JETIR.ORG ISSN: 2349-5162 | ESTD Year : 2014 | Monthly Issue
JOURNAL OF EMERGING TECHNOLOGIES AND INNOVATIVE RESEARCH (JETIR)
An International Scholarly Open Access, Peer-reviewed, Refereed Journal

A Review on Biological Activity of Thiadiazole Moiety and Its Derivatives

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ABSTRACT:

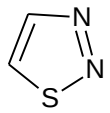
The most common type of organic compound is a heterocyclic compound. They're extremely important for a variety of synthetic, medicinal, and industrial uses, and they're well-known for their biological activities. Many compounds with a five-membered heterocyclic ring in their structure exhibit a diverse range of biological activity. Because of the high therapeutic qualities of these heterocycles, medicinal chemists have been able to develop a huge number of new chemotherapeutic drugs.[1]Because of their broad variety of biological activities. Derivatives of 1,3,4-thiadiazole have been the subject of several studies. They have been discovered to have antibacterial, anti-inflammatory, anticancer, antidiabetic, anticonvulsant, and antitubercular properties. There are many medications on the market that contain thiadiazole derivatives, such as acetazolamide, methazolamide, sulphamethazol, and cefazoline. The preparation of novel thiadiazole derivatives, as well as the study of their chemical and biological activities, has become increasingly important. The thiadiazole ring has been modified, resulting in increased potency and reduced toxicity. This page will go over the work that has been done in the past, as well as the chemistry and biological activity of thiadiazole.[2]

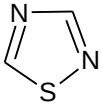
Keywords- Heterocyclic, 1,3,4-thiadiazole, Pharmaceutical, Biological, Chemotherapeutic

INTRODUCTION:

Heterocycles are by far the most important of organic chemistry's traditional divisions, with a wide range of biological and industrial applications. The occurrence of heterocycles in a wide range of organic molecules with applications in electronics, biology, optics, medicine, materials science, and other domains is well understood. In medicinal chemistry, the heterocyclic nucleus plays a significant role and serves as a crucial template for the synthesis of diverse therapeutic drugs. Throughout the history of organic synthesis, most researchers have maintained an interest in sulphur and nitrogen-containing heterocyclic molecules. The nucleus of one 1,3,4-thiadiazole is an outstanding pharmacophore with a wide range of actions.[3-4] In biomedical science, academic institutes and testing labs are likewise keen on the development and optimization of experimental medicines. The pharmaceutical industry's substantial research-based efforts in this field are not supported by a new molecule. The use of current commodities to meet anticipated medical requirements, as well as the investigation of novel chemical entities, are all part of drug development.[5]

According to an examination of standard reference texts, 1,3.4-thiadiazole has gotten more attention than other isomers. The 1,3,4-thiadiazole ring is a very weak base with a high aromaticity due to the inductive impact of the sulphur atom..


1,2,3-thiadiazole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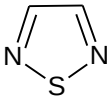
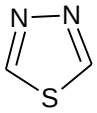

1,2,5-thiadiazole


1,3,4-thiadiazole

Isomers of thiadiazole

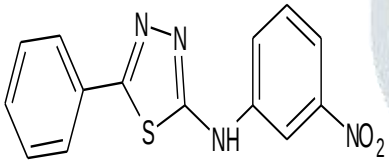
It is relatively stable in aqueous acid solutions, although it can ring cleave in aqueous base solutions. The ring is also shown to be very electron deficient due to the electron withdrawing effect of the nitrogen atoms, and relatively inert toward electrophilic substitution but susceptible to nucleophilic attack, whereas substitutions in the 2' or 5' positions of this ring are highly activated and readily react to yield diverse derivatives. Because of these properties, 1,3,4-thiadiazole is employed in a wide range of fields.[6]

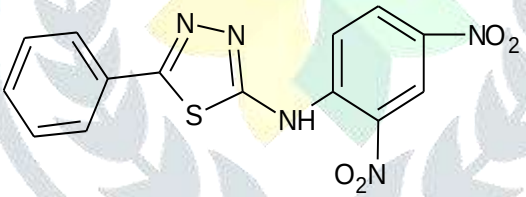
Structure and pharamacological activities

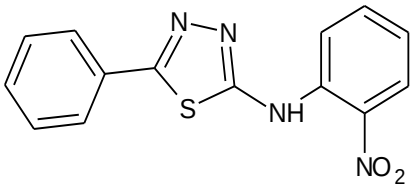
Thiadiazole is a five-membered aromatic ring heterocyclic molecule with two nitrogen atoms and one sulphur atom. Because of their distinct chemical features and biological actions, 1,3,4-thiadiazole are intriguing candidates for medicinal chemists. Thiadiazole derivatives exhibit anticancer, antibacterial, anti-inflammatory, antidepressant, antifungal, antitubercular, anticonvulsant, Antihypertensive and Antidiuretic effects, according to studies.[1-6]

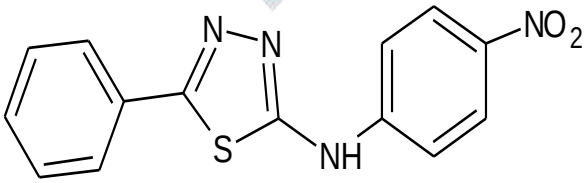
Anticancer activity

Cancer is a disease marked by the uncontrolled multiplication of a large number of cells that penetrate and, in some cases, spread throughout the body. As a result, a solid clump of cells known as a tumour or a liquid cancer forms. The anticancer characteristics of different substituted nitrobenzene 1,3,4-thiadiazole derivatives have been explored. The % inhibition of cell lines of breast cancer MCF-7 has been calculated by exposing the cell line to the test chemicals at varied doses. Because with the use of the tryphan blue exclusion method, all of the compounds found to have substantial activity, including docs MCF-7. The derivatives showing below was discovered to be more efficient. 5-fluorouracil is the typical chemical used.[7]



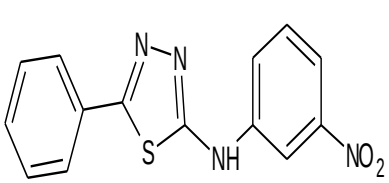
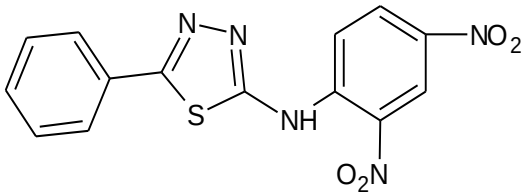
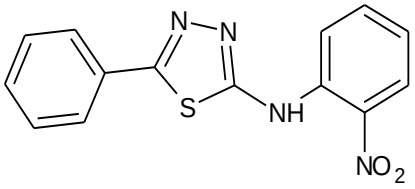
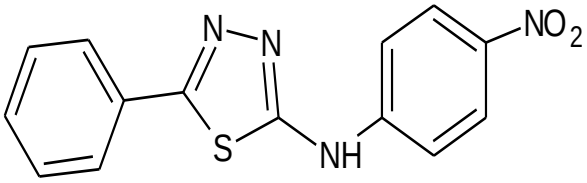






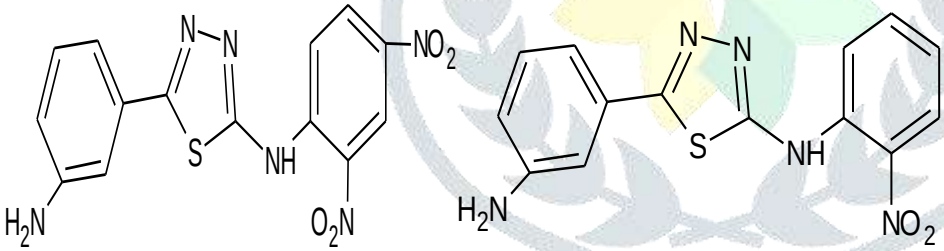
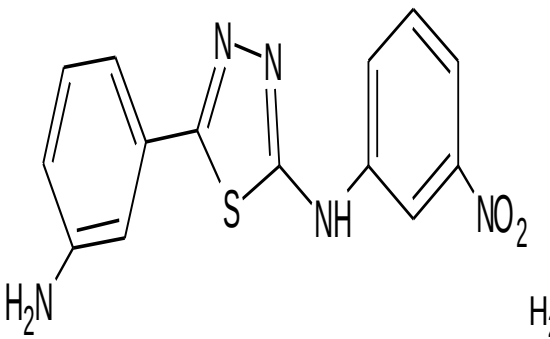
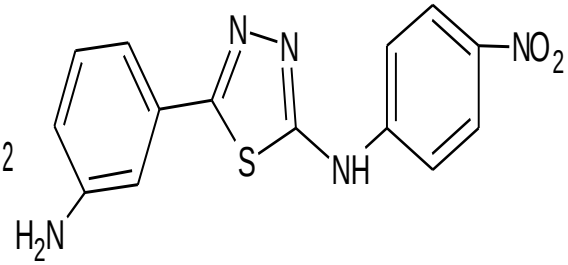
Antibacterial activity

All of the generated compounds were evaluated for antibacterial activity against Escherichia coli, Pseudomonas aeruginosa, Bacillus cereus, and Staphylococcus aureus using the disc diffusion method. Some of the compounds demonstrated good antibacterial activity when compared to standard medicines. This study adds to our ongoing efforts to develop more effective antibacterial medications through logical design.[8]

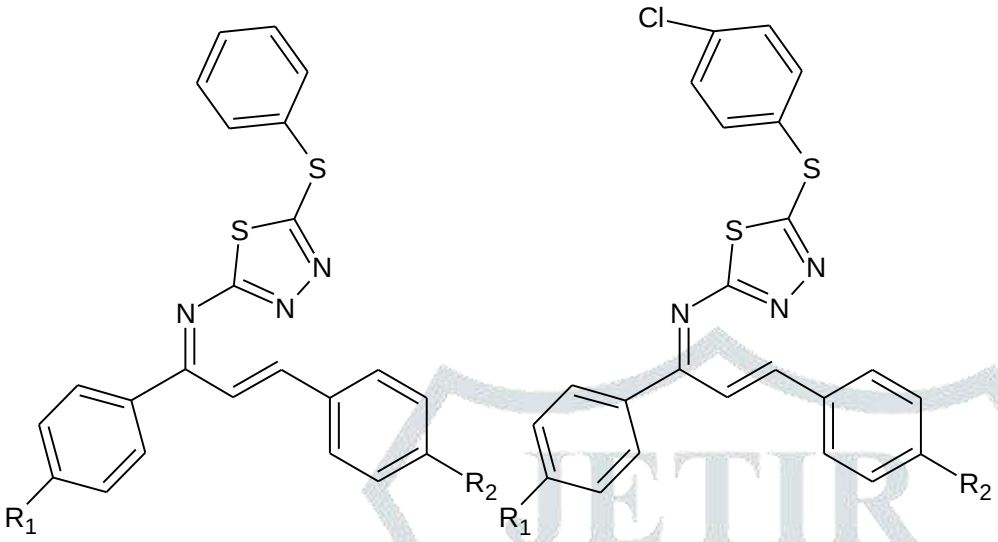
Anti-Inflammatory Activity

This study confirmed the anti-inflammatory activity of a new class of N- (substituted)-5-phenyl-1, 3, 4-thiadiazol-2-amine derivatives in vitro. Protein denaturation, a well-known source of inflammation, is the cause. In a dose-dependent way, some anti-inflammatory medicines have been shown to inhibit thermally induced protein denaturation. The anti-inflammatory actions of 1, 3, 4-thiadiazole may be due to its capacity to inhibit protein heat denaturation. Chemical code 3c, according to our findings, has anti-inflammatory characteristics.[9]

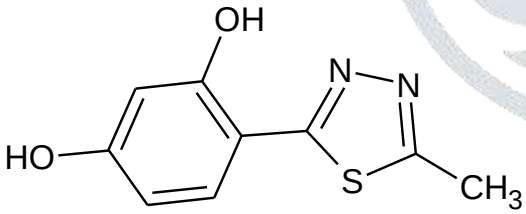
Antidepressant Activity

A number of new imine derivatives of 5-amino-1, 3, 4-thiadiazole-2-thiol have been synthesised, and their antidepressant efficacy has been assessed using imipramine as a reference drug. 5-[1-(4-chlorophenyl)-3-(4-methoxy-phenyl)prop-2-en-1-ylidene] 5-[1-(4-chlorophenyl)-3-(4-dimethyl-aminophenyl)prop-2-en-1-ylidene]amino-5-benzylthio-1,3,4-thiadiazole and 5-[1-(4-chlorophenyl)-3-(4-dimethyl-aminophenyl)prop-2-en-1-ylidene]amino-5-benz compounds shows (82 %)potency. [10]



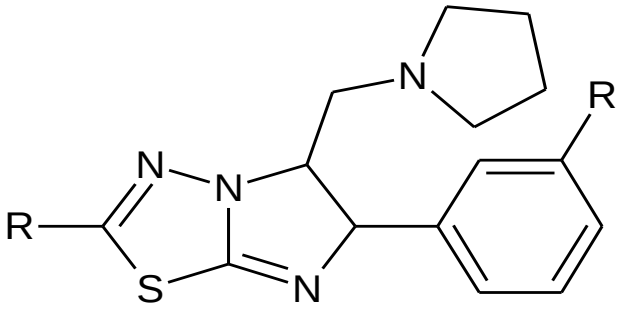
Antifungal Activity

Antibacterial, antifungal, and anticancer properties are all present in the group of 5-substituted 4-(1, 3, 4-thiadiazol-2-yl) benzene-1, 3- diols. The mechanism of antifungal activity of medicines in this class has yet to be discovered. Among the vast group of 5-substituted 4-(1, 3, 4-thiadiazol-2-yl) benzene-1, 3-diol derivatives, 4-(5-methyl-1, 3, 4-thiadiazole-2-yl) benzene-1, 3-diol derivatives, C1 was revealed to be one of the most efficacious agents against pathogenic fungus while also having the lowest toxicity to human cells.[11]



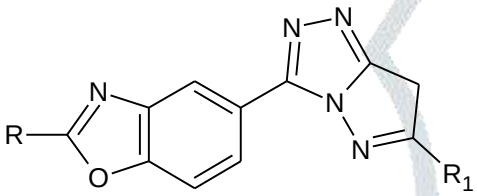
Antitubercular Activity

The compounds were examined in vitro for antitubercular activity against the Mycobacterium tuberculosis H37Rv strain of Mycobacterium tuberculosis as part of the TAACF TB screening programme, which is managed by the NIAID branch of the US National Institutes of Health. With a MIC of 3.14 l g/ml, 2-(1-methyl-1H-imidazol-2-yl)-6-(4-nitrophenyl) imidazo [2,1-b][1,3,4] thiadiazole showed the strongest (98 %) inhibitory activity when compared to the other compounds examined. Certain strong chemicals were also examined for cytotoxic action against a mammalian Vero cell line using the MTT assay. According to the findings, these compounds show antitubercular activity at non-cytotoxic dosages.[12]



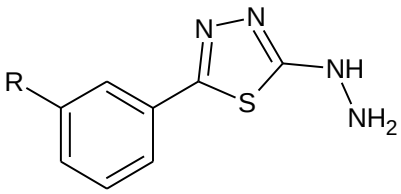
Anticonvulsant activity

The 1, 2, 4-triazolo-1, 3, 4-thiadiazoles were created using 3-amino-4-hydroxybenzoate as the starting material. The results of spectrum analysis were used to make ready-to-use compounds. To obtain better results, the MES test and scPTZ techniques were employed to screen compounds for anticonvulsant effect. To determine neurotoxicity, the rotarod method was used. With relatively little neurotoxicity, the majority of the compounds produced anticonvulsant effects that were almost equal to those of conventional medicines (phenytoin and carbamazepine).[13]



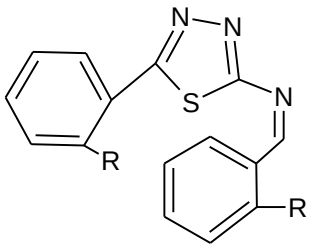
Antihypertensive Activity

Some 2-aryl-5-hydrazino-l,3,4-thiadiazoles have been synthesized and screened for antihypertensive activity. In general, compounds with a 2-substituted phenyl ring had higher activity than their 3- or 4-substituted counterparts or those containing heteroaryl groups. The 2-methylphenyl and 2-ethylphenyl derivatives 7 and 18 were the most potent members of the series. Preliminary studies indicated that the hypotensive action of these compounds was due to a direct relaxant effect on vascular smooth muscle.[14-15]



Antidiuretic activity

A series of 2-amino-substituted-5-phenyl-1, 3, 4-thiadiazole derivatives was synthesized with good yields and their structures were elucidated by spectral data. Compounds 7c and 7f were found to be less toxic which may be due to presence of an electron withdrawing group chlorine. Compound 7e showed the similar effect as compared to the standard drug Nitrofurazone used on 16th day. The period of epithelisation was 17.23 + 1.04 days for compound 7e against 13.15 + 1.47 for the standard drug treated group. Compound 7a and 7d was found to show good diuretic activity which may be due to the inhibition of the enzyme carbonic anhydrase which leads to the excretion of sodium, chloride ions along with water, a mechanism attributed to the standard drug used in this study.[16-17]



CONCLUSION:

The current review found that thiadiazole derivatives are a fascinating class of chemicals with a diverse range of biological actions. According to numerous literature reviews, thiadiazole compounds have anticancer, antibacterial, anti-inflammatory, depressive, antifungal, antitubercular, anticonvulsant, and other activities. Using the same approach, a series of compounds can be produced and then characterised and tested for desired pharmacological action with high potency and low toxicity. Furthermore, small changes in the substituents on the thiadiazole nucleus can increase action. Several recent novel therapeutic advancements in thiadiazole derivatives have demonstrated improved efficacy and reduced toxicity. So far, changes to the thiadiazole moiety have been observed to have important biological effects. It will be exciting to see if these changes may be used as effective medicinal agents in the future.

ACKNOWLEDGEMENT:

The authors are thankful to Principal, Ashokrao Mane Institute of pharmacy, Ambap for providing the necessary facilities**.**

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