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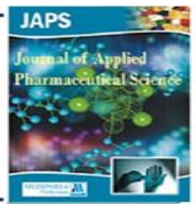

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Review on Biological Activities of 1,3,4-Thiadiazole Derivatives

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ABSTRACT

The Thiadiazole & their derivatives shown the number of pharmacological activity as anti microbial ,anti inflammatory activity, anti tubercular activity, ant diabetic activity, diuretics, anti depressant & cytotoxic activity. these thiadiazole are the heterocyclic compound which contain the five member ring & nitrogen & sulphur. In this paper we mention the recent derivatives of 1,3,4thiadiazole & their activity.

Key words: 1,3,4-Thiadiazole Derivatives, heterocyclic compounds, microbial ,anti inflammatory activity.

INTRODUCTION

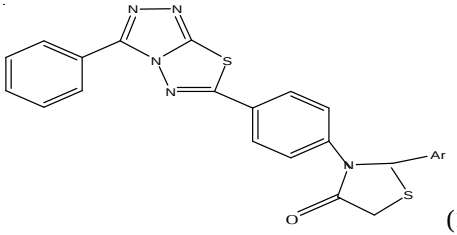
A heterocyclic compound is that which contain more than one kind of atoms if ring are only made up of the carbon atoms than that are called the homocyclic compounds but the heterocyclic ring contain more than one compounds as nitrogen, oxygen or sulfur for example, pyrole, furon, thiophene. during the recent year that has been found there are number of thiadiazole which contain the nitrogen in different position as 1,3,4-thiadaizole & 1,2,3-thiadiazole & 1,2,4- thiadiazole, & 1,2,5-thiadiazole etc. & the basic ring 1,3,4-thiadiazole are the fused heterocyclic ring compound have many biological activities as antimicrobial activity, anti inflammatory, anti fungal, antibiotic, diuretic, anti depressant etc have many example which shown these activity as acetazolamide (diuretic) sulfamethiazole (antibacterial) ceftazolene (antibiotic) atibeprone (anti-depressant) etc. In view of the standard reference work shows that more work has been carried out on the 1,3,4-thiadiazole than all other isomers combined. Members of this ring system have found their way into such diverse application as pharmaceuticals, oxidation inhibitors, cyanine dyes, & metal complexing agents. The literature review showed that the thiadiazole nuclei have antimicrobial, anti-inflammatory, anticancer, antitubercular, antifungal, analgesic, oxidative inhibitors, anti H-pylori, etc.

ANTIBACTERIAL AND ANTIFUNGAL ACTIVITY

Several five membered aromatic systems having three hetero atoms at symmetrical Position , 1,3,4-thia/oxa-diazole have been studied because of their interesting physiological properties. It is also well established that various derivatives of 1,2,4-triazole, 1,3,4-thiadiazole exhibit broad spectrum of pharmacological properties such as antibacterial and antifungal Activities.

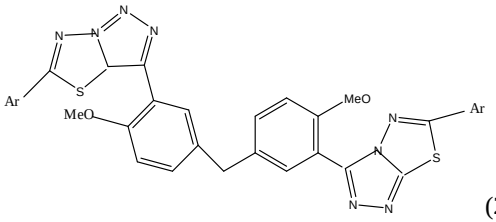
Kokila et al, introduces the various efficient procedure for synthesis of biologically active

1,2,4-triazoleo-[3,4-b]-1,3,4-thiadiazol-2-aryl-thiazolidine-4-one derivatives(1) and evaluated its antibacterial activity against B.subtilis, S.aureus, P.aeruginosa and E.coli (Kokila et al, 2011).



(1)

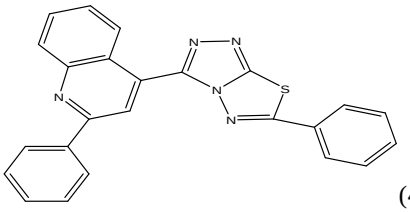
Reddy and others produced article on synthesis and evaluation of novel Bis[1,2,4]triazolo[3,4-b][1,3,4]thiadiazoles (2) as potent antimicrobial agents and evaluated the antibacterial activity against various gram negative and positive bacteria (Reddy et al,2010).



(2)

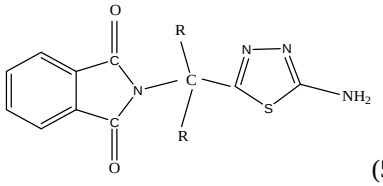
A series of some new 1,3,4-Thiadiazoles and 1,3,4-Thiadiazines containing 1,2,4-Triazolo Nucleus(3) introduced by (Purohit et al,2011) and these newly synthesized compounds were screened for their antimicrobial activity.(3)

Some Syntesis of Triazoles, Oxadiazoles and Condensed Heterocyclic compounds containing Cinchopheny(4) introduced by Peng-Fei Xu and studied of their antibacterial activities against sclerotium *blight of colza, gray mold of cucumber and cercospora brown spot of peanut* (Xu et al, 2004) .



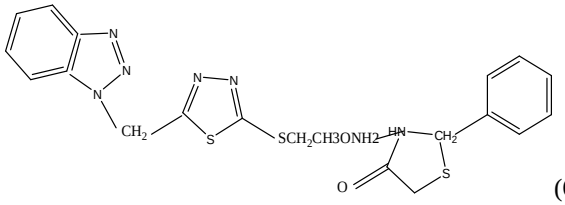
(4)

Yousif and colleague introduced the Synthesis of New Polymers Derived from Poly(vinyl Chloride) and study their biological evaluation as antimicrobial activity (Yousif et al,2009).



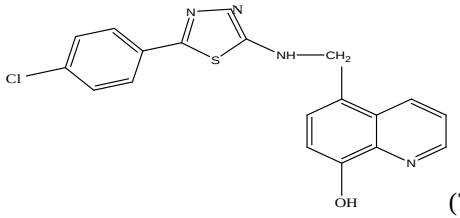
(5)

Conventional as well as eco friendly microwave irradiated synthesis and antimicrobial evaluationof some new benzotriazole derivatives(6) by Sen et al. The synthesized compounds were screened for their antibacterial activity against *Escherichia coli*, *Staphylococcus aureus Klebsiella pneumoniae* and *Bacillus substilis* (Sen et al,2011).



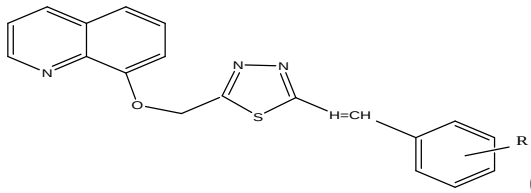
(6)

Patel et al, have been Synthesise metal chelates of 5-[4-Chlorophenyl(1,3,4)thiadiazol-2-ylaminomethylene]-8-hydroxy quinoline(7) , characterized and evaluated its anti-microbial activity (Patel et al,2009).



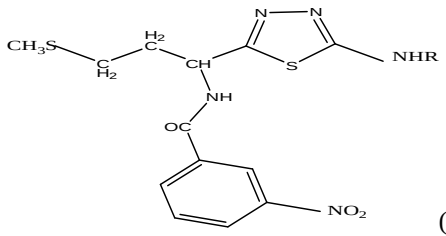
(7)

Some new series 1,3,4-thiadiazoles(8) synthesized by Madhaev and colleagues and further evaluated antimicrobial activity (Madhev et al,2011).



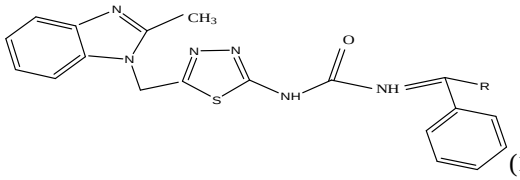
(8)

Pintilie, introduced the Synthesis of some new 1,3,4-Thiadiazole and 1,2,4- Triazole compounds having D,L,-Methionine(9) Moiety and screened its antimicrobial activity (Pintilie et al2007).



(9)

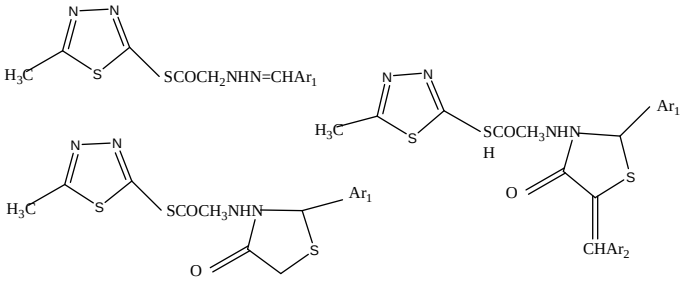
Rakak et al, introduced some new novel 2,5-disubstituted 1,3,4-Thiadiazoles(10) for their potential antimicrobial activity (Rajak et al,2009).



(10)

1,3-thiazolidin-4-one derivatives of 2-mercapto-5-methyl-

1,3,4-thiadiazole(11) Synthesise by Srivastava et al, and evaluated for their and antibacterial activity against B. substilis, E. coli. K. pneumonia and S. aureus bacteria and antifungal activity against A. niger, A. flavus, F. oxisporium and T. viride fungi respectively (Srivastava et al,2010).



Reddy et al, introduced a scientific paper on synthesis and evaluation of novel Bis[1,2,4]triazolo[3,4-b][1,3,4]thiadiazoles (2) as potent antimicrobial agents and evaluated the antifungal activity against Candida albicans, Aspergillus fumigatus, Trichophyton rubrum and Trichophyton mentagrophytes (Reddy et al,2010).

Some Syntesis of Triazoles, Oxadiazoles and Condensed Heterocyclic compounds containing Cinchopheny(4) introduced by Peng-Fei Xu and studied of the Chlorine substituted copounds against few Fungi (Peng-Fei Xu et al,2004).

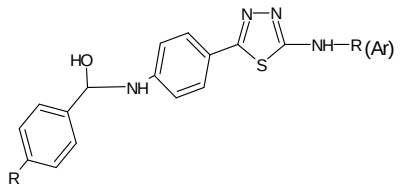
Conventional as well as eco friendly microwave irradiated synthesis and antimicrobial evaluationof some new benzotriazole derivatives(6) by Sen et al, were screened antifungal activity against *Aspergillus niger, Aspergillus flavus, Fusarium oxisporum* and *Trichoderma viride* (Sen et al,2011).

ANTICANCEROUS ACTIVITY

Various substituted 1,3,4-thiadiazoles and 1,2,4-triazoles are important for pharmacological activity. These compounds show antibacterial , antifungal , antimicrobial , antimycobacterial ,anti-inflammatory , antihypertensive , hypolipidemic and anticancer activity.

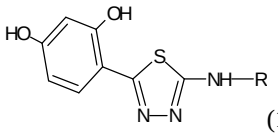
The Antileukemic action of two thiadiazole derivatives(12) introduced by Ciotti et al, and studied on retardation the growth of leukemia L1210 and extended the survival of time in mice (Ciotti et al,2011).

5-[-4-(4fluorobezoylolamino)phenyl]-2-subsitutedamino-1,3,4-thiadiazole derivatives(13) were synthesized by Sevgi et al, and evaluate the cytotoxic activity (Sevgi et al,2010).



(12)

A series of N-substituted 2-amino-5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazoles **(**14**)** were synthesized and evaluated for their antiproliferative activities against human cancer cell lines introduces by Matysiak et al. The cytotoxicity in vitro against the four human cell lines: SW707 (rectal), HCV29T (bladder), A549 (lung), and T47D (breast) was determined. The highest antiproliferative activity was found for 2-(2,4-dichlorophenylamino) 5-(2,4-dihydroxyphenyl)-1,3,4-thiadiazole, with ID_{50} two times lower (SW707, T47D) than for cisplatin studied comparatively as the control compound (Matysiak et al,2006).

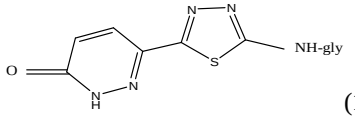


(14)

ANTIINFLAMMATORY AND ANALGESIC ACTIVITY

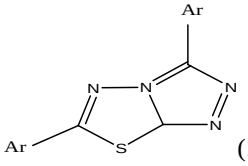
Heterocyclic compounds bearing a symmetrical triazole or 1,3,4-thiadiazole moieties, represent an interesting class of compounds possessing a wide spectrum of biological activities such as anti-inflammatory ,analgesic, antiviral and antimicrobial properties. It has also been reported that derivatives of 1,2,4-triazole and 1,3,4-thiadiazole condensed nucleus systems exert diverse pharmacological activities such as anti-inflammatory , analgesic etc.

Jing Tao has been developed the procedure related to Synthesis of 5-(6-Pyridazinone-3-yl)-2-glycosylamino-1,3,4-Thiadiazoles(15) (Tao et al,2010).



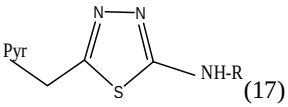
(15)

2,5-disubstituted s-Triazolo[3,4-b] [1,3,4]thiadiazoles(16) by new simple “one-pot” method introduced by Umer et al,1999 and expected the anti-inflammatory, antibacterial and cns depressant.



(16)

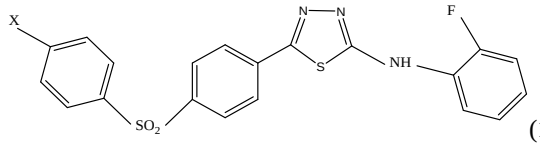
Burbuliene, was to develop simple and efficient procedures for the Synthesis and Characterization of newPurimidine- based 1,3,4-oxa(thia)diazoles, 1,2,4-triazoles and 4- thiazolidinones (17) and evaluated for anti-inflammatory activity (Burbuliene et al,2011).



(17)

New heterocyclic compounds from 1,2 4-triazole and 1,3,4-thiadiazole class having diphenylsulphone and 2-fluorophenyl fragments like 2-amino-1,3,4-thiadiazole)(18) from

cyclization of corresponding acylthiosemicarbazides by Babucianu et al, 2011, and with the purpose of investigating in the future their possible antimicrobial, analgesic or anti-inflammatory activities.

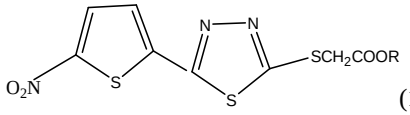


(18)

ANTITUBERCULAR ACTIVITY

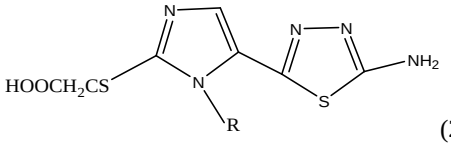
Tuberculosis is one of the very serious health problems caused by Mycobacterium tuberculosis. The treatment of mycobacterial infections especially the tuberculosis, has become an important problem due to the emergence of monodrug and multidrug-resistant strains of M. tuberculosis. Therefore, there is a need for new drugs of new structural classes. In this regard, since the last decade search for new antitubercular substances has ranked among the priority areas of chemotherapeutic research. During recent years, there have been intense investigations on thiadiazole compounds, have attracted the interest of researchers as antituberculosis agents. The purpose of the present work was to explore and develop the novel molecules with improved potential for treating tuberculosis.

Synthesis and in-vitro antimycibacterial activity of alkyl a-[5-(5-nitro-2-thienyl)-1,3,4-thiadiazole-2-ylthio]acetates(19) introduced by Foroumadi et al,2003 .



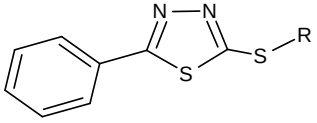
(19)

Synthesis of N-[5-(5-Amino-1,3,4-thiadiazol-2-yl)-2-imidazolylthio]acetic acids (20) introduced by Hadizadeh et al,2008 and these compounds showed the activity aginst mycobacterium tuberculosis.



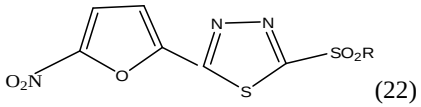
(20)

Foroumadi et al, showed interest in Synthesis of 2-(5-nitro-2-fufuryl)-and 2-(1-methyl-5-nitro-1H-imidazole-2-yl)-1,3,4-thiadiazole derivatives(21) and evaluated in vitro Antituberculosis activity of these derivatives (Foroumadi et al,2004).



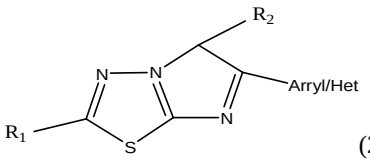
(21)

A new series of 2-(5-nitro-2-furyl)-1,3,4-thiadiazole-2-sulfide(22), sulfoxide and sulfones were synthesized and evaluated for in vitro antituberculosis activity against Mycobacterium tuberculosis strain H37Rv by Foroumadi et al,2002.



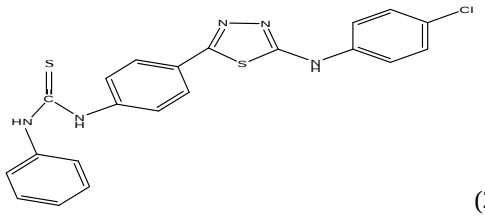
(22)

A series of 2-sulfonamido/trifluoromethyl-6-(40-substituted aryl/heteroaryl)imidazo[2,1-b]-1,3,4-thiadiazole derivatives(23) have been synthesized by Gadad et al,2004, and evaluated for anti-tubercular activity.



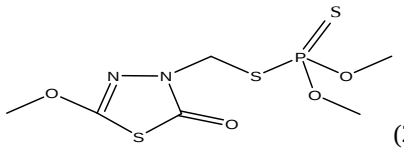
(23)

N-phenyl-*N*_-[4-(5-alkyl/arylamino-1,3,4-thiadiazole-2-yl) phenyl]thiourea derivatives(24) were synthesized by Karakus et al, 2002, and antituberculosis activity were screened in vitro using BACTEC 460 Radiometric System against *Mycobacterium tuberculosis* H37Rv at 6.25 _g/ml.



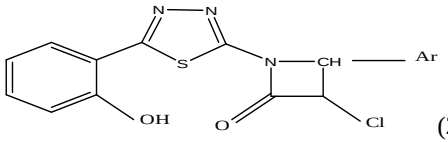
(24)

Methidathion (systematic name: *S*-2,3-dihydro-5-methoxy-2-oxo-1,3,4- thiadiazol-3-ylmethyl *O,O*-dimethyl phosphorodithioate)(25) by Kim et al, 2011, is one of the most widely used organophosphate insecticides in agriculture.



(25)

Gupta et al, have documented the synthesis of 5-(o-Hydroxyphenyl)-2-[4'aryl-3'chloro-2'azetidinon- 1 - yl] – 1 , 3 , 4 -thiadiazole (26) and further evaluated antifungal activity (Gupta et al,2011).

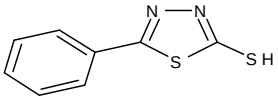


(26)

ANTI-H-PYLORY ACTIVITY

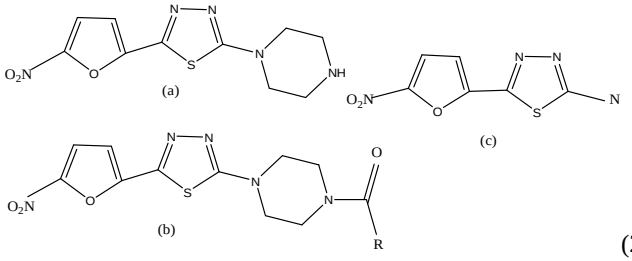
It is now identified that *Helicobacter pylori*, an S-shaped spiral microaerophilic Gram-negative bacterium first isolated in human gastric mucosa in 1982, is the main cause of gastric and duodenal ulcers, and gastric cancer. Hence, the World Health Organization (WHO) has proposed H. pylori as a class 1 carcinogen in humans.

Foroumadi et al, have been introduced a series of N-[5-(5-nitro-2-heteroaryl)-1, 3, 4-thiadiazol-2-yl] thiomorpholines(27) and some related compounds() and evaluated in-Vitro Anti-Helicobactor pylory activity and structure-activity relationship study. They found that nitrofuran analog containing thiomorpholine S,S-dioxide moiety have the potent activity (Foroumadi et al,2009).



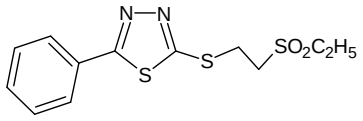
27

A series of 5-nitrofuran-containing (1,3,4-thiadiazol-2-yl)piperazine moieties (28) heterocyclic compounds were synthesized by Moshafi et al,2011, and evaluated those compounds as anti-Helicobacter pylori .



(28)

Abbas Shafiee and others, have synthesized a series of 5-(nitroaryl)-1,3,4-thiadiazoles(29) having certain sulfur containing alkyl side chain were synthesized and evaluated against *Helicobacter pylori*. They found that compound containing 2-[2-(ethylsulfonyl)ethylthio]-side chain from nitrothiophene series was the most potent compound tested against clinical isolates of *H. pylori* (Shafiee et al,2008).

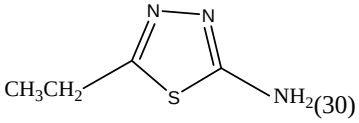


29

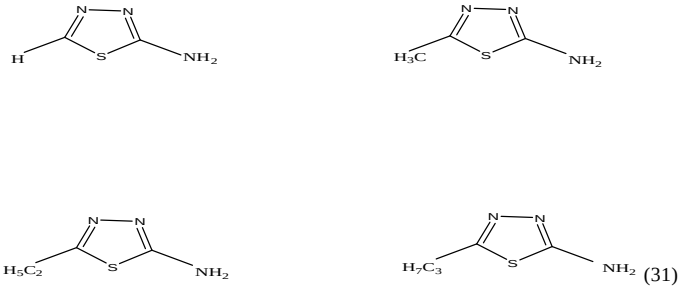
CORROSION INHIBITORS

Most of the well known corrosion inhibitors are organic compounds containing polar groups having nitrogen, sulfur and/or oxygen atoms and heterocyclic compounds with polar functional groups and conjugated double bonds. Organic heterocyclic compounds may act as inhibitors for corrosion of brass, copper, zinc etc. due to chelating action of heterocyclic molecules and the formation of a physical barrier on the brass surface by several mechanisms. The effectiveness of any corrosion inhibitor is dependent on the type of metal, properties of the corrosive environment as well as the state of inhibitor molecule. In these papers focuses on the behaviour of thiadiazole derivatives as corrosion inhibitors for brass in natural seawater, these compounds is expected to show a high inhibition efficiency for copper corrosion because it is a heterocyclic compound containing a variety of donor atoms, and it is nontoxic and inexpensive.

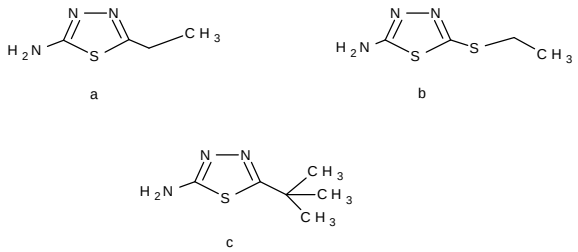
Some derivatives of thiadiazoles like 2-Amino-5-ethyl-1,3,4-Thiadiazole(30) as a corrosion inhibitors for copper in 3% NaCl solution have been introduced by Sherif et al,2006.



Khan et al, introduced the Synergistic effect of potassium iodide on inhibitive performance of thiadiazoles(31) during corrosion of mild steel in 20% sulfuric acid (Khan et al,2010).

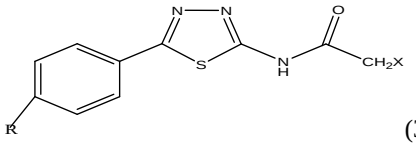


Corrosion inhibition effect of substituted thiadiazoles(32) on brass studied by Joseph Raj et al,2011, ICP-AES analysis confirms that dezincification was minimized to a greater extent in the presence of these inhibitors .



DIURETIC AGENTS

A comparative molecular field analysis study on 3D-QSAR of 2,5,-disubstituted-1,3,4-thiadiazole derivatives(33) as diuretic agents presented by Jain et al,2011.



(33)

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