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Use of NMR and Other Spectroscopy Techniques in Heterocyclic Oxadiazole Derivatives Studies: A Review

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Abstract

*It was possible to create a number of novel symmetrical 2,5-dialkyl-1,3,4-oxadiazoles with substituents including carboxymethylamino, isopropyloxycarbonylmethylamino, and bromine at the terminal positions of the alkyl groups. The multistep process that was devised used hydrazine hydrate, phosphorus oxychloride, and commercially available acid chlorides that varied in alkyl chain length and terminal substituent.Diisopropyliminodiacetate was an easy way to substitute the intermediate bromine-containing 2,5-dialkyl-1,3,4-oxadiazoles. This was followed we summarized the literature databy hydrolysis in an aqueous methanol solution, which produced the corresponding 1,3,4-oxadiazoles with carboxymethylamino substituents. All of the products' structures were verified using standard spectroscopic techniques such 1H NMR, 13C NMR, and HRMS.*One of the most significant heterocyclic fragments and a potential building block for drug discovery is the 1,3,4-oxadiazole scaffold. Substituted 1,3,4-oxadiazoles exhibit a wide range of pharmacological properties, including antitubercular, anticancer, anti-inflammatory, antibacterial, antiviral, antifungal, insecticidal, antioxidant, and analgesic effects. Additionally, licensed medications such as the antiviral drug Raltegravir, the anticancer drug Zibotentan, and the antihypertensive drugs Tiodazosin and Nesapidil contain the 1,3,4-oxadiazole core. This review compiles the primary methods for determining potential avenues for structural modification and pharmacological activity of non-condensed heterocyclic systems based on the 1,3,4-oxadiazole ring, highlighting their promise as targets in contemporary bioorganic and medicinal chemistry.

Keywords: 1,3,4-oxadiazoles; organic ligands; heterocycles; substitution; spectral characterization

INTRODUCTION

Oxadiazoles are heterocyclic compounds with five members. Oxadiazoles can take on several isomers depending on the position of the heteroatom. The most extensively researched of them is the 1,3,4-oxadiazole derivative, which has a broad spectrum of biological activity and great stability. They also show effects that reduce blood pressure and have anti-inflammatory, analgesic, antiviral, antibacterial, antifungal, and anticancer properties [1].

According to reports, the biological activity properties of oxadiazoles can be used in agriculture as plant protection agents, herbicides, and insecticides to control fungi, bacteria, and viruses. Oxadiazole compounds also have useful optical characteristics. Because of its electron-accepting property, the 1,2-dialzole fragment of 1,3,4-oxadiazole derivatives finds use in a variety of conducting systems Of special relevance are 1,3,4-Oxadiazoles modified with carboxymethylamino

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groups and featuring. One such heterocyclic molecule that can be produced is oxadiazole [2] Oxadiazole is heterocyclic compound that can be derived from nitrogen and oxygen-containing 5-member ring. The development in Oxadiazole synthesized compound show the biological activity A variety of these organic ligands are documented in the literature, some of which have been given the go-ahead to be used in agriculture and medicine. One of these is EDTA, or ethylene diamine tetra acetic acid [2].

It is noteworthy that in numerous instances, a synergistic effect emerged when the 1,3,4-oxadiazole core was combined with other heterocyclic fragments (Ahsan et al., 2011; Kotaiah et al., 2012; Padmavathi et al., 2011; Puthiyapurayil et al., 2012). Additionally, the 1,3,4-oxadiazole cycle is a bioisostere for carboxylic, amide, and ester groups. These groups mostly participate in hydrogen bonding interactions with receptors to boost pharmacological activity [3].

Urease is a metalloenzyme that is dependent on nickel and catalyzes the hydrolysis of urea to produce carbon dioxide and ammonia. By raising the pH in an aqueous solution, Helicobacter pylori was able to produce ammonia, which increased the bacteria's capacity to survive. Furthermore, it has been determined that Helicobacter pylorus is the root cause of a number of issues related to gastroduodenal function. These conditions include peptic ulcers, duodenal ulcers, stomach cancer, and urinary catheter encrustation. Additionally, ureease inhibitors stop ureolytic bacterial infections from becoming harmful. Regulation of urea breakdown is necessary. Medicinal chemists have focused a great deal of research into creating novel heterocyclic urease inhibitors as potential treatment alternatives due to the biological significance of organic heterocyclic compounds that function as urease enzyme inhibitors [4].

LITERATURE

Review motivated us to start creating a variety of new 1,3,4-oxadiazole compounds in an effort to increase activity while lowering toxicity. This study found that the activity of 1,3,4-oxadiazole derivatives may vary in both quantitative and qualitative ways depending on a small systemic change in the structural moiety of the compound. Over the past few decades, there has been a notable increase in the synthesis of novel 1,3,4-oxadiazole derivatives and the exploration of their biological and chemical characteristics. Oxadiazole was combined with additional heterocyclic moieties to create a compound that exhibited a variety of biological properties, antimalarial, anticancer, anti-inflammatory, anticonvulsant, analgesic, anti-allergic, and vasodilator properties. The oxadiazole nucleus is present in many commercially marketed medications, including as the anti-cancer medication Zibotentan, the HIV integrase Railtegraviras, and the hypertension medication Nesapidil [5].

In this research effort, we have designed and synthesized hybrid analogues based on benzothiazole containing oxadiazole as potent urease and alpha-glucosidase inhibitors, keeping in mind the biological significance of oxadiazole and benzothiazole derivatives. Figure 1 Shown: Pharmaceuticals with a bioactive oxadiazole component. This study's goal is to assess the biological significance of the produced compounds by contrasting their powerful molecule with previously reported compounds from the same series. The compounds' improved potentials have been discussed in relation to the various substituted moieties [6].

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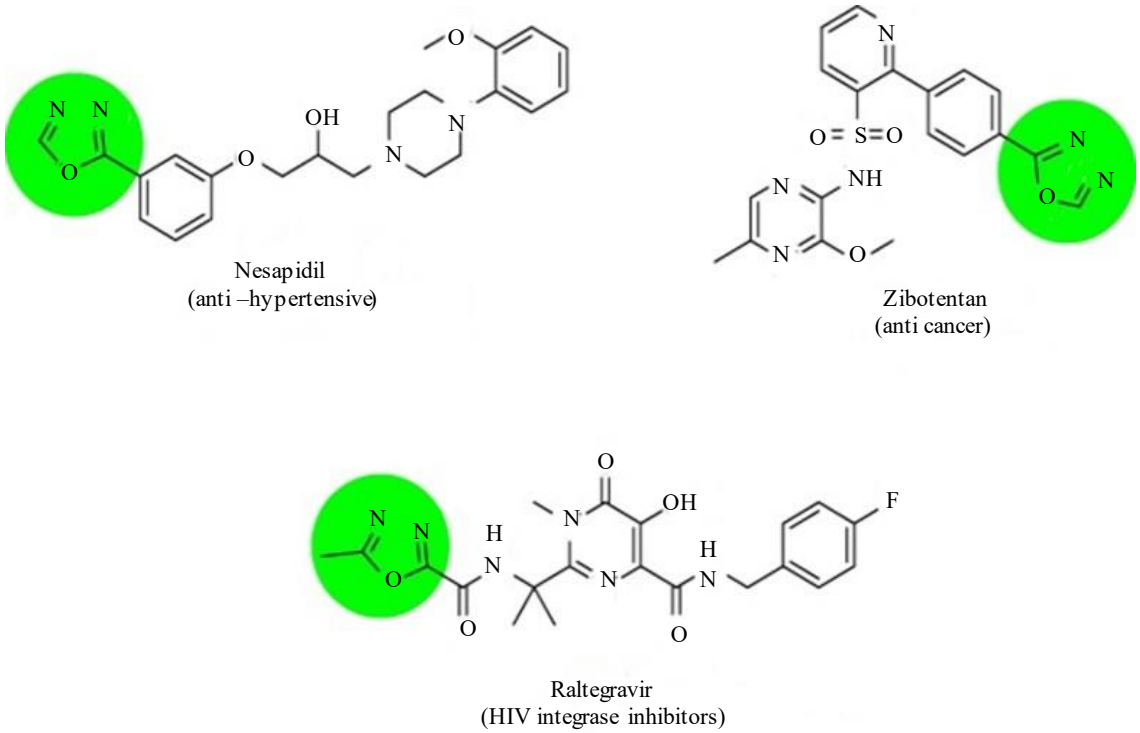

Figure 1. Shown pharmaceuticals with a bioactive oxadiazole component.

Antimicrobial Activity

Using the agar diffusion cup plate method, a quantitative in vitro antimicrobial investigation was conducted on Muller-Hinton agar (Hi-media) plates. The antibacterial activity of the compounds was evaluated against two bacterial strains: Escherchia coli (E. coli) (Gram-ve) and Staphylococcus aureus (S. Aureus) (Gram+ve). Using the cup plate method, antifungal activity was evaluated against Aspergillus Niger (A. Niger) at a concentration level of 200–25 µg/mL [7].

Clinical pharmacology of medicines for arrhythmias

Amiodarone's counterpart, benzofuran. Similar to amiodarone, dronedarone exhibits complicated electrophysical effects that fall into all four of the Vaughan Williams classes, albeit its precise mode of action is still unknown. Dronedarone is a class III medication that inhibits the potassium currents IKr, IK1, IKACh, and Isus, hence prolonging the cardiac action potential and refractory periods. Additionally, it inhibits the sluggish L-type calcium channels (a class IV effect) and sodium channels (a class IB impact), which causes the depolarization phase of the action potential to slope less [8].

Dronedarone has additionally demonstrated class II antiadrenergic properties. Dronedarone was observed to considerably extend the R-R and QT interval in healthy persons in a dose-dependent manner. Eliminating the iodine component mentioned before was also intended to lower the possibility of thyroid function problems that are known to arise after amiodarone medication. Dronedarone does not alter circulating plasma thyroid hormones, according to research on animals [9].

In naturally occurring compounds, furans, benzofurans, and their reduced counterparts are frequently found structural motifs. Furan heterocycles are also present in synthetic products, such as fire retardants, polymer polymers, and medicines. Because of this, chemists have focused a great deal of attention on creating ring syntheses for this particular class of heterocycles. the appearance of something new [9].

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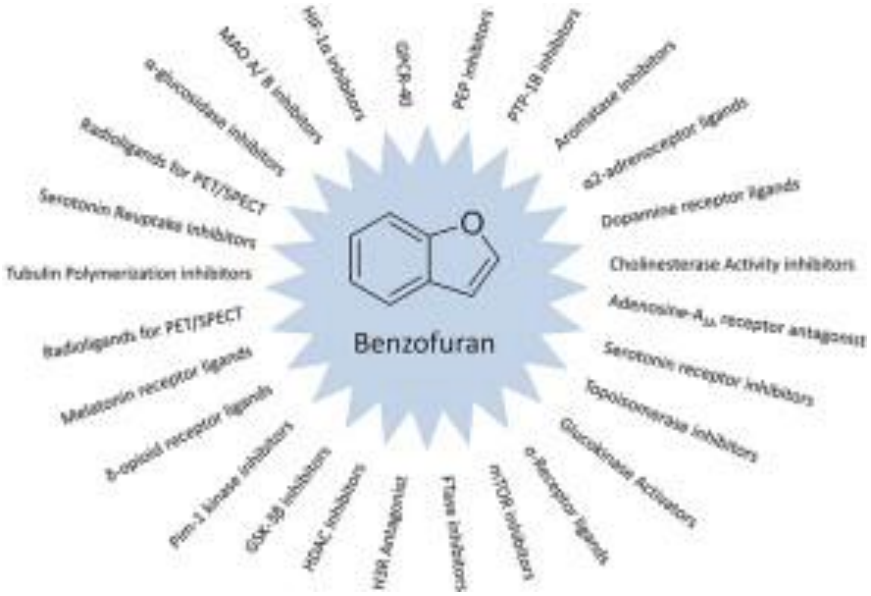

Figure 2. The extremely adaptable benzofuran core is found in numerous significant natural goods and natural medications.

Many synthetic medications and clinical prospects containing benzofuran are obtained from natural sources. Figure shows: 2 The extremely adaptable benzofuran core is found in numerous significant natural goods and natural medications. This review aims to shed light on the decade's top design advancements, clinical candidates, and PET tracer radio-ligands that contain benzofuran core, as well as provide a brief overview of target biology [10].

In naturally occurring substances, benzofurans and their reduced counterparts are frequently found structural motifs. Furan heterocycles are also present in synthetic products, such as fire retardants, polymer polymers, and medicines. Because of this, chemists have focused a great deal of attention on creating ring syntheses for this particular class of heterocycles. Furans and related chemicals are now much more accessible for synthetic synthesis thanks to the development of innovative asymmetric transformations and metal-catalyzed methodologies [11]. Figure 2

MTB, or Mycobacterium Tuberculosis

A pathogenic bacterium belonging to the Mycobacteriaceae family is a tiny, aerobic, nonmotile bacillus that can have a Gram-positive or Gram-negative appearance. MTB is the primary cause of tuberculosis (TB) and is worldwide in distribution. It usually thrives in a range of environmental conditions. Of the 1.7 billion people infected with MTB, 5–10% will get TB illness at some point in their lives. All across the world, Above the combined effects of HIV and AIDS, tuberculosis (TB) is the most common infectious agent-related cause of illness. According to WHO estimates, TB killed 1.3 million people in 2017 and affected at least 10 million people [12].

Many benzofuran derivatives have been created, manufactured, and tested in recent years for their anti-bacterial and anti-TB properties; some of them showed encouraging effectiveness. This study discusses the latest developments in benzofuran derivatives and their anti-bacterial and anti-TB qualities [13].

Antitubercular action

Prado et al. evaluated a number of benzofurobenzopyrans for their in vitro anti-TB, anti-bacterial, and anti-fungal properties. Given that they did not significantly harm mammal cells or inhibit the growth of different bacteria or fungus, these chemicals appear to be promising specialized anti-TB medicines [14].

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Activity Antimicrobial Action

The worldwide public health community places great importance on the development of new antibiotics due to the emergency and widespread spread of bacterial resistance. In vitro antimicrobial activities of eight benzofuran-pyrazole hybrids were assessed by Ashok et al. against Gram-positive pathogens Bacillus subtilis (B. subtilis) and Saphylococcus aureus (S. aureus), as well as Gram-negative pathogens Escherichia coli (E. coli) and Proteus vulgaris (P. vulgaris). All hybrids demonstrated moderate activity [15].

Chemistry

In the presence of a base, varying amounts of substituted benzonitrile (I) were combined with hydroxylamine to produce an intermediate moiety (II), which cyclized to produce distinct substituted oxadiazole moieties (III) when exposed to 2-chloroacetyl chloride. Following this, these moieties were put through a second step reaction in which 2-marcapto benzothiazole was combined with triethylamine in ethanol to produce the desired oxadiazole derivatives based on benzothiazole. One of the several spectroscopic tools used to precisely characterize all of the produced analogs was NMR (1H- and 13C-NMR). In addition, a molecular docking research was carried out for the majority of active analogs to investigate their binding interactions with the targeted enzymes' active sites; the findings corroborated the experimental data [16].

Equipment and Devices

With the use of the Perkin Elmer model 2400 CHNS/O analyzer, the unique synthesized compounds for C, H, N, and S underwent elemental analysis. Using KBr pellets, the produced products were further examined using an FT/IR (JASCO FT/IR 4100 Spectrophotometer). The chemical shifts were reported in δ (tau) ppm. Utilizing the Jasco V-630 Spectrophotometer for UV-Vis spectroscopy, the λ max of the produced compounds is examined. The open capillary method (Elico) was used to estimate the melting points, which are uncorrected [17].

Synthesis of 2-amino, 5-substituted 1, 3, 4-oxadiazole: general protocol (3, 4)

After adding 50.0g (0.5mol) of semicarbazide to 100mL of formic acid/acetic acid, the mixture was shaken for one hour at room temperature. After cooling the process, 100 mL of concentrated hydrochloric acid was added Ammonium hydroxide solution was used to basify the reaction after it had been cooled to 00C. The aforementioned chemical was obtained as an off-white solid by filtering, washing with water, and drying the solid. Finally, ethanol solvent is used to recrystallize the products [18].

Spectroscopic Characteristics

A detailed analysis of the novel compounds' photoluminescence pattern was conducted. BF and BDF scaffolds have the potential to be used as electron-rich building blocks in the creation of photoluminescent (PL) materials. We discovered that by utilizing the proper substituents and functional groups, their PL performance could be adjusted. In contrast to amino precursors, iminic derivatives exhibit photoluminescence in both concentrated solution and the solid state due to the aggregation-induced increased emission (AIE) effect [19].

Our method for achieving the AIE behavior involved building a sterically encumbered highly conjugated main plane, with the H-bond at the half-salen site and butyl substituents inducing restriction of intramolecular movements (RIM). Furthermore, because intramolecular H-bond interactions prevent sterically encumbered portions of the molecule from torsion, they can induce excited-state intramolecular proton-transfer (ESIPT), which is known to result in an emissive pattern in solution as well. Consequently, it is anticipated that the six chromophores will become active as dissolved or dispersed nanoaggregates in the aqueous physiological milieu [20].

CONCLUSION

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We address the efforts to find novel, promising drugs based on noncondensed 1,3,4-oxadiazole derivatives substituted with aryl/heteryl groups in this review. We also emphasize the primary methods for achieving a chemical alteration of the heterocycles in question as well as their pharmacological profile. The 1,3,4-Oxadiazole heterocycle, which has shown a wide range of biological properties including anticancer, antibacterial, antitubercular, anti-inflammatory, and analgesic effect, is a very fascinating and significant scaffold for contemporary organic and medicinal chemistry. Additionally, these ring systems can be found in a number of approved medicinal compounds, including the antiviral Raltegravir, the anticancer Zibotentan, and the antihypertensive drugs Tiodazosin and Nesapidil. Everything discussed above can be viewed as background information for more in-depth research on the chemistry and pharmacology of the heterocyclic systems with potential medical applications. Gaussian-03 software was used to perform DFT and TD-DFT calculations. Numerous chemical, electrical, and structural characteristics were examined.

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