Available online at www.ijpsdr.com
International Journal of Pharmaceutical Sciences and Drug Research 2009; 1(3): 136-143

Review Article ISSN 0975-248X

Thiazoles: A Valuable Insight into the Recent Advances and Biological Activities

Nadeem Siddiqui*, M. Faiz Arshad, Waquar Ahsan, M. Shamsher Alam

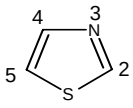
Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard (Hamdard University), New Delhi 110062, India

ABSTRACT
Thiazoles displayed broad range of biological activities and found in many potent biologically active molecules such as Sulfathiazol (antimicrobial drug), Ritonavir (antiretroviral drug), Abafungin (antifungal drug) and Tiazofurin (antineoplastic drug). So far, modifications of the thiazole ring have proven highly effective with improved potency and lesser toxicity. The present review highlights the recently synthesized thiazoles possessing important biological activities.

Keywords: Thiazoles derivatives; Biological activities.

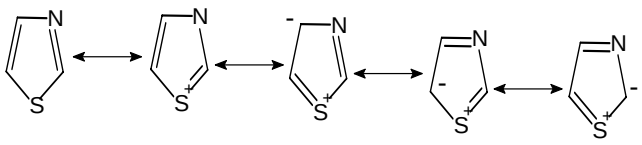
INTRODUCTION

Thiazole is a heterocyclic compound featuring both a nitrogen atom and sulfur atom as part of the aromatic five-membered ring. Thiazole and related compounds are called 1, 3-azoles (nitrogen and one other heteroatom in a five-membered ring). They are isomeric with the 1, 2-azoles, the nitrogen and sulfur compound being called isothiazole. The numbering system is shown below for naming derivatives of thiazole.



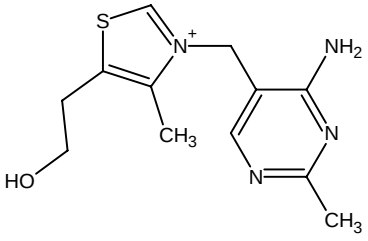
1
Numbering system of thiazole ring

Thiazole is aromatic on the basis of delocalization of a lone pair of electrons from the sulfur atom completing the needed 6 π electrons to satisfy Huckel's rule. The resonance forms are:



***Corresponding author: Prof. Nadeem Siddiqui,**
Department of Pharmaceutical Chemistry, Faculty of Pharmacy, Jamia Hamdard (Hamdard University), New Delhi 110062, India **Tel:** +91 11 26059688 Extn 5639.
Email:nadeems_03@yahoo.co.in,
nadeems_03@rediffmail.com

Thiazole is a clear to pale yellow liquid with a boiling point of 116-118°C. Its specific gravity is 1.2 and it is sparingly soluble in water. It is soluble in alcohol and ether. The odor of thiazole is similar to pyridine. It is used as an intermediate to manufacture synthetic drugs, fungicides, and dyes. A thiazole ring is found naturally in the essential vitamin B_1 (thiamin).



Thiamin

Thiamin is a water soluble vitamin that helps the body release energy from carbohydrates during metabolism. It also helps in the normal functioning of the nervous system by its role in the synthesis of acetylcholine, a neurotransmitter. Thiamin is found mostly in pasta and breads made from refined flours. It is also found in ready-to-eat cereals and in navy and kidney beans.

1.2. BIOLOGICAL ACTIVITIES

Thiazoles are important class of heterocyclic compounds, found in many potent biologically active molecules such as Sulfathiazol (antimicrobial drug), Ritonavir (antiretroviral drug), Abafungin (antifungal drug) with trade name Abasol cream and Bleomycine and Tiazofurin (antineoplastic drug).
It has been noticed continuously over the years that interesting biological activities [1-2] were associated with

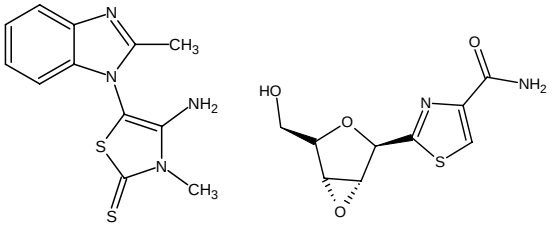
thiazole derivatives. Recently the applications of thiazoles were found in drug development for the treatment of allergies [3], hypertension [4], inflammation [5], schizophrenia [6], bacterial [7], HIV infections [8], hypnotics [9] and more recently for the treatment of pain [10], as fibrinogen receptor antagonists with antithrombotic activity [11] and as new inhibitors of bacterial DNA gyrase B. [12] A brief review of thiazoles associated with large number of biological activities is presented below.

1.2.1. Antitumor activity

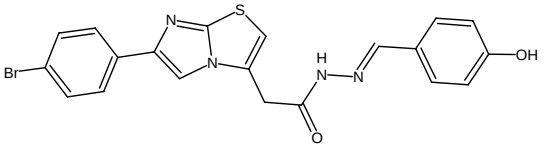
Ramla et al [13] synthesized a variety of 1-substituted-2-methyl-5-nitrobenzimidazoles and evaluated them for anti-tumor activity. The anti-tumor effect of compound [**1**] was found to be significant.

Popsavin et al [14] reported a set of 2-(2, 3-anhydrofuranosyl) thiazole-4-carboxamide (2', 3'-anhydro tiazofurin) derivatives and screened them for their anti-tumor activity. The most active compound was found to be [**2**] against K_{562} malignant cells, with IC_{50} vlues ranging from 0.09-0.49 μM.

Gulsory et al [15] presented a series of arylidene hydrazides from [6-(4-bromophenyl) imidazol-3yl] acetic acid hydrazide. The synthesized compounds were evaluated one dose primary cytotoxicity assay. Compound [**3**] demonstrated the most effective agents on a prostate cancer cell lines.



[**1**] [**2**]



[**3**]

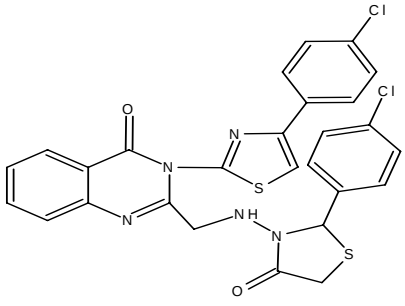
1.2.2. Anti-inflammatory activity

Kumar et al [16] synthesized a group of 3-[4'(*p*-chlorophenyl) thiazol-2'-yl]-2-[(substituted azetidinone/thiazolidinone)-aminomethy]-6-bromoquinazolin-4-ones and screened them for anti-inflammatory and analgesic activities. Compound [**4**] was found to be highly active in both the activities. They found that the presence of thiazolidinone ring have shown much better anti-inflammatory as well as analgesic activity at 50 mg/kg po as compared to their parent compounds. Compound substituted with chloro group at 2nd position of phenyl ring has shown almost equal anti-inflammatory activity to that of the standard drug phenylbutazone at 50 mg/kg.

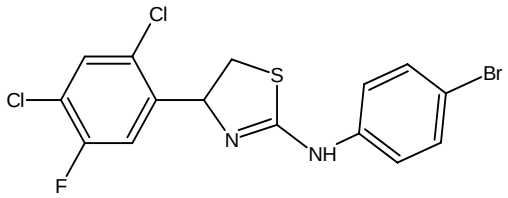
Holla et al [17] reported different series of arylaminothiazoles, arylidene/5-aryl-2-furfurylidene hydrazinothiazoles and screened them for their antibacterial and anti-inflammatory activities. Two of the newly synthesized compounds [**5**] and [**6**] showed anti-inflammatory activity comparable with that of ibuprofen.

Kalkhambkar et al [18] reported triheterocyclic thiazoles containing coumarin and carbostyril (1-aza coumarin). The newly synthesized compounds were tested for their *in vitro* analgesic and anti-inflammatory activities. Among the tested compounds, [**7**] and [**8**] significantly inhibited the acetic acid induced writhing.

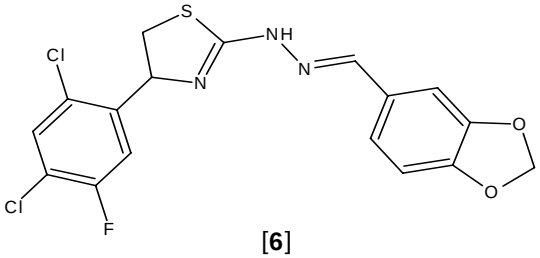
Rostom et al [19] reported two groups of structure hybrids comprising basically the antipyrine moiety attached to polysubstituted thiazole or 2, 5-disubstituted-1, 3, 4-thiadiazole counterparts through various linkages. Twelve compounds were evaluated for their anti-inflammatory activity, ulcerogenic effects and acute toxicity. The analgesic activity of the same compounds was also evaluated. Additionally, their *in vitro* antimicrobial activity was evaluated. Some compounds [**9**] and [**10**] displayed remarkable anti-inflammatory and analgesic profiles with a fast onset of action together with a super GI safety profile and safety margin. Additionally, some compounds exhibited broad-spectrum antimicrobial activity.



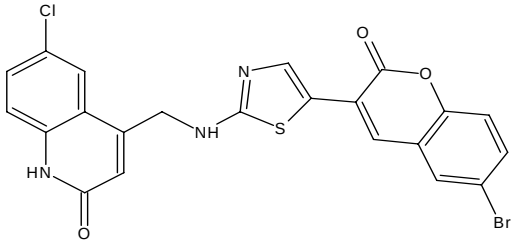
[**4**]



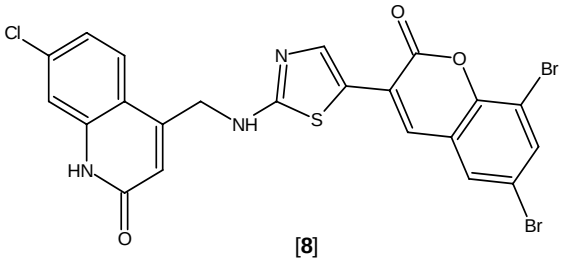
[**5**]



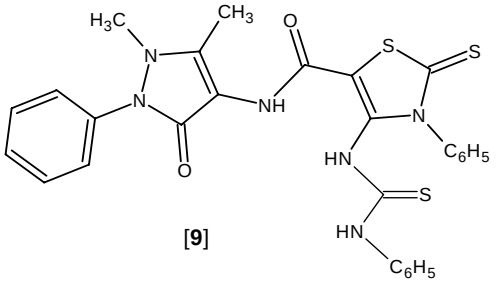
[**6**]



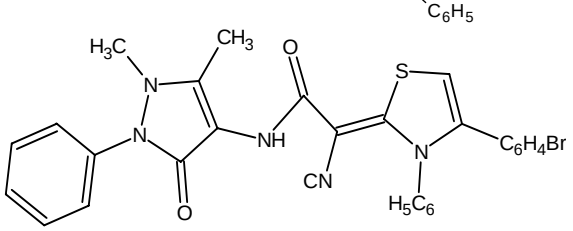
[**7**]



[**8**]



[**9**]



[**10**]

1.2.3. Antimicrobial activity

Pandeya et al [20] prepared a series of Schiff and Mannich bases derived from isatin derivatives and *N*-[4-(4'chlorophenyl) thiazol-2-yl] thiosemicarbazide. Investigation of antimicrobial activity of compounds was done by agar dilution method against 28 pathogenic bacteria, 8 pathogenic fungi and anti-HIV-1 (IIIB) in MT-4 cells. Among the compounds tested [**11**] showed the most favorable antimicrobial activity.

Shiradkar et al [21] reported a series of *N*-{4-[(4-amino-5-sulphanyl-4*H*-1, 2, 4-triazol-3-yl) methyl]-1, 3-thiazol-2-yl}-2-substituted amide derivatives. The compounds were tested for their preliminary *in vitro* antibacterial activity against *S. aureus*, *E. coli*, *P. aeroginosa* and *S. typhosa* and then were screened for antitubercular activity against *M. tuberculae* $H_{37}Rv$ strain by both micro dilution assay method. Compound [**12**] and [**13**] showed best activity. They revealed that the compounds that have shown more than 90% inhibition were obtained by S-alkylation with acetonitrile. It was noted that the cyano group may not have any role in increase in the activity. When the sulfhydryl group were optimized and investigated, it resulted into the loss of activity.

Xin et al [22] reported sixteen novel oxazolidinone analogue containing substituted thiazole/ fused bicyclic [imidazo[1,2-b] pyradazine/imidazo [2,1-b] thiazole groups were designed and synthesized. All the compounds were evaluated for their *in vitro* antibacterial activity against *S. aureus*. Among them compound [**14**] displayed promising antibacterial activity comparable to that of linezolid.

Vicini et al [23] produced a new set of 2-thiazolylimino-5-arylidene-4-thiazolidinones and assayed *in vitro* for their antimicrobial activity against Gram positive and Gram negative bacteria, yeast and mould. All the compounds especially compound [**15**] exhibited potent against Gram positive bacteria. They have studied the structure-activity relationship and found that the 5-arylidene derivatives showed a significant antibacterial efficacy greater than that of the parent compound suggesting that the unsubstituted and substituted 5-arylidene moiety plays an important role in enhancing the antimicrobial properties of this class of compounds.

Dundar et al [24] presented a set of thiazolyl thiazolidine-2,4-dione derivatives and screened them for their antibacterial and antifungal activities against methicillin resistant *S. aureus*, *E. coli* and *C. albicans*. All the compounds particularly [**16**] were found to be moderately potent against screened microorganisms. The structure-activity relationships showed that the anti-fungal activity of the substituents at the phenyl ring is H, Cl, Br, *o*,*p*-diCl > F, NO_2 for benzylic 2,4-TZD compounds. As for phenacyl 2,4-TZD compounds, it is Cl, Br > H, F, *o*,*p*-di-Cl, NO_2.

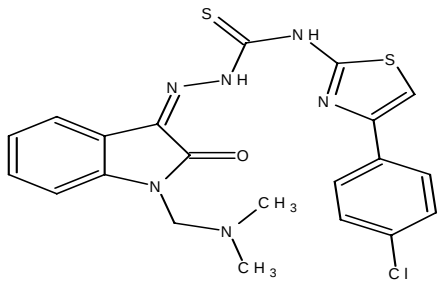
Cukurovali et al [25] reported a series of Schiff bases containing 2, 4-disubstituted thiazole and cyclobutane rings and hydrazones moieties in the same molecule and evaluated them for antibacterial and antifungal activities. Among the tested compounds, the most effective compound providing a MIC value of 16 μg ml^{-1} was found to be [**17**] against *C. tropicalis* and *B. subtilis*. They studied the lowest effective substance against all the microorganisms and found that despite all the substances have very similar structures, their antibacterial and antifungal activities are very different. Most of them demonstrate weak activity against gram-positive and gram-negative bacteria and fungi in comparison to the reference drugs.

Zitouni et al [26] reported new thiazole derivatives of triazoles and evaluated for antifungal and antibacterial activity. Their antimicrobial activities against *Candida albicans* (two strains), *C. glabrata*, *E. coli*, *S. aureus*, *P. aeruginosa* were investigated. The results showed that some of the compounds [**18**] have very strong antifungal activity.

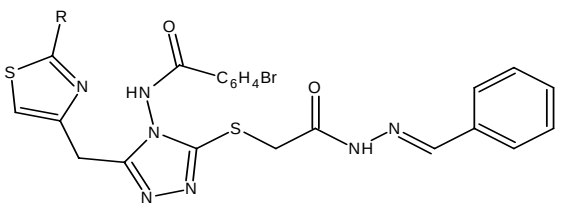
Abdel-Wahab et al [27] synthesized a series of 1-(benzofuran-2-yl)-4-nitro-3-arylbutan-1-ones and 3-(benzofuran-2-yl)-4,5-dihydro-5-aryl-1-[4-(aryl)-1,3-thiazol-2-yl]-1*H*-pyrazoles. All the synthesized compounds were screened for their antibacterial and antifungal activities. Compound [**19**] showed a significant activity against *E. coli* higher than that of the control drug, whereas antifungal activity against *Aspergillus niger* was also exhibited by some of the compounds equal to that of the reference drug.

Karegoudar et al [28] synthesized a series of novel 4-aryl-2-(2, 3, 5-trichlorophenylidenehydrazino)-1, 3-thiazoles in good yield. The newly synthesized compounds were screened for their antibacterial and antifungal activities. Preliminary results reveal that derivatives of synthesized compound [**20**] are showing promising antimicrobial activity.

.

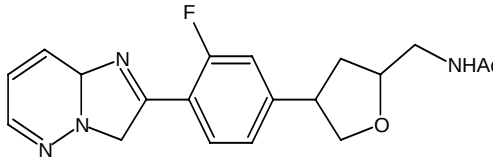


[**11**]

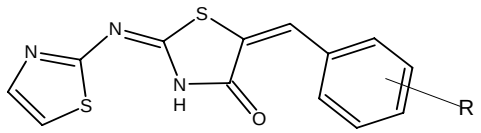


[**12**] R=NHCOCH$_3$, Ar=3-NO$_2$.C$_6$H$_4$

[**13**] R=NHCOC$_6$H$_5$, Ar=3-NO$_2$.C$_6$H$_4$

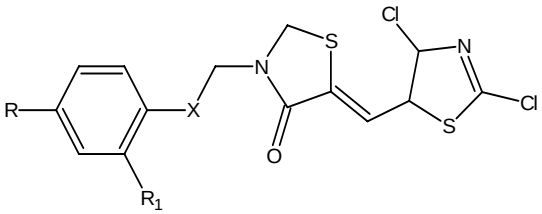


[**14**]



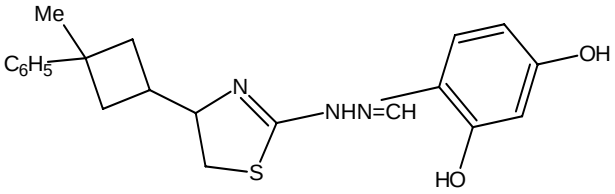
R = H, OH, OCH_3, NO_2, Cl

[**15**]

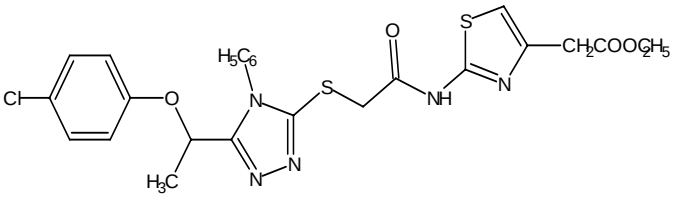


R = H, F, Cl, Br, NO_2: R_1 = H, Cl: X = CH_2, CO

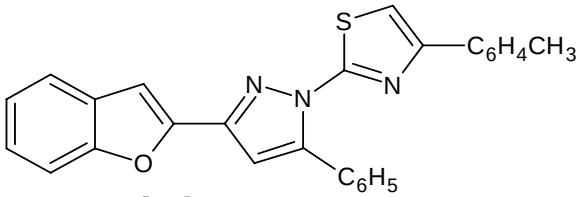
[**16**]



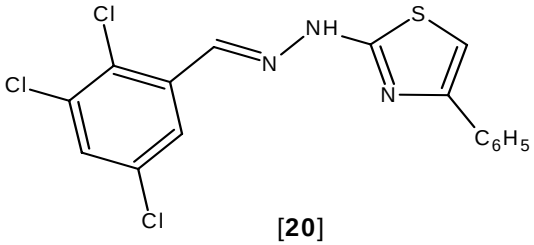
[**17**]



[**18**]



[**19**]



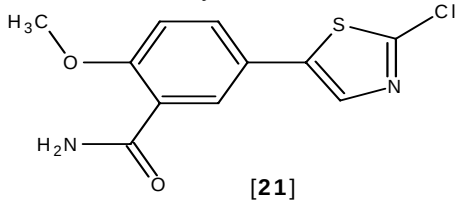
[**20**]

1.2.4. Antifungal activity

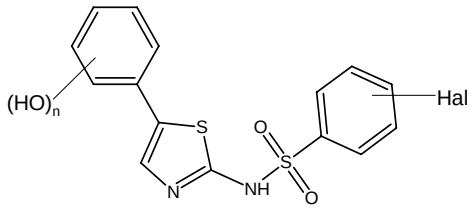
Narayana et al [29] prepared a series of 5-{2-[(*N*-substituted aryl) amino]-1, 3-thiazol-5-yl} 2-hydroxy benzamides by reacting 5-(bromoacetyl) salicylamide with thiourea, thioformamide, thioalkylamide and substituted thioureas in absolute ethanol. These compounds were converted to 5-(2-substituted–1, 3-thiazol-5-yl)-2-alkoxybenzamides and 5-(2-*N*-(substituted aryl)-1, 3-thiazol-5-yl)-2-alkoxy benzamides by reacting with *n*-alkylbromides in presence of a base. The newly synthesized compounds were screened for their antifungal activity. The derivatives of compound [**21**] exhibited significant activity.

Beuchet et al [30] synthesized polymethoxylated and polyhydroxylated derivatives of 2-amino-4-arylthiazoles bearing a halogenobenzenesulfonamide moiety at position 2 as azole antifungal analogues. *In vitro* assays against various pathogenic fungal strains (*Candida* and *Trichophyton* species) showed no activity in comparison to econazole as reference.

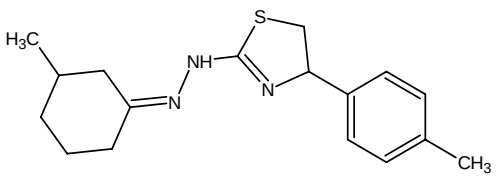
Chimenti et al [31] reported the synthesis of a novel series of 2-thiazolylhydrazone derivatives and the influence of the substituents on the thiazole ring on antifungal activity. All synthesized compounds were screened for their *in vitro* activities against 22 clinical isolates of *Candida* sp., representing six different species, compared to clotrimazole as a reference compound. Some of the tested compounds were found to possess significant antifungal activity when compared to clotrimazole, in particular compound [**23**] which exhibited higher potency against most of the *Candida* sp. considered. The compounds that were most active as anti-Candida agents were also submitted to cytotoxic screening by the Trypan Blue dye exclusion assay and in general they were shown to induce low cytotoxic effects.



[**21**]



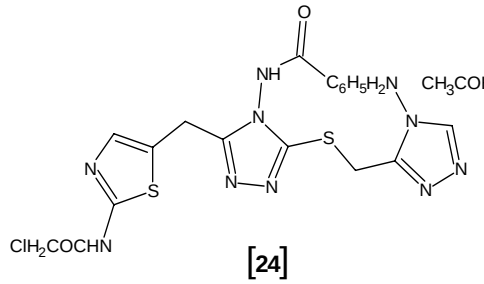
[**22**]



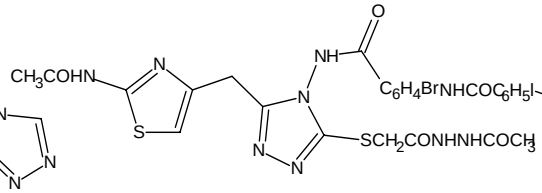
[**23**]

1.2.5. Antitubercular activity

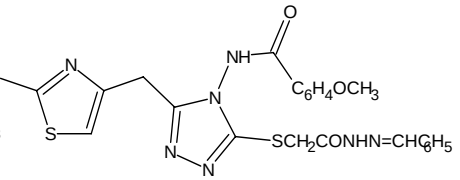
Shiradkar et al [32] synthesized a series of *N*-{4-[(4-amino-5-sulfanyl-4H-1, 2, 4-triazol-3-yl) methyl]-1, 3-thiazol-2-yl}-2-substitutedamide [**24**], [**25**] and [**26**] derivatives in good yields. The compounds were evaluated for their preliminary



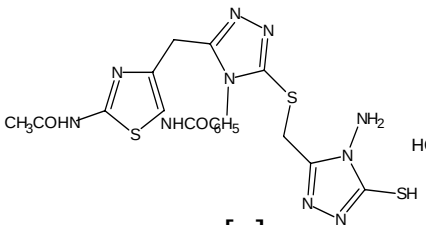
[24]



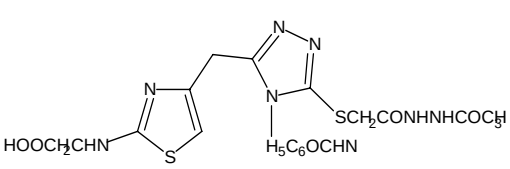
[25]



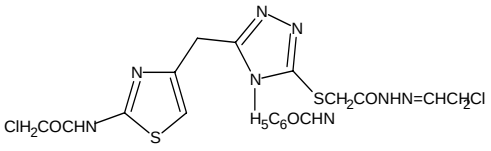
[26]



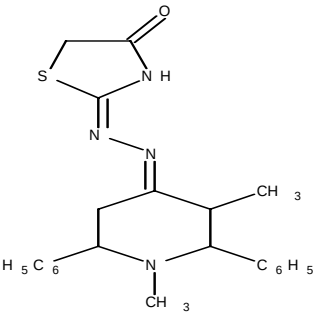
[27]



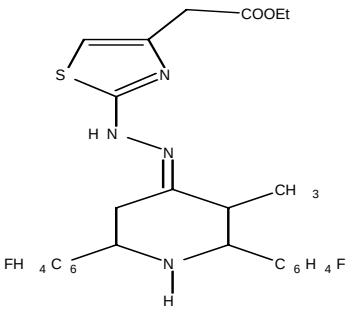
[28]



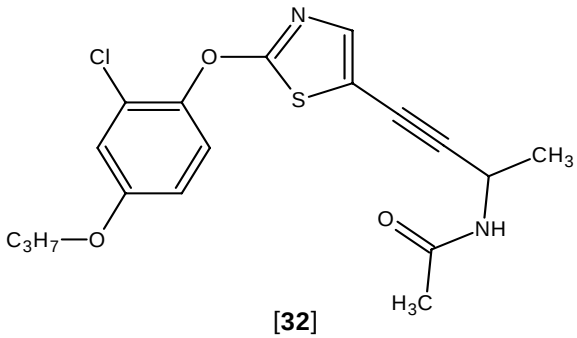
[29]



[30]



[31]



[32]

in vitro antibacterial activity against *S. aureus, E. coli, P. aeruginosa* and *S. typhosa* and then were screened for antitubercular activity against *Mycobacterium tuberculosis* H37 Rv strain by broth microdilution assay method. The antibacterial data of the tested compounds indicated that most of the synthesized compounds showed better activity against bacteria compared to reference drugs. The *in vitro* antitubercular activity reports of tested compounds against *M. tuberculosis* strain H37 Rv showed moderate to better activity. It was noted that the cyano group may not have any role in increase in the activity. When the sulfhydryl group were optimized and investigated, it resulted into the loss of activity.

Shiradkar et al [33] reported the synthesis of thiazolyl triazole derivatives, starting from ethyl acetoacetate, by microwave organic reaction enhancement method (MORE). Results of investigations of their antimycobacterial and antimicrobial activities were also produced. Many compounds [**27**], [**28**], [**29**] have shown promising activity while others were inactive. They found that two compounds that have shown 97% and 100% inhibition were obtained by the S-alkylation with acetonitrile. When the acetate derivatives were converted into the hydrazide derivatives, the antimycobacterial activity was quite interesting as all of these compounds have shown inhibition above 90 %.

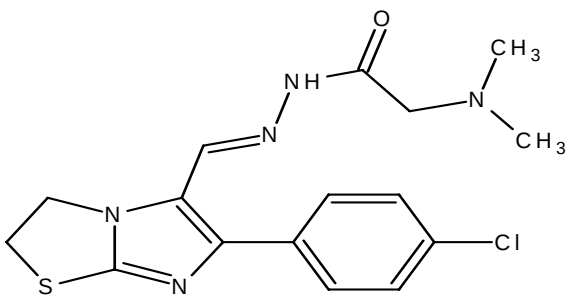
Aridoss et al [34] synthesized some new thiazolidinones and thiazoles based on t-3-alkyl-r-2,c-6-diarylpiperidin-4-ones and evaluated them for antimycobacterial and antimicrobial activity and it was revealed after screening that substitution of electron withdrawing or donating substituents at the para position of the phenyl groups besides methyl group at N-1 and C-3 exerted better biological profiles [**30**], [**31**].

1.2.6. Acetyl-Co-A carboxylase inhibitors

Clark et al [35] presented a new series of phenoxy thiazolyl derivatives and screened them for their acetyl-Co-A carboxylase inhibitory profile. Compound [**32**] was found to be highly active in the inhibition of acetyl-Co-A carboxylase isozyme.

1.2.7. Diuretic activity

Andreani et al [36] synthesized a series of imidazo[2,1-b] thiazole acetohydrazones and screened them for their diuretic activity. A potent diuretic activity was confirmed for the 2-methyl derivative bearing a phenyl ring at position C-6 [**33**]. Evaluation of the diuretic activity of both the saturated compounds and their unsaturated analogues shows that among the 6-position substituents, which were synthesized, a phenyl or substituted phenyl group was superior. This was confirmed by the results obtained with the analogues, 2- and 3-methyl derivatives which, considering the dose employed and the acute toxicity were the most promising derivatives.

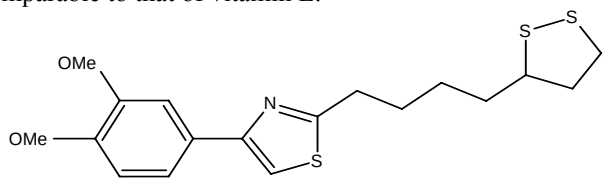


[33]

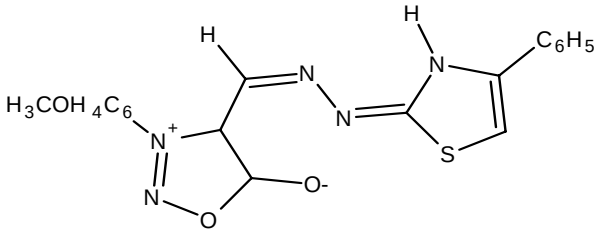
1.2.8. Neuroprotective and antioxidant activity

Koufaki et al [37] designed synthesized new analogues containing 1, 2-dithiolane derivatives and screened for neuroprotective activity. Compound [**34**] was found to be highly neuroprotective. The structure-activity relationship revealed that when the amide functionality was replaced by the tetrazole ring, they were found to be the strngest neuroprotectant, while the 1, 3, 4-oxadiazole derivative was somewhat less potent. Thus, it appeared that the replacement of the amide functionality by the aromatic heterocycles conveyed greater neuroprotective activity to the resulting compounds.

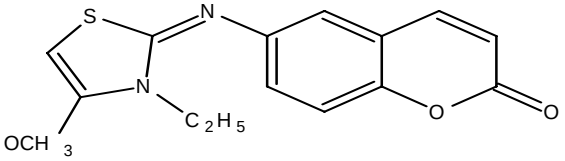
Shih et al [38] synthesized a series of sydnonyl substituted thiazolidinone and thiazoline derivatives and evaluated them for antioxidant activity. The antioxidant activity of derivatives of compound [**35**] exhibited the significant DPPH (1, 1-diphenyl-2-picrylhydrazyl) radical scavenging activity, comparable to that of vitamin E.



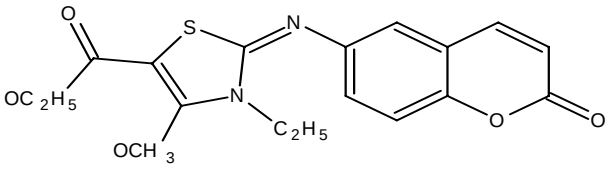
[**34**]



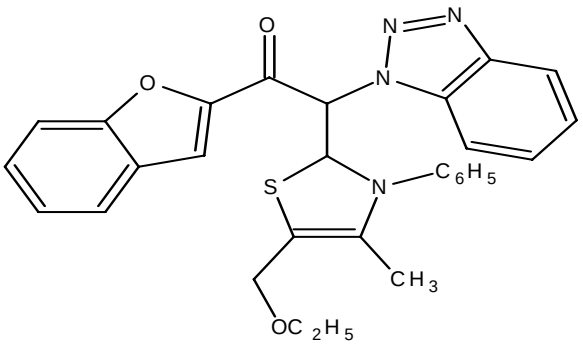
[**35**]



[**36**]



[**37**]



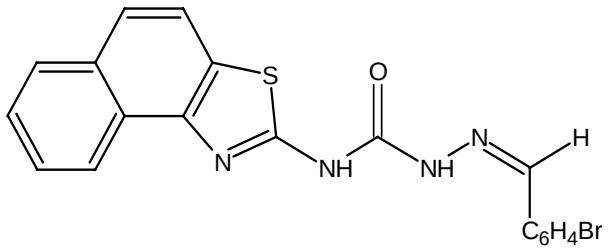
[**38**]

1.2.9. Anticonvulsant activity

Amin et al [39] reported some new substituted coumarinyl thiazolines, coumarinyl thiazolidin-4-ones and substituted chromenothiazoles and evaluated for anticonvulsant activity. Compounds [**36**] and [**37**] were the most active of the series against PTZ induced seizures

Dawood et al [40] reported a series of newly synthesized compounds and evaluated them for anti-inflammatory and anticonvulsant activity. The newly synthesized compounds [**38**] were found to possess anticonvulsant and anti-inflammatory activities with the same mechanism of action of selective COX-2 inhibitors. From the structure-activity relationship viewpoint, the anti-inflammatory activity of 5-acetyl-1, 3, 4-thiadiazole derivatives were found to be high in the case of unsubstituted phenyl derivatives and decreases with substitution in the order H > 4-CH_3 > 4-Cl. Also, the anti-inflammatory effect of the thiazolidine ester derivative is higher than that of its acetyl derivatives. In addition, the chlorinated ester derivatives of 1, 3, 4-thiadiazole system was found to be more effective than its non-chlorinated derivatives.

Azam et al [41] designed and synthesized a series of N^4-(naphtha[1,2-*d*]thiazol-2-yl)semicarbazides [**39**] and evaluated for their anticonvulsant and neurotoxicity studies. The biochemical estimations of malondialdehyde (MDA), superoxide dismutase (SOD) and glutathione peroxidase (GSH-Px) from brain homogenate for selected compounds were performed to study their antioxidant property.



[**39**]

1.3. CURRENT ASPECTS OF THIAZOLE

Zhu et al [42] have performed the structure-based 3D-QSAR studies on 20 thiazoles against their binding affinities to the 5-HT_3 receptor with comparative molecular field analysis (CoMFA) and comparative molecular similarity indices analysis (CoMSIA). The thiazoles were initially docked into the binding pocket of a human 5-HT_{3A} receptor homology model, constructed on the basis of the crystal structure of the snail acetylcholine binding protein (AChBP), using the GOLD program. The docked conformations were then extracted and used to build the 3D-QSAR models, with cross-validated τ^2_{cv} values 0.785 and 0.744 for CoMFA and CoMSIA, respectively. An additional five molecules were used to validate the models further, giving satisfactory predictive r^2 values of 0.582 and 0.804 for CoMFA and CoMSIA, respectively. The results would be helpful for the discovery of new potent and selective 5-HT_3 receptor antagonists.

Deeb et al [43] have performed the QSAR analysis of a set of 96 heterocyclics with antifungal activity. The results revealed that pyridine ring was more favorable than benzene as the 6-membered ring, for high activity, but thiazole was

unfavorable as the 5-membered ring relative to imidazole or oxazole. Methylene was the spacer leading to the highest activity. The descriptors used were indicator variables, which account for identity of substituent, lipophilicity and volume of substituent, and total polarizability.

This has been noticed so far, that modifications on thiazole moiety displayed valuable biological activities. It will be interesting to observe that these modifications can be utilized as potent therapeutic agents in future. Thus the quest to explore many more modifications on thiazole moiety needs to be continued.

REFERENCES

1. Quiroga J, Hernandez P, Insuasty B, Abonia R, Cobo J, Sanchez A, Nogueras M, Low JN. Control of the Reaction Between 2-Aminobenzothiazoles and Mannich Bases: Synthesis of pyrido[2,1-*b*][1,3]benzothiazoles *versus* [1,3]benzothiazolo[2,3-b]quinazolines. J Chem Soc Perkin Trans1. 2002; 4:555-559.
2. Hutchinson I, Jennings SA, Vishnuvajjala BR, Westwell AD, Stevens MFG. Antitumor Benzothiazoles. 16 Synthesis and Pharmaceutical Properties of Antitumor 2-(4-Aminophenyl)benzothiazole Amino Acid Prodrugs. J Med Chem. 2002; 45:744-747.
3. Hargrave KD, Hess FK, Oliver JT. N-(4-Substituted-thiazolyl)oxamic acid Derivatives, New Series of Potent, Orally Active Antiallergy Agents. J Med Chem. 1983; 26:1158-1163.
4. Patt WC, Hamilton HW, Taylor MD, Ryan MJ, Taylor Jr. DG, Connolly CJC, Doherty AM, Klutchko SR, Sircar I, Steinbaugh BA, Batley BL, Painchaud CA, Rapundalo ST, Michniewicz BM, Olson SCJ. Structure-activity relationships of a Series of 2-Amino-4-thiazole Containing Renin Inhibitors. J Med Chem. 1992; 35:2562-2572.
5. Sharma RN, Xavier FP, Vasu KK, Chaturvedi SC, Pancholi SS. Synthesis of 4-Benzyl-1,3-thiazole derivatives as potential anti-inflammatory agents: An Analogue-based Drug Design Approach. J Enz Inhib Med Chem. 2009; 24:890 – 897.
6. Jaen JC, Wise LD, Caprathe BW, Tecle H, Bergmeier S, Humblet CC, Heffner TG, Meltzner LT, Pugsley TA. 4-(1,2,5,6-Tetrahydro-1-alkyl-3-pyridinyl)-2-Thiazolamines: A Novel Class of Compounds With Central Dopamine Agonist Properties. J Med Chem. 1990; 33:311-317.
7. Tsuji K, Ishikawa H. Synthesis and Anti-pseudomonal Activity of New 2-Isocephems with a Dihydroxypyridone Moiety at C-7. Bioorg Med Chem Lett. 1994; 4:1601-1606.
8. Bell FW, Cantrell AS, Hogberg M, Jaskunas SR, Johansson NG, Jordon CL, Kinnick MD, Lind P, Morin Jr. JM, Noreen R, Oberg B, Palkowitz JA, Parrish CA, Pranc P, Sahlberg C, Ternansky RJ, Vasileff RT, Vrang L, West SJ, Zhang H, Zhou XX. Phenethylthiazolethiourea (PETT) Compounds, a New Class of HIV-1 Reverse Transcriptase Inhibitors. 1. Synthesis and Basic Structure-Activity Relationship Studies of PETT Analogs. J Med Chem. 1995; 38:4929-4936.
9. Ergenc N, Capan G, Gunay NS, Ozkirimli S, Gungor M, Ozbey S, Kendi E. Synthesis and Hypnotic Activity of New 4-Thiazolidinone and 2-Thioxo- 4,5-Imidazolidinedione Derivatives. Arch Pharm Pharm Med Chem. 1999; 332:343-347.
10. Carter JS, Kramer S, Talley JJ, Penning T, Collins P, Graneto MJ, Seibert K, Koboldt C, Masferrer J, Zweifel B. Synthesis and Activity of Sulfonamide-Substituted 4,5-Diaryl Thiazoles as Selective Cyclooxygenase-2 Inhibitors. Bioorg Med Chem Lett. 1999; 9:1171-1174.
11. Badorc A, Bordes MF, De Cointet P, Savi P, Bernat A, Lale A, Petitou M, Maffrand JP, Herbert JM. New Orally Active Non-Peptide Fibrinogen Receptor (GpIIb-IIIa) Antagonists: Identification of Ethyl 3-[N-[4-[4-Amino[(ethoxycarbonyl)imino]methyl]phenyl]- 1,3-thiazol-2-yl]-N-[1- (ethoxycarbonyl)methyl]piperid-4-yl]amino]propionate (SR 121787) as a Potent and Long-Acting Antithrombotic Agent. J Med Chem. 1997; 40:3393-3401.
12. Rudolph J, Theis H, Hanke R, Endermann R, Johannsen L, Geschke FU. seco-Cyclothialidines: New Concise Synthesis, Inhibitory Activity toward Bacterial and Human DNA Topoisomerases, and Antibacterial Properties. J Med Chem. 2001; 44:619-626.
13. Ramla MM, Omar MA, El-Khamry AMM, El-Diwan HI. Synthesis and Antitumor Activity of 1-Substituted-2-methyl-5-nitrobenzimidazoles. Bioorg Med Chem. 2006; 14:7324-7332.
14. Popsavin M, Spaic S, Svircev M, Kojic V, Bogdanovic G, Popsavin V. Synthesis and Antitubercular Activity of New Tiazofurin Analogues Bearing a 2, 3-Anhydrofunctionality in the Furanose Ring. Bioorg Med Chem Lett. 2007; 17:4123-4127.
15. Gulsory E, Guzeldemirci NU. Synthesis and primary cytotoxicity evaluation of new imidazo [2,1-b] thiazole derivatives. Eur J Med Chem. 2007; 42:320-326.
16. Kumar A, Rajput CS, Bhati SK. Synthesis of 3-[4'-(p-chlorophenyl) thiazol-2'-yl]-2-[(substituted azetidinone/thiazolidinone)-aminomethyl]-6-bromoquinazolin-4-ones. Bioorg Med Chem. 2007; 15:3089-3096.
17. Holla BS, Malini KV, Rao BS, Sarojini BK, Kumari NS. Synthesis of some new 2, 4- disubstituted thiazoles as possible antibacterial and anti-inflammatory agent. Eur J Med Chem. 2003; 38:313-318.
18. Kalkhambkar RG, Kulkarni GM, Shivkumar H, Rao NR. Synthesis of novel triheterocyclic thiazoles as anti-inflammatory and analgesic agents. Eur J Med Chem. 2007; 42:1272-1276.
19. Rostom SAF, El-Ashmawy IM, Abd El Razik HA, Badr MH, Ashour HMA. Design and synthesis of some thiazolyl and thiadiazolyl derivatives of antipyrine as potential non-acidic anti-inflammatory, analgesic and antimicrobial agents. Bioorg Med Chem. 2009; 17:882-895.
20. Pandeya SN, Sriram D, Nath G, DeClerq E. Synthesis, antibacterial, antifungal and anti-HIV activities of Schiff and Mannich bases derived from isatin derivatives and N-[4-(4'-chlorophenyl) thiazol-2-yl] thiosemicarbazide. Eur J Pharm Sci. 1999; 9:25-31.
21. Shiradkar MR, Murahari KK, Gangadasu HR, Suresh T, Kalyan CA, Panchal D, Kaur R, Burange P, Ghogare J, Mokale V, Raut M. Synthesis of new S-derivatives of clubbed triazole as anti-*Mycobacterium tuberculosis* agents. Bioorg Med Chem. 2007; 15:3997-4008.
22. Xin Z, Yang-fang Z, Jia W, Wei J, Liang H, Ping G. Synthesis and antibacterial activity of novel oxazolidinone analogues containing substituted thiazole/fused bicyclic groups. Chem Res Chinese U. 2006; 22:459-464.
23. Vicini P, Geronikaki A, Anastasia K, Incerti M, Zani F. Synthesis and antimicrobial activity of novel 2-thiazolyl imino-5-arylidene-4-thiazolidinones. Bioorg Med Chem. 2006; 14:3859-3864.
24. Dundar OB, Ozgen O, Mentese A, Altanlar N, Ath O, Kendj E, Ertan R. Synthesis and antimicrobial activity of some new thiazolyl thiazolidine-2,4- dione derivatives. Bioorg Med Chem. 2007; 15:6012-6017.
25. Cukurovali A, Yilmaz I, Gur S, Kazaz C. Synthesis antibacterial and antifungal activity of some new thiazolylhydrazone derivatives containing 3-substituted cyclobutane ring. Eur J Med Chem. 2006; 41:201-207.
26. Zitouni GT, Kaplancıklı ZA, Yıldız MT, Chevallet P, Kaya D. Synthesis and antimicrobial activity of 4-phenyl/cyclohexyl-5-(1-phenoxyethyl)-3-[N-(2-thiazolyl)acetamido]thio-4H-1,2,4-triazole derivatives. Eur J Med Chem. 2005; 40:607–613.
27. Abdel-Wahab BF, Abdel-Aziz HA, Ahmed EM. Synthesis and antimicrobial evaluation of 1-(benzofuran-2-yl)-4-nitro-3-arylbutan-1-ones and 3-(benzofuran-2-yl)-4,5-dihydro-5-aryl-1-[4-(aryl)-1,3-thiazol-2-yl]-1H-pyrazoles. Eur J Med Chem. 2009; 44:2632-2635.
28. Karegoudar P, Karthikeyan MS, Prasad DJ, Mahalinga M, Holla BS, Kumari NS. Synthesis of some novel 2,4-disubstituted thiazoles as possible antimicrobial agents. Eur J Med Chem. 2008; 43:261-267.
29. Narayana B, Vijaya Raj KK, Ashalatha BV, Kumari NS, Sarojini BK. Synthesis of some new 5-(2-substituted-1,3-thiazol-5-yl)-2-hydroxy benzamides and their 2-alkoxy derivatives as possible antifungal agents. Eur J Med Chem. 2004; 39:867–872.
30. Beuchet P, Varache-Lembège M, Neveu A, Léger JM, Vercauteren J, Larrouture S, Deffieux G, Nuhrich A. New 2-sulfonamidothiazoles substituted at C-4: synthesis of polyoxygenated aryl derivatives and in vitro evaluation of antifungal activity. Eur J Med Chem. 1999; 34:773−779.
31. Chimenti F, Bizzarri B, Maccioni E, Secci D, Bolasco A, Fioravanti R, Chimenti P, Granese A, Carradori S, Rivanera D, Lilli D, Zicari A, Distinto S. Synthesis and *in vitro* activity of 2-thiazolylhydrazone derivatives compared with the activity of clotrimazole against clinical isolates of Candida spp. Bioorg Med Chem Lett. 2007; 17:4635–4640.
32. Shiradkar MR, Murahari KK, Gangadasu HR, Suresh T, Kalyan CA, Panchal D, Kaur R, Burange P, Ghogare J, Mokalec V, Raut

M. Synthesis of new S-derivatives of clubbed triazolyl thiazole as anti-*Mycobacterium tuberculosis* agents. Bioorg Med Chem. 2007; 15:3997–4008.
33. Shiradkar M, Kumar GVS, Dasari V, Tatikonda S, Akula KC, Shah R. Clubbed triazoles: A novel approach to antitubercular drugs. Eur J Med Chem. 2007; 42:807-816.
34. Aridoss G, Amirthaganesan S, Kima MS, Kim JT, Jeong YT. Synthesis, spectral and biological evaluation of some new thiazolidinones and thiazoles based on t-3-alkyl-r-2,c-6-diarylpiperidin-4-ones. Eur J Med Chem. 2009; 44:4199-4210.
35. Clark RF, Zhang T, Wang X, Wang R, Zhang X, Camp HS, Beutel BA, Sham HL, Gu YJ. Phenoxy thiazole derivatives as potent and selective acetyl Co-A carboxylase-2 inhibitors: Modulation of isozyme selectivity by incorporation of phenyl ring substituent. Bioorg Med Chem Lett. 2007; 17:1961-1965.
36. Andreani A, Rambaldi M, Mascellani G, Rugarli P. Synthesis and diuretic activity of imidazo [2,1-b] thiazole acetohydrazones. Eur J Med Chem. 1987; 22:19-22.
37. Koufaki M, Kiziridi C, Nikoludaki F, Alexis MN. Design and synthesis of 1,2-dithiolane derivatives and evaluation of their neuroprotective activity. Bioorg Med Chem Lett. 2007; 17:4223-4227.
38. Shih MH, Ying KF. Syntheses and evaluation of antioxidant activity of sydnonyl substituted thiazolidinone and thiazoline derivatives. Bioorg Med Chem. 2004; 12:4633-4643.
39. Amin KM, Rahman ADE, Al-Eryani YA. Synthesis and preliminary evaluation of some substituted coumarins as anticonvulsant agents. Bioorg Med Chem. 2008; 16:5377-5388.
40. Dawood KM, Gawad HA, Rageb EA, Ellithey M, Mohamed HA. Synthesis, anticonvulsant, and anti-inflammatory evaluation of some new benzotriazole and benzofuran-based heterocycles. Bioorg Med Chem. 2006; 14:3672–3680.
41. Azam F, Alkskas IA, Khokra SL, Prakash O. Synthesis of some novel *N*4-(naphtha[1,2-d]thiazol-2-yl)semicarbazides as potential anticonvulsants. Eur J Med Chem. 2009; 44:203-211.
42. Zhu LP, Ye DY, Tang Y. Structure-based 3D-QSAR studies on thiazoles as 5-HT_3 receptor antagonists. J Mol Model. 2007; 13:121-131.
43. Deeb O, Clare BW. QSAR of heterocyclic antifungal agents by flip regression. J Comp Aid Mol Des. 2008; 22:885-895.