect humans and often cause fatal infections. Surprisingly, only 20 of them—mostly bacteria—are responsible for over two thirds of the fatal cases. The number of predicted infections-related deaths in high-developed countries has been falling consistently, with estimates of 13 million in 2050 compared to 16 million in 1990. Nonetheless, the toll that pneumonia, HIV/AIDS, and other diseases take on people is still rather high.diarrhea, tuberculosis, malaria, and a host of other ailments. Developing innovative treatments and discovering new, effective antibacterial/antiviral drugs are two issues of the greatest significance considering the numerous pandemic threats that Europe and the rest of the world are facing [13].

### Agents Anticonvulsant

Over 50 million people worldwide of all ages suffer with epilepsy, a neurological illness marked by frequent and unexpected seizures. Although some cases of epilepsy are brought on by brain injuries, tumors, infections, or congenital defects, the exact etiology of the condition is still unknown. These days, there are many examples of commercially available medications (such as carbamazepine, phenobarbital, phenytoin, diazepam, etc.); however, about 30% of patients do not respond well to these medications, and some unfavorable side effects, like sleeplessness, lightheadedness, and gastrointestinal issues, have been reported. This makes the creation of fresh, secure, and efficient anti-epilepsy medications essential [14].

A number of 1,2,4-oxadiazoles based on acridone and coumarin were recently presented by Mohammadi-Khanaposhtani M. and colleagues. These compounds were tested as effective anticonvulsants against seizures in mice generated by maximum electroshock (MES) and pentylenetetrazole (PTZ) [15].

### Anti-Drowsiness Drugs

Inadequate or insufficient sleep duration is associated with a health condition called insomnia. It usually shows up as insomnia, trouble focusing, trouble learning, low mood, anger, and sometimes even as a heart disease, hypertension, dementia, or melancholy risk factor. Sleeplessness is estimated to affect up to 70% of individuals globally, making it a significant public health concern. For a long while, GABA antagonists were the cornerstone of treatment for insomnia; however, their high risk of addiction and subsequent worsening of mood encouraged the development of other sleep aids. Clinical trials for the neuropeptides known as orexin A and B's antagonists, lemborexant and almorexant, were started in 1998 after the neuropeptides were identified [16].

### Anti-Diabetic Intent

Diabetes Mellitus is a group of metabolic diseases characterized by a blood sugar level that is consistently elevated. The three most common signs of diabetes are increased thirst, increased hunger,

 

and frequent urination. Untreated diabetes can result in a number of health problems. Serious long-term effects of diabetes include nerve damage, stroke, cardiovascular disease, cognitive decline, eye damage, foot ulcers, and chronic kidney failure. Diabetes is brought on by either the pancreas's inability to create enough insulin or the body's cells' inability to use the insulin that is produced. Diabetes mellitus can be treated with a vast array of drugs that lower blood glucose levels. All of them—aside from insulin, exenatide, and pramlintide—are taken orally, earning them the moniker "oral hypoglycemic medications [17]."

In order to investigate the antidiabetic effect of benzothiazole derivatives, Prabhat et al. synthesized them. Compared to other compounds, the produced compounds resulted in a higher decrease in blood glucose levels in diabetic rats In order to investigate the antidiabetic effect of benzothiazole derivatives, Prabhat et al. synthesized them. Compared to other compounds, the produced compounds resulted in a higher decrease in blood glucose levels in diabetic rats. According to estimates, the produced compounds had values between 100 and 1000 mg/kg, respectively. Nabil and colleagues developed heterocyclic compounds based on curcumin that had potent antidiabetic properties, exhibiting values of 200.2 μM and 95.5 μM, respectively. The authors found that curcumin's pyranone and pyrimidinone derivatives showed great promise in the fight against diabetes [18].

**1,3,4-Oxadiazoles' Pharmacological and Antimicrobial Activities**

The necessity for novel, safer, and more effective antimicrobial drugs has been highlighted by the recent growth of antibiotic resistance in the treatment of infectious diseases. Excellent antibacterial activity for compounds containing the 1,3,4-oxadiazole core has been reported by numerous studies [19].

Oliveira et al. have recently reported the production and anti staphylococcal activity of 1,3,4-oxadiazolines against methicillin- and amino glycoside-resistant strains of Staphylococcus aureus that encode efflux proteins (multidrug-resistant; MDR). All of the compounds exhibited effective anti-staphylococcal activity, making them 2–8 times more potent than the common medication chloramphenicol [20].

## CONCLUSIONS

One of the most important classes of organic molecules in medical chemistry are heterocyclic compounds, which are utilized as drugs to treat a variety of illnesses. Heterocyclic compounds have been demonstrated to have a broad range of medicinal pharmacological uses through a number of remarkable achievements. Because of their fascinating biological activity, heterocyclic molecules are useful synthetic targets and important structural elements in organic synthesis and medicinal chemistry. The pharmaceutical world is very interested in the prospective uses of heterocycles as antiviral, anticancer, anti-inflammatory, antifungal, antibacterial, anti-Alzheimer's, and antidiabetic medicines, among other uses. It's interesting to note that in continuing drug development, a growing number of heterocycles have been identified as possible therapeutic candidates.

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