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# SYNTHESIS AND EVALUATION OF THIADIAZOLE DERIVATIVES

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**ABSTRACT**

Thiadiazole nucleus is found in natural and synthetic products of biological interest. A wide variety of biological and pharmacological properties are associated with thiadiazole nucleus. Various substituted thiadiazole have been reported to have a very wide range of biological activities, such as anti-inflammatory, anticonvulsant, antibacterial, antifilarial, antihelmintic activities etc. In view of proven potentiality of thiadiazole, it has been felt worthwhile to get then incorporated with the suitable pharmacophores by molecular conjunction method. Accordingly it has been planned to synthesize substituted thiadiazoles.2-cyano-3-phenyl-N-(5-phenyl-1,3,4-thiadiazol-2-yl)acryl amides with thiadiazole pharmacophore group is planned to be synthesized as they incorporate many interesting structural features associated with antibacterial activity. As physico-chemical properties influence the biological activity to a great extent, various ring substituted derivatives have been synthesized.

**Keywords**: Thiadiazole, Biological activities, Anti-inflammatory, Anticonvulsant, Antibacterial.

## INTRODUCTION

### Objectives

- To synthesize the various substituted thiadiazoles.
- To purify the intermediate and final compounds by appropriate recrystalisation and or chromatographic techniques.
- To characterize all the new compounds by analytical and spectral methods.
- To evaluate anti-bacterial anti inflammatory and antioxidant activities of the compounds and an effort will be made to study the SAR of the compounds.

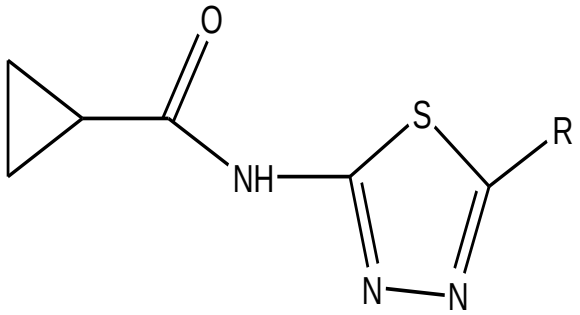
### Review of 1, 3,4 Thiadiazoles [1-4]

1,3,4-thiadiazole derivatives have been of interest to the medicinal chemists because of their diverse pharmacological activities such as Antifungal, Anticancer, Antidepressant, Antitrypanocidal, Antileishmanicidal, Analgesic, Antihelicobacterpylori, Antimicrobial, Anticonvulsant, Antituberculosis, Antimycobacterial, Antibacterial, Anti-inflammatory activities.

### Antifungal Activity [5,6]

Some N-(5-substituted-1,3,4 thiadiazol-2-yl) cyclopropane carboxamide derivatives **(1)** were synthesized and evaluated for antifungal activity. Based on COMFA these compounds were found to display a good anti fungal activity.

R=Ph or O-MePh




Han song CHEN *et al.*, in 1999 reported the synthesis of active pyrazolyl substituted 1,3,4 thiadiazole compounds **(2)** showed fungicidal activity against *Rhizoctonia solons.*

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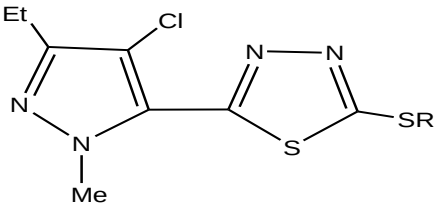
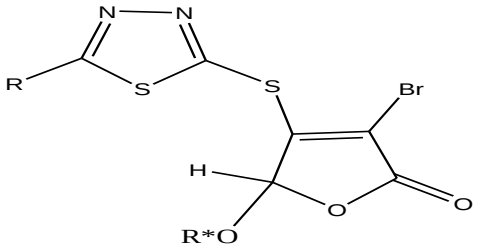
R=Me,Pr,Allyl, **2**



**Anticancer Activity**

A new series of chiral 1,3,4-thiadiazole derivatives **(3)** possessing γ-substituted butenolide moiety and evaluated for *in vitro* anticancer properties. These compound exhibited best inhibitory activity. All the compounds showed good anticancer activities against hela cell lines.

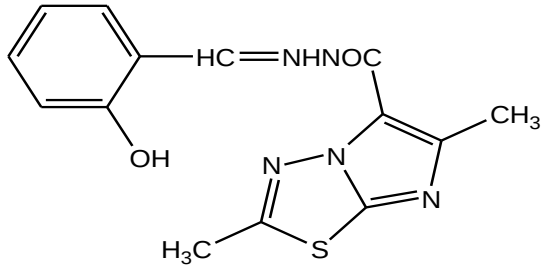


R*=1-Methyl;R=p-$NO_2$-$C_6H_4$

**3**

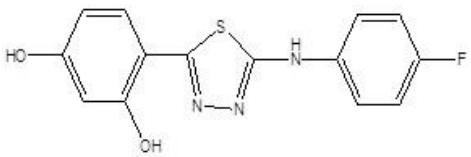
Wojciech rzeski *et al.,* in 2007 reported the synthesis of 2-(4-fluorophenyl amino)-5-(2,4-dihydroxy phenyl)-1,3,4 thiadiazole (FABT) **(29)** Which is the derivative of 2-amino 1,3,4-thiadiazoles and it showed anticancer activity.

**FABT 4**



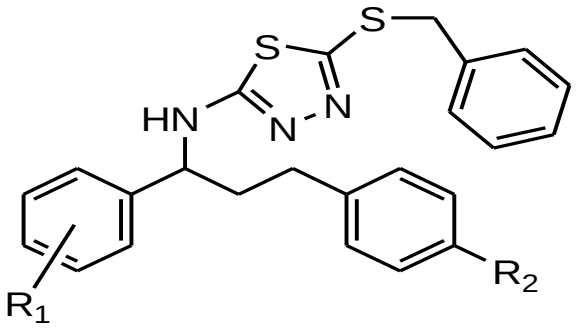
Novel 2,6-dimethyl-N′-substituted phenyl methylene imidazo [2,1-b]-[1,3,4] thiadiazole-5-carbohydrazides were synthesized. 2, 6-dimethyl-N′-(2-hydroxy-phenyl methylidene) imidazo [2,1-b][1,3,4] thidiazole-5-carbohydrazide **(5)** showed the most favorable cytotoxicity.

**5**



**ANTIDEPRESSANT ACTIVITY**

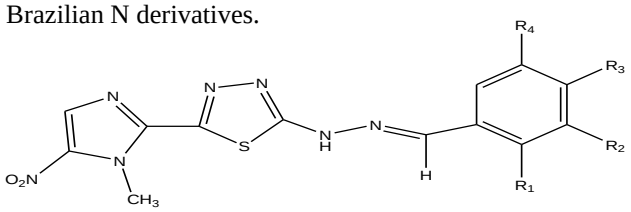
A number of new imine derivatives of 5-amino 1,3,4 thiadiazole-2-thiol were synthesized .The compounds 5-{[1-(4-chloro phenyl)-3-(4-methoxy-phenyl)prop-2-en-1-ylidene]-amino}-5-benzyl thio -1,3,4 thiadiazole **(6)** and 5-{[1-(4- chloro phenyl)-3-(4-dimethyl-amino-phenyl)prop-2-en-1-ylidene]-amino}-5-benzyl thio -1,3,4 thiadiazole **(7)** shown sufficient antidepressant activity using imipramine as reference drug.



**6**=$R_1$=$OCH_3$,:$R_2$=Cl
**7**=$R_1$= $N(CH_3)_2$ $R_2$=Cl

**ANTITRYPANOCIDAL ACTIVITY**

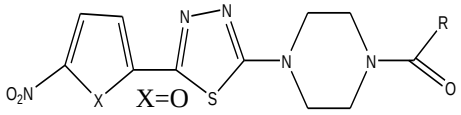
Samir A. carvalho *et al.,* in 2008 synthesized structurally related 1,3,4-thiadiazole 2-aryl hydrazone derivatives and are screened for antitrypanocidal activity. The most active hydrazone compounds of this new series were 3-nitrophenyl and 5-nitrovanillyl **(8) & (9)** named Brazilian N derivatives.

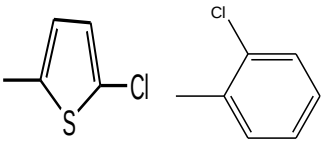


| | $R_1$ | $R_2$ | $R_3$ | $R_4$ |
|---|---|---|---|---|
| **8** | H | OH | OH | H |
| **9** | H | $NO_2$ | OH | $OCH_3$ |

**ANTILEISHMANICIDAL ACTIVITY**

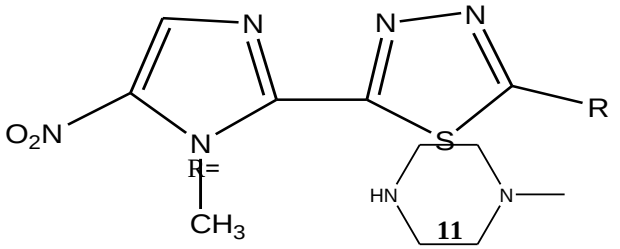
some nitro heteroaryl -1,3,4 thiadiazole based compounds including 1-[5-(5-nitrofuran -2-yl)-1,3,4 thiadiazole-2-yl]-4-aroyl piperazines and 1-[5-(5-nitrothiophen -2-yl)-1,3,4 thiadiazole-2-yl]-4-aroyl piperazines were synthesized and evaluated for anti leishmanicidal activity.5- nitro furan derivatives **(10)** were more active than the corresponding 5-nitrothiophen analogues.





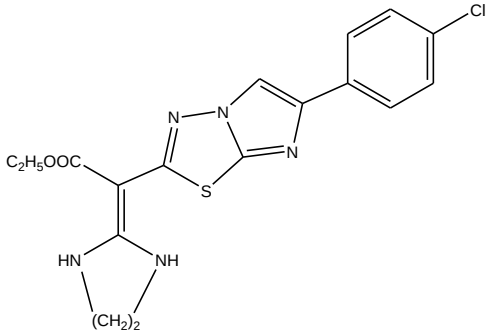
R= **10**

A series of 2-(1-methyl-5-nitroimidazol-2-yl)-5-(1-piperazinyl, 1-piperidinyl and 1-morpolinyl)-1,3,4-thiadiazole were synthesized and evaluated for antileishmanicidal activity against *Leismania major* promastigotes. All the compounds in this series showed strong & much better activity. Compound **(11)** was the most active compound among all the compounds.



**11**

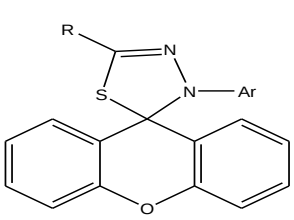
Ram V.J *et al.,* in 1997 synthesized a series of imidazo[2,1-b] 1,3,4- thiadiazole derivatives and evaluated for antileishmanicidal activity. Compound **(12)** showed better leishmanicidal activity.

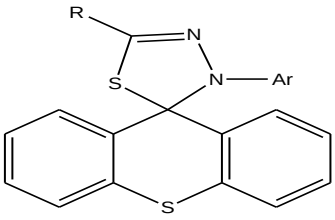


**12**

## ANALGESIC ACTIVITY

A novel spiro-thioxanthene-9', 2-[1, 3,4] thiadiazoles and spiro-xanthene-9',2-[1,3,4] thiadiazole derivatives were synthesized and evaluated for analgesic activity. Compounds **(13)** &**(14)** were obtained in good yields and they showed significant activity compared to standard drug.

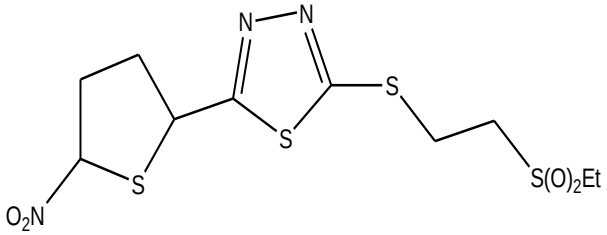




**13.**R= $C_6H_5$, $COCH_3$ **14.** Ar=$C_6H_5$, p-$C_6H_4$-Cl, p-$C_6H_4$-$NO_2$

## ANTI-HELICOBACTERPYLORI ACTIVITY

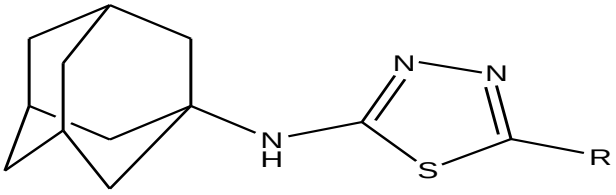
A series of 5-(nitroaryl)-1,3,4 thiadiazoles bearing certain sulfur containing alkyl side chain and evaluated against helicobacter pylori using disk diffusion method. The compound 2-[2-(ethyl sulfonyl) ethyl thio] side chain from nitrophen series **(15)** was the most potent compound tested against clinical isolates of *H.pylori*.



**15**

## ANTI-MICROBIAL ACTIVITY

A series of 2-(1-adamantyl amino)-5-substituted 1,3,4 thiadiazoles were synthesized and evaluated for antimicrobial activity. Compound **(16)** showed potent activity against gm +ve bacteria *Bacillus subtilis.*



R=4-Cl $C_6H_4$, 4-$NO_2C_6H_4$,1-Adamantyl **16**

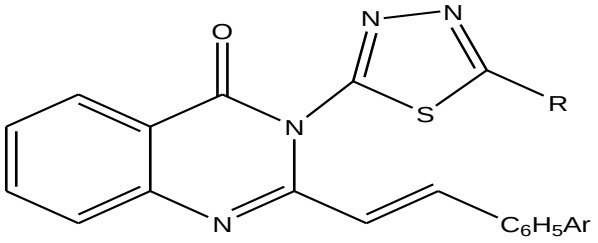
## ANTI-CONVULSANT ACTIVITY

A series of new 3-[5-substituted phenyl]-1, 3,4 thiadiazole-2-yl]-2-styryl quinazoline-4(3H) ones were synthesized and evaluated for anticonvulsant activity. Compound **(17)** showed favorable anticonvulsant activity.

Ar=p-$ClC_6H_4$

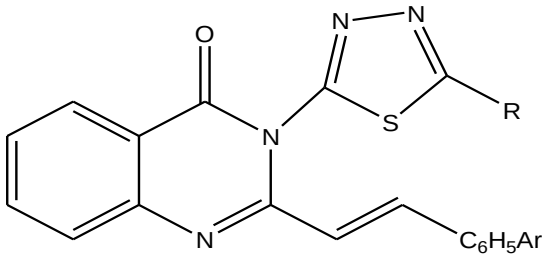
R=$C_6H_5$,m-$ClC_6H_4$, p-$ClC_6H_4$

**17**



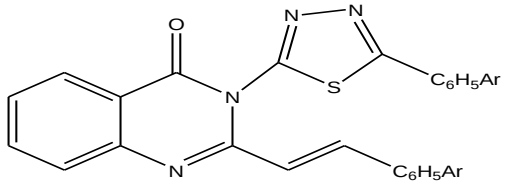
Bhandari *et al.,* in 2008 reported the synthesis of 3-[5-substituted 1, 3, 4-thiadiazole-yl]-2-styryl quinazoline-4(3H)-ones and these derivatives were tested *in vivo* for their anticonvulsant activity using MES and

PTZ models. The compound **(18)** was found to be more potent among all the synthesized compound using PTZ model.



R=$N(CH_3)_2$ Ar=4-F **18**

The compounds (**19)** and (**20)** were found to be significantly potent using MES model.

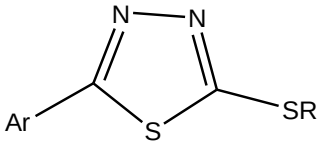


| | **(19)** | **(20)** |
|---|---|---|
| R | $N(CH_3)_2$ | 3-$NO_2$ |
| Ar | 3-$NO_2$ | 4-Br |

**ANTITUBERCULOSIS ACTIVITY**

Alireza foroumadi *et al*., in 2004 reported the synthesis of two series of 2-(5-nitro-2-furyl) and 2-(1-methyl-5-nitro-1H-imidazol-2-yl)-5-propyl,allyl and propargyl) thio -1,3,4 thiadiazoles and 2-(5-nitro-2-furyl) and 2-(1-methyl-5-nitro-1H-imidazol-2-yl)-5-(nitro benzyl) thio -1,3,4 thiadiazoles derivatives.

The compounds **21(a-e)** were evaluated for antituberculosis activity, all the compounds in this series showed significant inhibition effects against *M.tuberculosis*.

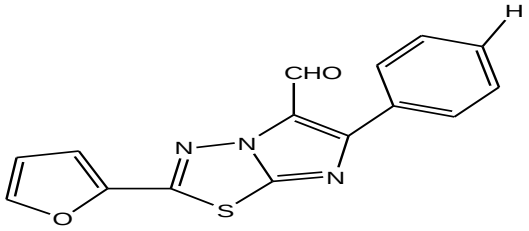


**21(a-e)**

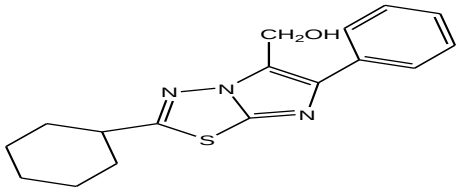
| | Ar | R |
|---|---|---|
| A | 1-methyl 5-nitro1H-imidazol-2-yl | n-propyl |
| B | 5-nitro 2-furyl | Propargyl |
| C | 5-nitro 2-furyl | 2-nitro benzyl |
| D | 5-nitro 2-furyl | 3-nitro benzyl |
| E | 5-nitro 2-furyl | 4-nitro benzyl |

A series of 2,6-disubstituted and 2,5,6 trisubstituted imidazo [2,1,b][1,3,4] thiadiazoles were synthesized, the structures of the compounds were elucidated and screened for anti-tubercular activity against *M.tuberculosis* $H_{37}$Rv.

Among the tested compounds 2-(2-furyl)-6-phenylimidazo[2,1,b][1,3,4] thiadiazole-5-carbaldehyde **(22)** and 2-(2-furyl)-6-phenylimidazo [2,1,b][1,3,4] thiadiazole-5-yl methanol **(23)** have shown the highest (100%)activity.



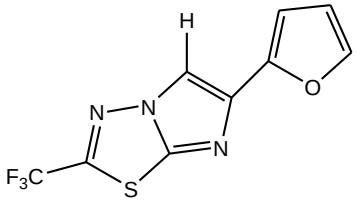
**22**



**23**

**ANTIMYCOBACTERIAL ACTIVITY**

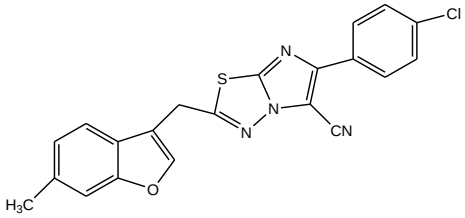
Various 2-sulfonamide/triflouromethyl-6-(4'-substituted aryl/ heteroaryl imidazo [2,1,b][1,3,4] thiadiazole derivatives were synthesized and evaluated for antimycobacterial activity. Compound **(24)** was the most promising derivative for antimycobacterial activity.



**24**

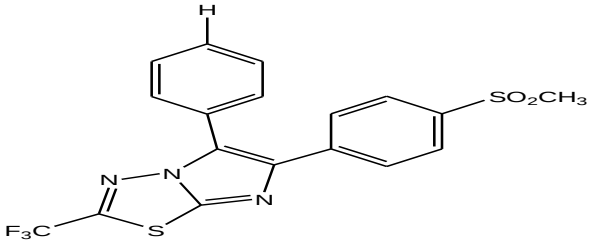
**ANTI-INFLAMMATORY ACTIVITY:**

A series of 6-substituted and 5,6-disubstituted 2-(6-methyl-benzofuran-3-yl-methyl)-imidazo[2,1-b][1.3,4] thiadiazoles **(25)** were synthesized and showed anti-inflammatory activity.

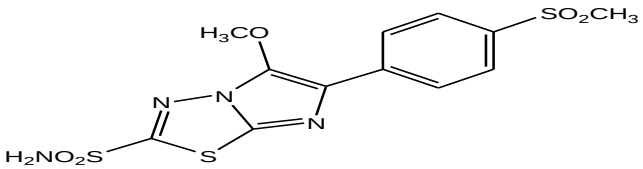


**25**

A series of 2-trifluoromethyl/ sulfonamide 5,6-diaryl substituted imidazo [2,1,b]-1,3,4 thiadiazole derivatives were synthesized and screened for their anti-inflammatory activity. The compounds **(26) &(27)** showed appreciable COX-2 inhibitory activity.



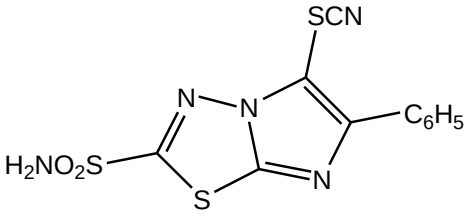
**26**



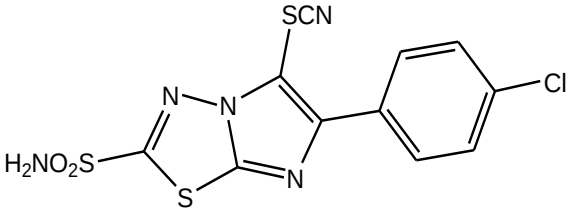
27

**ANTIBACTERIAL ACTIVITY:**

Some 5-guanylhydrazone/thiocynate-6-aryl-imidazo [2,1,b] - [1,3,4]-thiadiazole-2-sulphonamide derivatives were synthesized and screened for anti-bacterial activity. compounds **(28)&(29)** showed promising activity during antibacterial screening against *E.coli* and *S.aereus* and moderate activity against *salmonella typhi, P.aeruginosa*.



**28**



**29**

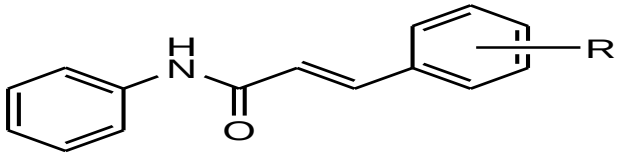
Novel methylene bridged benzisoxazolyl-imidazo[2,1-b][1,3,4] thiadiazoles were synthesized and these derivative **(30)** showed highest activity against *E.coli, S.aureus*-ATCC 25923,*B.subtilis*.

**REVIEW OF LITERATURE OF CINNAMIDES**

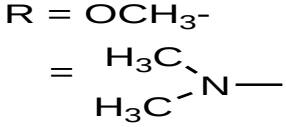
Literature survey reveals that cinnamide derivatives were reported to possess varied pharmacological activities such as anticancer, anticonvulsant, antifungal, KCNQ2 opener antimicrobial, vasodilative, antiatherogenic TRPV1 antagonist, NMDA receptor antagonist etc.

**Cinnamides with Antimicrobial Activity**

A new microwave procedure for the rapid and efficient synthesis of N-phenyl-3-(substituted phenyl) propenamides (3**1**) has been developed. The microwave heating effectively reduced the reaction time from 12h-16h to a few min (4-7 min) and improved the yields. The compounds were active against all the three strains of *C. albicans*. All the compounds inhibited growth of the fungi at a concentration ranging between 12.5-19 μg/ml.



**31**



A series of esters, substituted derivatives and amides of cinnamic acid (3**2**) were synthesized and evaluated as antibacterial and antifungal agents. All the derivatives showed antimicrobial activity comparable to the standard. The quantitative models relating the structural features of cinnamic acid derivatives and their antimicrobial activity showed that Gram negative *Escherichia coli* and candida albicans were the most sensitive microorganisms.

$C_6H_5$-CH=CH-COR (3**2**)

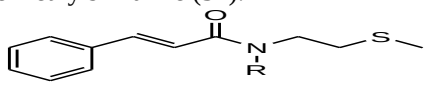
R = $N(C_2H_5)_2$

= $N(C_2H_5OH)_2$

= Morpholinyl

= Piperidinyl

The synthesis and antimicrobial evaluation of some aryl cinnamides and imidazolones derivatives based on2-(N-phthalimidomethyl)-4-benzylidene-5(4)-oxazolone were reported. Analysis of the methanolic leaf extract of *glycosmis cyanocarpa* (Rutaceae) led to the isolation of a new type of sulfur containing cinnamides with antifungal activity: Sinharine (cinnamic acid methyl sulfidoethylamide) **(33)** and the corresponding N-methyl derivative methylsinharine (3**4**).

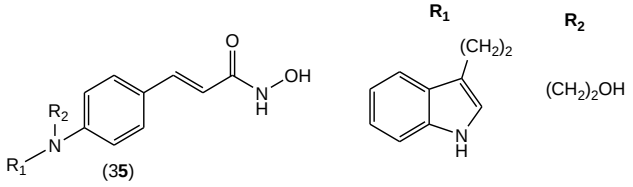


**33** R = H
**34** R = $CH_3$

**Cinnamides with Anticancer Activity**

A series of N-hydroxy-3-substituted phenyl-2-propenamide were prepared as novel inhibitors of human histone deacetylase (HDAC). These compounds were potent enzyme inhibitors, in a partially purified enzyme assay. However, potency in cell growth inhibition assays ranged over 2 orders of magnitude in two human carcinoma cell lines i.e. H 1299 and HCT116 cells. Four

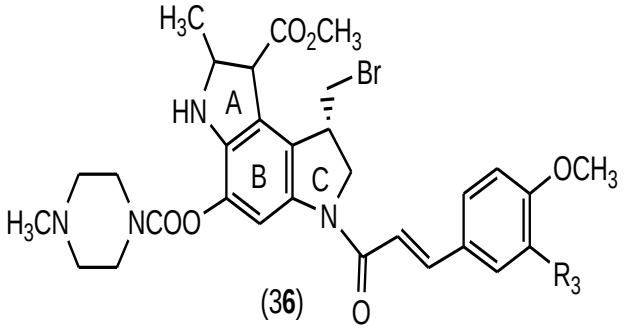
compounds having MTD≥100 mg/kg were selected for dose-reponse studies in HCT116 xenograft model and one compound (3**5**) (NVP-LAQ824) had significant dose-releated activity in the HCT 116 colon and A549 lung tumor models, high MTD, and low gross toxicity. On the basis of these properties, Compound 3**5** has entered human clinical trials as a novel anticancer agent.




(3**5**)

(NVP-LAQ824)

A series of N-cinnamates of A-ring pyrrole compound of duocarmycin (3**6**) were synthesized and evaluated for *in vitro* anticellular activity against He La S3 cells and *in vivo* antitumor activity against murine sarcoma 180 in mice. The 4'-methoxy and 4'-BoCNH-cinnamates exhibited strong *in vitro* anticellular activity among the synthesized compounds. Most of the 8-O-(N,N-dialkyl carbamoyl) derivatives of the 4'-methoxycinnamates displayed remarkably superior *in vivo* antitumor activity to duocarmycin A or B2. It was showed that the 4'-position of these cinnamates plays a significant role for the biological activity, and the substituent at the 3'-position contributes to an enhancement of water solubility.




(36)

$R_3 = NEt_2$

**Cinnamides with Vasodilative Activity**

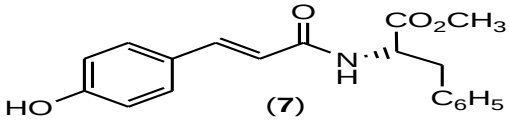
The synthesis and vasodilative activities of cinnamides and o-phenyl cinnamide derivatives were studied for searching new compounds with strong vasodilating effect. The classic knoevenagel condensation and mixed anhydride method were used.

Nine cinnamides and phenyl cinnamide derivatives were synthesized. Vasodilative activity screening (*in vitro)* showed that the olefinic linkage inserted between the benzene ring and carbonyl group was unfavourable to inhibit, the contraction activity of rat aortic strip induced by noradrenaline while the introduction of bulky groups (substituted phenyl) at a position of the cinnamoyl carbonyl group might selectively enhance the inhibition activity against contraction of rat aortic strip.

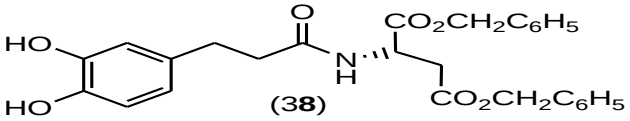
Han Xiao-bing reported the synthesis and biological activities of a substituted N-(phenylethyl) cinnamides. The results showed that title compounds had remarkable immunity and vasodilating effects.

**Cinnamides with Anti–Atherogenic Activity**

A series of cinnamic acid derivatives were synthesized and their biological abilities on lipoprotein metabolism were examined. Among the tested compounds, 4-hydroxy cinnamic acid (L-phenylalanine methyl ester) amide (3**7**) and 3,4-dihydroxyhydrocinnamic acid (L-aspartic acid dibenzyl ester) amide (3**8**) inhibited human acyl-CoA : cholesterol acyl transferase-1 and 2-activities. Compounds 3**7** and 3**8** also served as antioxidants against copper mediated low-density lipoproteins (LDL) oxidation. These new cinnamic acid derivatives possess useful biological activity as antiatherosclerotic agent with inhibition of cellular cholesterol storage and transport by both ACAT, inhibition of LDL-oxidation, HDL particle size.

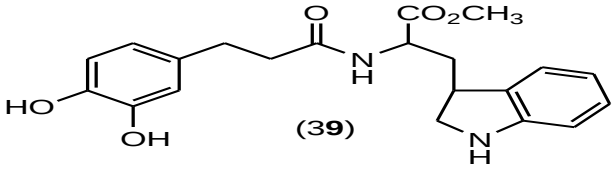



(7)

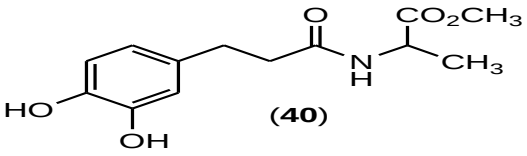



(38)

3,4-dihydroxy hydrocinnamides 3**8** and 3**9** exhibited the antiatherogenic activities by inhibiting the formation of aortic fatty streak in high cholesterol-fed rabbits.



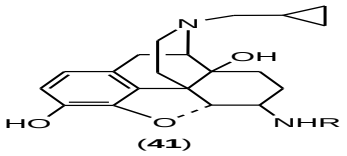

(39)




(40)

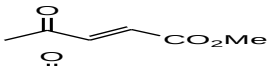
**Cinnamides as Opioid Antagonists**

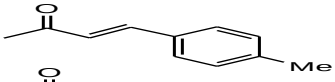
Cinnamoyl derivatives of β-naltrexamine (β-NTA) (**41**) have been prepared and evaluated as potential irreversible opioid antagonist β-FNA and the cinnamoylamido analogues (Bu42, 59 and 60) were prepared from β-naltrexamine (β-NTA) in 60-70% yields by acylation with the appropriate acid chloride in dichloromethane in presence of triethylamine.

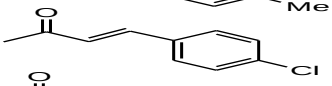


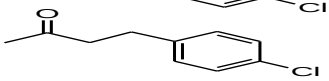
(41)

(β - NTA) R = H

(β - NTA) R = 

(BU42) R = 

(BU59) R = 

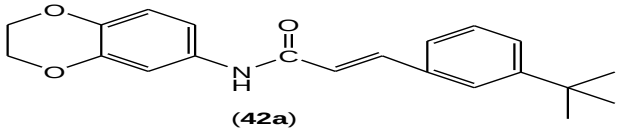
(BU60) R = 

**Cinnamides as TRPVI Antagonists**

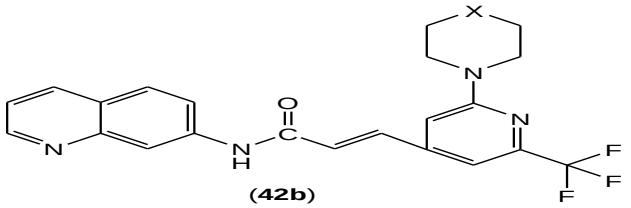
The vanilloid receptor-I (TRPVI or VRI) is a member of the transient receptor potential (TRP) family of ion channels and plays a role in regulating the function of sensory nerves. A growing body of evidence demonstrates the therapeutic potential of TRPVI modulators, particularly in the management of pain.

Elizabeth M. Doherty *et al* identified the potent TRPVI antagonist (E)-3-(4-tert-butylphenyl)-N-2,3-dihydrobenzo[b][1,4]dioxin-6-yl)acryl-amide (**42a**). Replacement of benzodioxan-7-yl group i.e. compound (**42b)** with the 7-quinolinyl group resulted in a significant improvement in functional activity.

Alterations to the acrylamide core were detrimental to activity, consequently the amide was preferred over the N-methyl amide, thioamide, or ester, and the *trans*-cinnamide was preferred over the dihydrocinnamide, *cis*-cinnamide, or cyclopropanated analog. With respect to potency, the optimum groups in the para position of the phenyl ring of the cinnamide were tert-butyl, isopropyl and trifluoromethyl. These investigators provided an understanding of the SAR of this class of compounds, resulting in the discovery of potent new TRPV1 antagonists with good oral bioavailability.



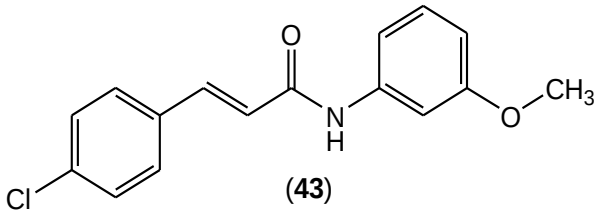
(42a)



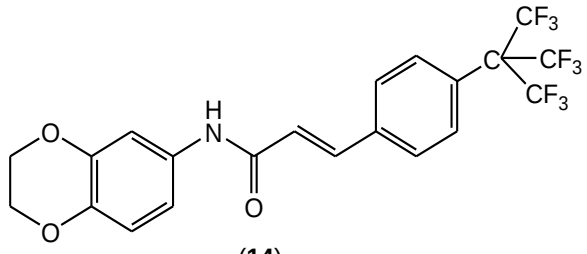
(42b)

X = O
X = $CH_2$

A group of TRPVI antagonists based on cinnamides include AMG 9810 (**44**) and SB-366791 (N-(3-methoxyphenyl)-4-chlorocinnamide. SB-366791 (**43**) inhibited capsaicin-induced hypothermia, eye wiping movements and vasodilatation of the knee joint at 500 µg/kg i.p dose 2mg/kg. The potency of cinnamides depends on the optimum groups being in the para position of the phenyl ring of the cinnamide. These groups were tert-butyl, isopropyl and trifluoromethyl.



(**43**)

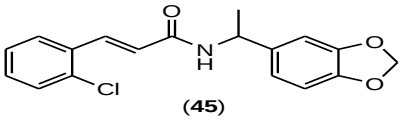


(**14**)

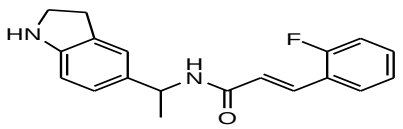
**Cinnamides as KCNQ2 Channel Openers**

A new class of acrylamides was synthesized, and the effects of these evaluated by using two electrode voltage clamp recordings from xenopus laevis ooctyes expressing cloned mKCNQ2 channels. SAR studies indicated that the pharmacophore of the acrylamide series includes the (S) absolute configuration at the (1-phenyl) ethyl moiety and the α, β-unsatured acrylamide functionality with a free NH. The study identified (S)-N-[1-(3-morpholin-4yl-phenyl)-ethyl]-3-phenyl-acrylamide and (S)-N[1-(4-fluoro-3-morpholin-4-yl-phenyl)-ethyl]-3-(4-fluorophenyl)-acrylamide as KCNQ2 openers for further electrophysiological evaluations. These two acrylamides demonstrated significant activity in the cortical spreading depression model of migraine (Yong-Jin WU *et al.*, 2004).

Biosteric replacement studies led to the identification of N-(1-benzo[1,3]dioxol-5-yl-ethyl)-3-(2-chlorophenyl) acrylamide (**45**) as a highly potent KCNQ2 opener, and 3-(2,6-difluorophenyl)-N-[1-(2,3-dihydro-benzofuran-5-yl)-ethyl]-acrylamide and N-[1-(2,3-dihydro-1H-indol-5-yl) - ethyl] -3 - (2-fluoro-phenyl)-acrylamide (**46**) as highly efficacious KCNQ2 openers. In contrast, their respective R enantiomers showed significantly less or no appreciable KCNQ2 opener activity even at the high concentration tested (100 µM).



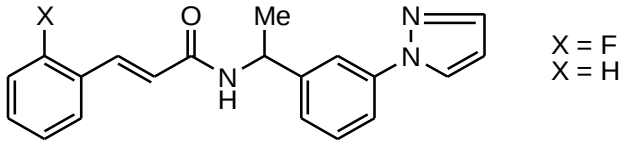
(45) (S)-3



(46) (S)-5

Alexandre *et al.* reported the synthesis and KCNQ2 opener activity of heteroaryl substituted acrylamides. Among this series of heteroaryl substituted acrylamides (S, E)-N-[3-(1H-pyrazol-1-yl) phenyl-ethyl-3-(2-fluorophenyl) acrylamide (**47**) exhibits balanced potency and efficacy.

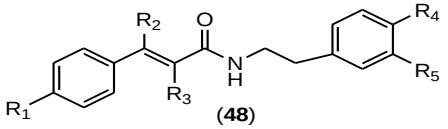
KCNQ2 (K = potassium, CN=channel, Q long QT designation).




(**47**)

**Cinnamide as NMDA Receptor antagonist**

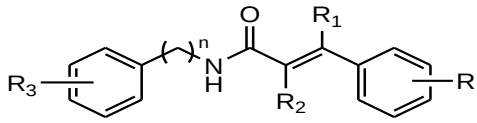
A series of N-(2-phenethyl) cinnamides was synthesized and assayed for antagonism at three N-methyl-D-aspartate (NMDA) receptor sub types (NRIA/2A-C). N-(2-(4-hydroxyphenyl)ethyl)-4-chloro-cinnamide (**48**) was identified as a highly potent and selective antagonist of the NRIA / 2B subtype.




(**48**)

$R_1$ = Cl $R_2$ = H = $R_3$
$R_4$ = OH

The N-(phenylalkyl) cinnamide (**49**) series provides a novel and structurally diverse framework for designing new NR2B-selective NMDA antagonists as potential CNS therapeutics. For this series, the primary determinants of potency at the NR2B containing NMDA receptors are (1) the phenolic 4-OH group which presumably serves as a H-bond donor (2) the length of linking chain from the nitrogen atom of the cinnamide moiety to the B-ring. 3) an electrostatic interaction between the receptor and the amide functional group in the linking chain. 4) Rigidification of the linker through inclusion of a double bond.




(**49**)

**A-ring** **B-ring**

n = 4, R = -40 H
$R_1$ = $R_2$ = $R_3$ = H

**SUMMARY**

The reported 2-phenyl 5-(2-cyano cinnamide) 1, 3, 4,-thiadiazole derivatives are important precursors for the synthesis of many bioactive molecules belonging to various therapeutic categories such as anti microbial, anti fungal, anti cancer, anti inflammatory, anti convulsant etc. A series of 2-phenyl 5-(2-cyano cinnamide)1,3,4,-thiadiazole derivatives were synthesized by refluxing 2-amino 5-phenyl 1,3,4,-thiadiazole with Ethyl 2-cyano 3-(substituted phenyl ) acrylates in presence of tryethylamine and tetrahydrofuran. The 2-amino-5-phenyl-1,3,4-thiadiazole was obtained by oxidative cyclization of thiosemicarbazide and benzoic acid in the presence of sulphuric acid and the Ethyl 2-cyano 3-( substituted phenyl) acrylates were prepared by stirring of substituted benzaldehydes with ethylcyanoacetate in presence of piperidine and ethanol. A total of twelve compounds were synthesized in this series. The chemical structures of synthesized compounds were confirmed by means of IR, $^1$H NMR and Mass data.

The final compounds were screened for anti-oxidant activity was evaluated by the methods namely nitric oxide scavenging activity and reduction of DPPH. The present work from our laboratory has been shown that antioxidant activity.Out of these compounds, unsubstituted compound showed good antioxidant activity Substitution by 4-dimethylamino, 4-hydroxy, 4 -chlorine showed increase in anti-oxidant activity.

**ACKNOWLEDGEMENT: NIL**

**CONFLICT OF INTEREST: NIL**

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