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Review Article

Exploring the Therapeutic Potential: Oxadiazole Derivatives as Promising Anticancer Agents

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Abstract

The exploration of oxadiazole derivatives as promising anticancer agents holds significant promise for the development of novel therapeutics. Through extensive research and experimentation, these compounds have demonstrated remarkable potential in targeting cancer cells with high specificity and efficacy. The diverse structural modifications available for oxadiazole derivatives offer a wide range of opportunities for further optimization and fine-tuning of their anticancer properties. Despite the challenges ahead, continued investigation and refinement of oxadiazole-based compounds are essential for advancing cancer treatment strategies and ultimately improving patient outcomes. With ongoing efforts, the therapeutic potential of oxadiazole derivatives in combating cancer remains a compelling area of research warranting further exploration and development.

Keywords: oxadiazole, anticancer, novel therapeutics, cancer cells, structural modifications**.**

Introduction

Certainly! Cancer is a complex group of diseases characterized by the uncontrolled growth and spread of abnormal cells. These cells can invade and destroy normal tissue and can spread to other parts of the body through the bloodstream and lymphatic system, a process known as metastasis.
There are more than 100 different types of cancer, each with its own set of causes, risk factors, symptoms, and treatment options. Some common types of cancer include breast cancer, lung cancer, prostate cancer, colorectal cancer, and skin cancer.

Risk factors for cancer include genetic factors, exposure to carcinogens such as tobacco smoke and ultraviolet radiation, unhealthy lifestyle choices such as poor diet and lack of physical activity, certain infections such as human papillomavirus (HPV) and hepatitis B and C viruses, and environmental factors such as pollution and radiation. Cancer treatment options depend on the type and stage of cancer, as well as the individual's overall health and preferences. Treatment may include surgery, chemotherapy, radiation therapy, immunotherapy, targeted therapy, hormone therapy, or a combination of these approaches.

Early detection through screening tests such as mammograms, Pap smears, colonoscopies, and PSA tests can significantly improve the chances of successful treatment and survival. Additionally, lifestyle changes such as maintaining a healthy weight, quitting smoking, limiting alcohol consumption, eating a balanced diet, and staying physically active can help reduce the risk of developing cancer. Research into cancer prevention, early detection, and treatment is ongoing, and advances in medical science continue to improve outcomes for cancer patients

Drug Information: Oxadiazole

Oxadiazole is a chemical compound that belongs to the class of heterocyclic compounds, specifically a five-membered ring containing two nitrogen atoms and one oxygen atom.

It has various applications in medicinal chemistry, including its use as a scaffold for the synthesis of biologically active molecules, such as pharmaceuticals and agrochemicals. Here's a comprehensive overview of oxadiazole:

Chemical Structure

Oxadiazole has a bicyclic structure consisting of one oxygen atom and two nitrogen atoms in a five-membered ring. The molecular formula for oxadiazole is C2H2N2O.

Types of Oxadiazoles

There are several types of oxadiazoles, including 1,2,4-oxadiazole, 1,2,5-oxadiazole, and 1,3,4-

oxadiazole. These derivatives differ based on the positions of the nitrogen and oxygen atoms in the ring.

Synthesis

Oxadiazoles can be synthesized through various methods, including cyclization reactions involving hydrazides and amidoximes, as well as condensation reactions between amidoximes and acid chlorides or carboxylic acids.

Applications

Medicinal Chemistry

Oxadiazoles serve as important scaffolds in the design and synthesis of pharmaceutical compounds, particularly as anticancer, antibacterial, antifungal, antiviral, and anti-inflammatory agents.

Agrochemicals

Some oxadiazole derivatives have pesticidal properties and are used in the formulation of agricultural chemicals.

Materials Science

Oxadiazoles are also employed in materials science for the development of polymers, liquid crystals, and optoelectronic materials.

Biological Activity

Anticancer Activity: Certain oxadiazole derivatives exhibit promising anticancer activity by inhibiting specific molecular targets involved in cancer cell proliferation and survival.

Antibacterial and Antifungal Activity

Oxadiazole compounds have demonstrated antibacterial and antifungal properties against a variety of pathogens, making them potential candidates for the development of new antimicrobial agents.

Other Biological Effects

Oxadiazoles may also possess other biological effects, such as antioxidant, anti-inflammatory, and antiviral activities, depending on their chemical structure and functional groups.

Drug Development

Oxadiazole derivatives are of interest in drug discovery and development due to their diverse biological activities and potential therapeutic applications.

Researchers continue to explore and optimize oxadiazole-based compounds for various medical and agricultural purposes.

A Brief Description of Review/Research Work on Oxadiazole for Anticancer Activity

Table 1:

S. No.	Title	Conclusion
1.	Novel 1,3,4-Oxadiazole Fused Thiadiazole Derivatives: Synthesis and study of Anticancer Activities	Background: In search of novel anticancer agents, a series of 1,3,4-oxadiazole derivatives (12a-j) containing 1,3,4-thiadiazole moieties were synthesized, and their structures were confirmed by 1HNMR, 13CNMR and ESI-MS spectral analysis. Methods: Cytotoxicity of these compounds was evaluated by MTT assay in vitro against four human tumor cell lines, i.e. A549 (lung), MCF-7 (breast), A375 (melanoma) and HT-29 (colon). Results: Here, CA4 used as positive control. Among them, compounds 12b, 12c, 12f, 12g, 12h and 12j were exhibited promising activity than control drug. Conclusion: In conclusion, we have synthesized a novel series of 1,3,4-oxadiazole fused 1,3,4- thiazdiazole derivatives and their structures were confirmed by spectral analysis.
2.	Synthesis, characterization and anticancer activity of certain 3-{4-(5-mercapto-1,3,4-oxadiazole-2-yl) phenylimino}indolin-2-one derivatives	A series of 5- or 7-substituted 3-{4-(5-mercapto-1,3,4-oxadiazol-2-yl) phenylimino}-indolin-2-one derivatives were synthesized by treating 5-(4-aminophenyl)-1,3,4-oxadiazole-2-thiol with different isatin derivatives. The newly synthesized compounds were characterized on the basis of spectral (FT-IR, 1H NMR, MS) analyses. All the synthesized derivatives were screened for anticancer activity against HeLa cancer cell lines using MTT assay. All the synthetic compounds produced a dose dependant inhibition of growth of the cells. The IC50 values of all the synthetic test compounds were found between 10.64 and 33.62 μM. The potency (IC50 values) of anticancer activity of compounds VIb–d was comparable with that of known anticancer agent, Cisplatin. Among the synthesized 2-indolinones, compounds VIb–d with halogen atom (electron withdrawing groups) at C5 position showed the most potent activity. These

		results indicate that C5 substituted derivatives may be useful leads for anticancer drug development in the future
3.	Design, synthesis and in vitro anticancer activity of novel quinoline and oxadiazole derivatives of ursolic acid	A series of new quinoline derivatives of ursolic acid were designed and synthesized in an attempt to develop potential anticancer agents. The structures of these compounds were identified by 1H NMR, 13C NMR, IR and ESI-MS spectra analysis. The target compounds were evaluated for their in vitro cytotoxicity against three human cancer cell lines (MDA-MB-231, Hela and SMMC-7721). From the results, compounds 3a-d displayed significant antitumor activity against three cancer cell lines. Especially, compound 3b was found to be the most potent derivative with IC50 values of 0.61±0.07, 0.36±0.05, 12.49±0.08μM against MDA-MB-231, HeLa and SMMC-7721 cells, respectively, stronger than positive control etoposide. Furthermore, the Annexin V-FITC/PI dual staining assay revealed that compound 3b could significantly induce the apoptosis of MDA-MB-231 cells in a dose-dependent manner. The cell cycle analysis also indicated that compound 3b could cause cell cycle arrest of MDA-MB-231 cells at G0/G1 phase.
4.	Synthesis and evaluation of selected 1,3,4-oxadiazole derivatives for in vitro cytotoxicity and in vivo anti-tumor activity	The oxadiazole moiety is known for its anticancer activity through its antiangiogenic and mitostatic potential. Taking this as a cue, the present study was designed to investigate the anti-cancer potential of selected oxadiazole derivatives. Twelve 1,3,4-oxadiazole derivatives (AMK OX-1 to AMK OX-12) were synthesized and were tested for IC50 values through brine shrimp lethality assay and MTT assay on HeLa and A549 cell lines. Four compounds, AMK OX-8, 9, 11 and 12 showed potential cytotoxicity activity with low IC50 value. These compounds produced considerable cytotoxic effect on Hep-2 and A549 cancer cell lines. However, they were found to be comparatively safer to normal cell lines, viz., V-79 cell lines than to the tested cancer cell lines, such as HeLa, A 549, and Hep2 cell lines. The mechanism of cytotoxicity was evaluated through nuclear staining and DNA ladder assay. Although DNA ladder assay showed DNA fragmentation (apoptotic phenomenon) in Hep-2 cells treated with only AMK OX-12, the staining procedures using acridine orange, ethidium bromide and propidium iodide showed apoptotic bodies in cells treated with AMK OX-8, 9 and 12 also. In JCI staining on isolated mitochondria of Hep2 cells, AMK OX-8, 9-11 and 12 displayed increasing fluorescence intensity with time which confirmed involvement of mitochondrial pathway and intrinsic pathway of apoptosis. All four compounds were found to be safe in acute oral toxicity study in Swiss albino mice. These derivatives were effective in reducing tumor size and weight in the in vivo DLA-induced solid tumor model. They were found to be significantly effective in reducing tumor volume and tumor weight.
5.	1,3,4-Oxadiazole-containing hybrids as potential anticancer agents: Recent developments, mechanism of action and structure-activity relationships	Chemotherapy is an important therapeutic approach for the treatment of cancer. Currently, many anticancer drugs are available in the market that plays an important role in cancer treatment, but concerns such as, drug resistance and side effects create an urgent need for the development of new anti-tumor drugs with high potency and less side effects. Heterocycles are of great interest due to their fascinating anticancer activity. Among them, 1,3,4-oxadiazoles showed attracting anti-tumor activity and its derivatives are under clinical trials for the treatment of cancer. Hybridization of 1,3,4-oxadiazole moiety with other heterocyclic pharmacophoresis a promising approach to overcome various disadvantages of current anticancer drugs such as drug resistance, toxicity, and other side effects. Thus, 1,3,4-oxadiazole-

		heterocycle hybrids occupy a significant position in the discovery of anti-tumor drugs. Among the reported oxadiazole-based hybrids reviewed here, compounds 45i, 59j, and 62x showed the highest anticancer activity with IC50 values in the nanomolar range. This review summarizes the recent developments in the anticancer potential, structure–activity relationships, and mechanisms of actions of 1,3,4-oxadiazole-heterocycle hybrids.
6.	Synthesis, Biological Evaluation and Docking Studies of 1,3,4-Oxadiazole Fused Benzothiazole Derivatives for Anticancer Drugs	Hetero atom containing compounds are well studied class of organic compounds exhibits variety of properties and applications. Design and synthesis of new heterocyclic compounds are always of great interest in synthetic and medicinal organic chemistry. Benzothiazole or 2-aminobenzothiazole scaffold-based derivatives were reported to display a wide range of biological activities including anticancer, anti-tubercular, antiviral, fungicidal, etc. On the other hand, 1,3,4-oxadiazoles were permit to increase their biological activities due to H-bonding with receptors. These derivatives possess diverse biological activities which include anticancer, antiviral, antifungal, antibacterial and antidepressant etc. Due to interesting biological activity information of about these hetero cyclic moieties, benzothiazole/2-aminobenzothiazole and 1,3,4-oxadiazoles moieties, we chose to design a new series of heterocyclic compounds by mimicking these two types of scaffolds in a single molecule for our study. Methods: The 1,3,4-oxadiazole linked benzothiazole derivatives were synthesized by condensation of, 2-(4-(5-(benzo[d]thiazol-2-yl)-1,3,4-thiadiazol-2-yl)-2,6-dimethoxyphenoxy) acetohydrazide and POCl3 under reflux conditions. All these ten compounds' structures were confirmed by spectral data 1H & 13C NMR, Mass, CHN analysis etc. Further, these compounds were evaluated for their anticancer activity against four human cancer cell lines, A549, MCF7, A375 and HT-29 in comparison to CA4 as a reference drug. We also carried out docking studies of these compounds in the Colchicines binding site of Tubulin (PDB_ID: 1SA0) using Glide docking tool indicated that the ligands show good interactions with active site residues. Results: A new series of 1,3,4-oxadiazole fused benzothiazole derivatives were synthesized successfully in totally six steps starting with 4-hydroxy-3,5-dimethoxybenzoyl chloride. All these newly synthesized compounds structures were confirmed by spectral studies and elemental analysis. As we designed for anticancer activity, they were assessed for their anticancer activity against four human cancer cell lines in comparison to a reference drug CA4. As expected, all the ten compounds exhibited anticancer activities against four cancer cell lines with half maximal inhibitory concentration (IC50) values ranging from 0.01 μM to 12.3 μM. The docking studies indicated all the compounds exhibited good binding energies with the receptor.

Conclusion

The investigation of oxadiazole derivatives as potential anticancer drugs offers great promise for the development of new therapies. Following significant study and experimentation, these chemicals have proven great promise for targeting cancer cells with high selectivity and potency. The many structural alterations accessible for oxadiazole derivatives provide several chances for further optimizing and fine-tuning their anticancer activities. Notwithstanding the difficulties that lie ahead, further research and development of molecules based on oxadiazole is imperative to progress cancer therapy approaches and eventually enhance patient outcomes. With continued efforts, the therapeutic potential of oxadiazole derivatives in cancer treatment remains an intriguing field of study that requires additional investigation and advancement.

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