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A Potential Review On Thiadiazoles

Rushda Parveen[1], Shamim Ahmad[2], Rakhi Mishra[1]*, Shamsher Alam[1]

[1]Department of Pharmaceutical Chemistry, Translam Institute of Pharmaceutical Education & Research, Mawana Road, Meerut 250001, U.P. India

[2]Department of Pharmacognosy, Translam Institute of Pharmaceutical Education & Research, Mawana Road, Meerut 250001, U.P. India

***Corres author: rakhi.misra84@rediffmail.com**
Tel.: +91 7599310341

Abstract: Thiadiazole and their derivatives have been studied extensively because of their wide range of biological activity. They are found to be effective as antibacterial, antimalarial, antiviral, antiinflammatory, anticancer and antianthelminthic agents. Diverse biological activities, such as antibacterial, anti-inflammatory, and antiviral have been associated with 1,3,4- Thiadiazole derivatives. The substituted-1,3,4- Thiadiazole nucleus is particularly common, and examples can be found in marketed drugs such as vermox, albanza, mintizol, mansil vansil.
The synthesis of 1,3,4- Thiadiazole derivatives has attracted widespread attention due to their diverse biological activities, including antimicrobial, anti-inflammatory, analgesic, and antianthelmintic. Therefore, we have synthesized some 1,3,4- Thiadiazole derivatives possessing antimicrobial activity.
Key Word: Thiadiazole,anti inflammatory,antimicrobial and antihelminthics.

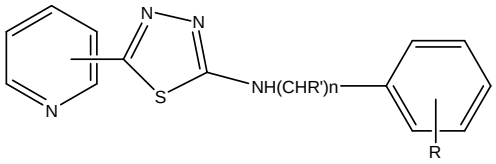
INTRODUCTION

Several 1,3,4 thiadiazole derivatives are also known to exibit diverse biological properties like antimicrobial, antitubercular, anti-inflammatory and anticonvulsant.several new 2,5-disubstituted derivatives of 1,3,4-thiadiazoles containing isomeric pyridyl were obtained from cyclization of corresponding thiosemicarbazides under acidic conditions. some other 1,2,4-triazole and 1,3,4-thiadiazole theterocyclic entities that are very interesting components in terms of their biological properties, such as antifungal, antibacterial, herbicidal and plant growth regulator activites have been reported.the therapeutic effects of compounds containing 1,3,4 thiadiazole and 1,3,4-thiadiazine rings have been well studied for a number of pathological conditions including inflammation, pain and hyprertension the synthesis and in vitro cytotoxic activity of a series of 3 ,6-disubstituted 1,2,4-triazolo,-1,3,4-thiadiazole derivatives used against breast and ovarian human cell lines.the therapeutic effects of compounds containing 1,3,4-thiadizole and 1,2,4-triazole rings have been well studied for a number of pathological conditions including inflammation (1,2),pain (3-5) or hypertension.the biological profile of 1,3,4-thiadiazole derivatives is very extensive various compounds comprising a hetrocyclic ring of the 1,2,5-thiadiazole type present interesting properties in the pharmaceutical or agrochemical industry ,and in the

field of polymers.1,3,4-thiadiazole exhibit broad spectrum of biological activites possibly due to the presence of toxophoric N-C-S moiety.in literature revealed ,some derivaties of (1,2,4)-triazole-(3,4-b)-(1,3,4)-thiadiazoles have been show as optically active with L-amino acid.

ANTIMICROBIAL:

Several new 2,5-disubstituted derivatives of 1,3,4-thiadiazoles **(1)** containing isomeric pyridyl were obtained from cyclization of corresponding thiosemicarbazides under acidic conditions was reported by **Zamani *et al.*** Most of the synthesized compounds have been found to be active against both gram-positive and gram-negative bacteria at less than 3.6 mg/ml. The compound is most active against all seventeen used gram-positive and gram-negative bacteria.[(1)]

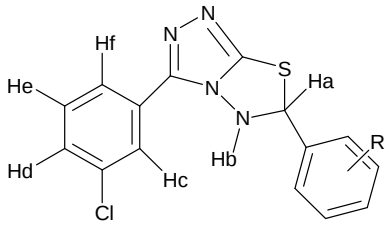


R=R'=H

R=H,R'=CH_3

(1)

The desired fused ring system 3-(3-chlorophenyl)-6-aryl-5,6-dihydro[1,2,4]triazolo[3,4-*b*][1,3,4]thiadiazoles **(2)** were synthesized by the reaction of 4-amino-5-(3 chlorophenyl)-4*H*-1,2,4-triazole-3-thiol reported by **Purohit *et al.*** All the newly synthesized compounds were screened for their antimicrobial activity. Some of the compounds exhibited significant inhibition on bacterial and fungal growth as compared to standard drugs.[(2)]

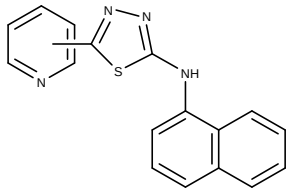


R=$C_6H_5^-$

R=3-Cl-$C_6H_4^-$

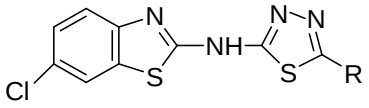
(2)

This compound was synthesised i.e. new 1,2,4-tri and 1,3,4-thiadiazoles **(3)** bearing isomeric pyridyl and 1-naphthyl was reported by **Zamani *et al.*** using 1,4-disubstituted thiosemicarbazides in alkaline and acidic media, respectively. The antibacterial studies of some of the synthesized compounds against *S. aureus* and *E. coli* as MIC values are reported. None of them have important antibacterial activities.[(3)]



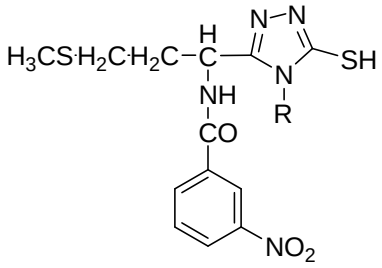
(3)

Thiosemicardazide of 6-chloro-2-aminobenzotiazole on cyclization with different carboxylic acid in $POCL_3$ and substituted azlactones in pyridine provide the corresponding 2-aryl-5-(6chloro-1,3benzothiazole-2-yl-amino)-1,3,4-thiadiazoles**(4)** was reported by **Amir *et al*.** all the compounds have been evaluated in vitro for their antimicrobial activities against several microbes and show significant activity.[4]



(4)

The New synthesis that is 1,3,4-thiadiazole**(5)** and 1,2,4-triazolecompounds containing a *D,L*-methionine moiety were synthesized by intramolecular cyclization of 1,4-disubstituted thiosemicarbazides in acid and alkaline media, respectively was reported by **Otilia Pintilie *et al***[5]

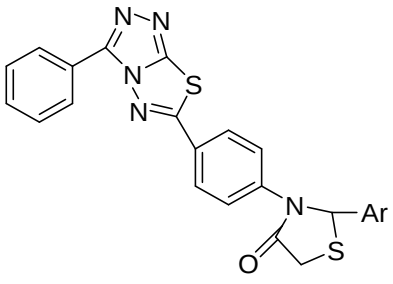


R=CH_3, C_6H_5, C_6H_4-CH_3

(5)

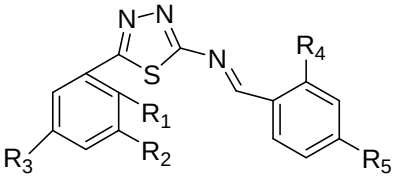
ANTIHELMINTHICS:

Some new and biologically active [1,2,4] triazolo [3,4-b][1,3,4] thiadiazole-2-aryl-thiazolidinone-4-ones**(6)** were synthesized by reaction of Schiff bases with mercapto acetic acid in presence of THF with adding anhydrous ZnCl2 reported by **Parmar Kokila *et al.*** The compounds have been evaluated for antibacterial activity against B. subtilis, S. aureus, P. aeruginosa.[6]



(6)

This research was concentrates on the synthesis of some Schiff bases of 5-phenyl substituted, 2-amino 1, 3, 4 thiadiazole **(7)**derivates. The synthesis was reported by **Mathew *et al*,** this reaction between various aryl carboxylic acids with thiosemicarbazide in presence of dehydrating agent like Conc. H_2SO_4 to form 5-phenyl substituted, 2-amino 1, 3, 4 thiadiazole derivates. These derivatives on further treatment with various aldehydes to form Schiff base.[7]



R_1=OH, H

R_2=H, NO_2

R_3=H, NO_2

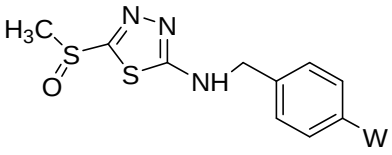
R_4= OH, H

R_5=Cl, OCH_3, H

(7)

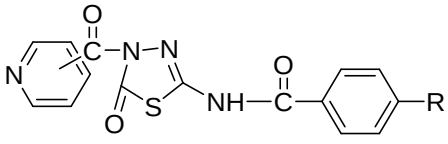
ANTI INFLAMMATORY:

In this work was reported by **Varandas *et al,*** the design, synthesis and evaluation of the anti-inflammatory, analgesic, and antiplatelet properties of new 1,3,4-thiadiazole**(8)** derivatives, structurally planed by exploiting the molecular hybridization approach between diuretic drug acetazolamide and a 1,3-benzodioxole COX-2 inhibitor, previously developed. The *in vivo* pharmacological evaluation of these new compounds lead us to identify the *para*-fluoro-substituted derivative 8b as a new prototype, more active that celecoxib at the same molar concentration.[8]



(8)

Two series of 3-arylsulphonyl-5-arylamino-1,3,4-thiadiazol-2(3H)ones **(9)** with potential anti-inflammatory and analgesic activity were prepared and tested. Pharmacological results revealed that all the title compounds, endowed with an arylsulphonyl side chain, possess good antalgic activity and fair anti-inflammatory properties. The analgesic profile of the two series, evaluated by the acetic acid writhing test, showed that compouds 2c, 2f and 2h, in particular, were the most active, this experiment was reported by **Schenone *et al***.[9]



R=C_6H_5, $C_6H_4PCH_3$

(9)

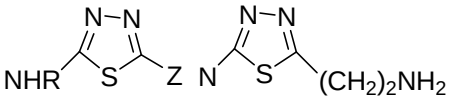
In order to reduce the ulcerogenic effect of ibuprofen, its carboxylic group has been converted into 5-membered heterocyclic rings. Various 1,3,4-oxadiazoles, 1,2,4-triazoles, 1,3,4-thiadiazoles, and 1,2,4- -triazine derivatives of ibuprofen were prepared by cyclization of 2-(4-*i*-butylphenyl) propionic acid hydrazide and *N1*-[2-(4-*i*-butylphenyl)-propionyl]-*N4*-alkyl/aryl- -thiosemicarbazides under various reaction conditions this experiment was reported by Amir *et al*. The cyclized derivatives were screened for their anti-inflammatory activity by the

carrageenan induced rat paw edema method and showed 50 to 86% inhibition, whereas the standard drug ibuprofen showed 92% inhibition at the same oral dose.[10]

In this work was reported by **Varandas *et al,*** the design, synthesis and evaluation of the anti-inflammatory, analgesic, and antiplatelet properties of new 1,3,4-thiadiazole derivatives, structurally planed by exploiting the molecular hybridization approach between diuretic drug acetazolamide and a 1,3-benzodioxole COX-2 inhibitor, previously developed. The *in vivo* pharmacological evaluation of these new compounds lead us to identify the *para*-fluoro-substituted derivative 8b as a new prototype, more active that celecoxib at the same molar concentration.[11]

ANTIVIRAL:

Starting from 4-chlorobenzoic acid, 10 new 5-(4 chlorophenyl)-*N*-substituted-*N*- 1,3,4-thiadiazole-2-sulfonamide**(10)** derivatives were synthesized in six-steps. Esterification of 4-chlorobenzoic acid with methanol and subsequent hydrazination, salt formation and cyclization afforded 5-(4-chlorophen-yl)-1,3,4-thiadiazole-2-thiol. Conversion of this intermediate into sulfonyl chloride, followed by nucleophilic attack of the amines gave the title sulfonamides, this experiment was reported by **Chen *et al***.[12]



(10)

The efficacy and safety of oral LY217896 for prevention of experimental influenza A/Kawasaki/86 (HIN1) virus infection were assessed in susceptible males randomly assigned to receive LY217896 (75 mg) or placebo once daily for 7 days beginning 24 h prior to viral challenge. The rates of virus shedding (100% in both groups), days of viral shedding (3.1 ± 1.3 for the LY217896 group; 2.8 ± 1.3 for the placebo group), and titers of virus in nasal washings did not differ between the groups. Mild upper respiratory tract illness (72% in the LY217896 group; 69% in the placebo group) developed in similar proportions of each group. LY217896 was associated with asymptomatic rises in serum uric acid levels and was ineffective in modifying the virologic or clinical course of experimental influenza A (HiN1) virus infection, this is reported by **Hayden *et al***.[13]

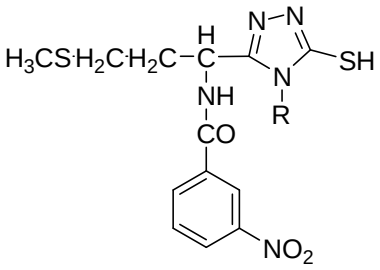
Isosorbide-2-aspirinate-5-salicylate is a true aspirin prodrug in human blood because it can be effectively hydrolyzed to aspirin upon interactionwith plasma BuChE. We show that the identity of the remote 5-ester dictates whether aspirin is among the products of plasma-mediated hydrolysis. **Jones *et al*** observing the requirements for aspirin release from an initial panel of isosorbide-based esters, we were able to introduce nitroxymethyl groups at the 5-position while maintaining ability to release aspirin. Several of these compounds are potent inhibitors of platelet aggregation. The design of these compoundswill allowbetter exploration of cross-talk betweenCOXinhibition and nitric oxide release and potentially lead to the development of selective COX-1 acetylating drugs without gastric toxicity.[14]

In this experiments, the compound 2-amino-5-(2-sulfamoylphenyl)- 1,3,4-thiadiazole(11) (G413) was shown to possess high activity against DNA viruses (herpes simplex viruses 1 and 2 and adenovirus 17) and RNA viruses (poliovirus 1, echovirus 2, and coxsackievirus B4) reported by Bonina *et al*. Experiments on the replicative cycle of poliovirus 1 and production of infectious RNA viruses demonstrate that this compound probably prevents assembly of virus particles by acting on structural proteins. In the present experiments, results concerning the activity of derivatives of G-413 after side-chain modification are reported. Modification of the primary amine H to CH_3 or CH_2-CH=CH_2 produced a loss of activity against DNA viruses, but inhibitory action on RNA viruses was preserved. Modification to CH_2CH_3 resulted in the loss of antiviral activity.[15]

ANTICANCER:

Some 2-R-5-formyl-1,3,4-thiadiazole derivatives have been synthesized and characterized by their spectral data. Thus, **Şerban *et al*** described in the present paper the formation and hydrolysis, through Sommelet reaction, of some hexamethylenetetramine salts from which some new heterocyclic aldehydes resulted.[16]

A facile synthesis of 3,6-disubstituted-1,2,4-triazolo-[3,4-b]-1,3,4-thiadiazoles**(11)** has been achieved by condensing 3-aryl substituted 4-amino-5-mercapto (4H)-1,2,4-triazole with various aromatic acids was reported by **Ilango *et al***.[17]



$R=C_6H_5$

(11)

CONCLUSION:

The review article shows that [1,3,4]thiadiazole heterocycles has resulted in some therapeutically potential analogs. Some compounds have shown more pharmacological action than standard. Thus it is of need for the researchers to do some more work on thiadiazole derivatives which serves as a core structural component in an array of drug categories such as antimicrobial, anti-inflammatory, analgesic, antiepileptic, antiviral, antineoplastic, and antitubercular agents. The broad and potent activity of thiadiazole and their derivatives has established them as pharmacologically significant scaffolds. In this study, an attempt has been made with recent research findings on this nucleus, to review the structural modifications on different thiadiazole derivatives for various pharmacological activities.

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