Heterocyclic Letters
Vol. 7| No.4|1185-1210|Aug-Oct|2017
ISSN : (print) 2231–3087 / (online) 2230-9632
CODEN: HLEEAI
http://heteroletters.org

DIVERSE PHARMACOLOGICAL ASPECTS OF 2-AMINO-4-PHENYLTHIAZOLE DERIVATIVES-A REVIEW

Mohammed Arifuddin*, Neeraj Kumar Chauhan, Laxmi Keshav Kritika, Pramod Kumar Dubey

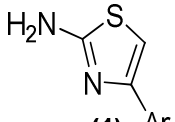
**Department of Medicinal Chemistry,*
National Institute of Pharmaceutical Education and Research. (NIPER-Hyderabad)
Balanagar, Hyderabad-500 037. India
Email:- arifabib@yahoo.com

Abstract: Thiazole derivatives are known for their wide range of biological activities such a cardiotonic, fungicidal, sedative, anaesthetic, bactericidal and anti-inflammatory. Among thiazole class of compounds 2-amino-4-arylthiazoles and their derivatives occupy a unique position. They have long been used as precursors for the synthesis of a series of other biologically active molecules. In this review article we wish to describe the various biological activities of 2-amino-4-arylthiazoles along with their synthetic methods.

Keywords: Diverse pharmacological activities, 2-amino-4-arylthiazoles, synthesis, anti-microbial, anticancer.

1. Introduction

Thiazoles are a well known group of compounds in medicinal chemistry with diverse types of biological activities. A thiazoloe ring is a five-memebered ring structurally similar to thiophene with a sp^2 nitrogen in the 3-position instead of a sp^2 carbon. Thiazole derivatives are known for their wide range of biological activities such a cardiotonic, fungicidal, sedative, anaesthetic, bactericidal and anti-inflammatory.[1] Among thiazole derivatives 2-amino-4-arylthiazoles (**1**) and their derivatives occupy a unique position. They have long been used as precursors for the synthesis of biologically active molecules. 2-Aamino-4-arylthiazoles (**1**) have also shown a variety of biological activities notable among them being antibacterial, antifungal, antitubarcular, anti-HIV, anti-inflammatory, anticancer anticonvulsant, antidiabatic, antihypertensive, antiprotozoal etc.[2] Structurally, 2-amino-4-arylthiazoles are derivable from thaizoles by substituting amino group in the 2nd position and aryl group in the 5th position as shown in **Figure-1**.



(1)

Figure-1
Some of the marketed drugs molecules, containing the 2-amino-4-arylthiazoles moiety are shown in **Figure-2**.

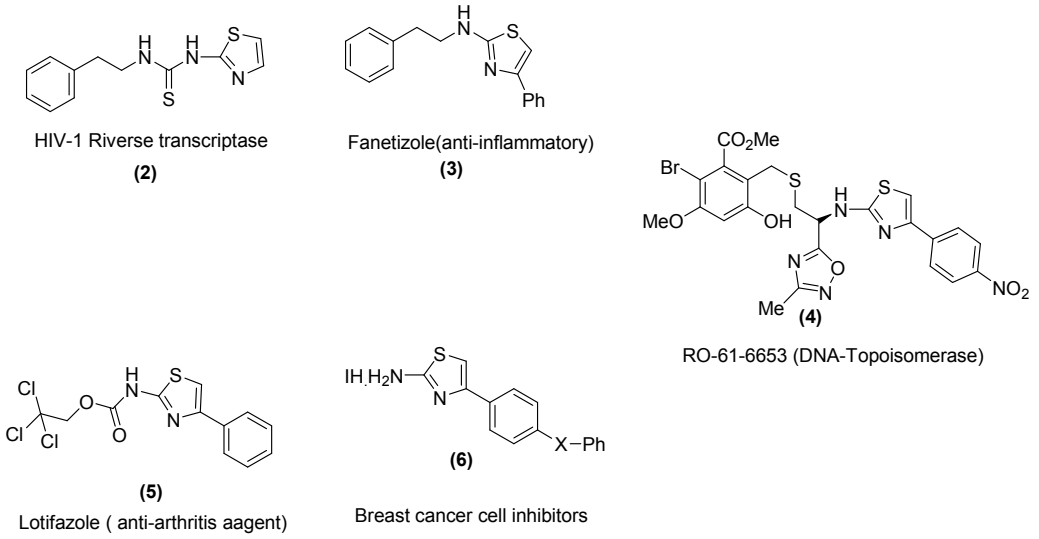
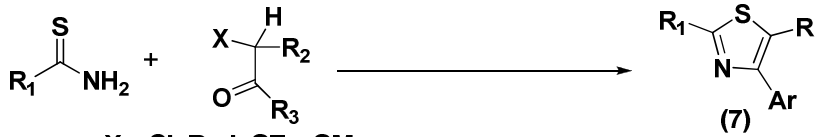


Figure-2: Structure of some drugs containing 2-aminothiazole rings

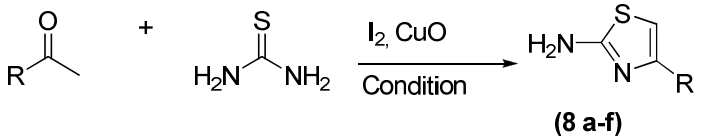
Furthermore, the pharmacological properties as well as therapeutic application of 2-amino-4-arylthiazoles depend on the substitution pattern and it is been reported that they are exhibiting various pharmacological activities. In the present review we will highlights the pharmacological importance of 2-amino-4-arylthiazoles in last two decade. Additionally, this review will also highlight the latest synthetic methods for the synthesis of 2-amino-4-arylthiazoles reported in last two decades.

2. New methods developed for the synthesis of 2-amino-4-arylthiazoles

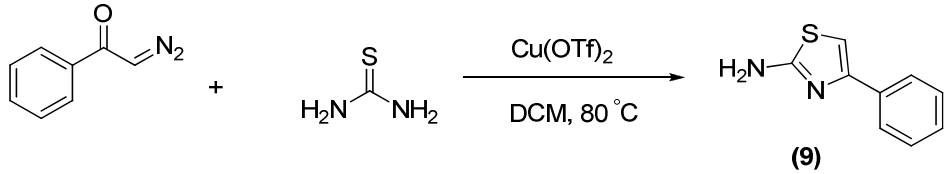
The 2-amino-4-arylthiazoles (**7**) are commonly synthesised by using the procedure reported first by Hantzch in 1887 which involves the condensation of haloketones and thiourea or thioamides in refluxing alcohol. This method has disadvantages such as long reaction times (24-25 hr) and harsh reaction conditions.[3] Hence, several new approaches and methods have been developed to overcome the drawback of the classical methods. Few of the methods of synthesis of 2-amino-4-arylthiazoles reported in recent years are described below.



A concise and efficient one-pot process from easily available methyl ketones/unsaturated ketones and thiourea was developed for the synthesis of 2-aminothiazoles in the presence of I_2/CuO by An-Xin Wu and coworkers.[4] The method is highly stereo-selective as only E-isomers of 4-ethenyl-2-aminothiazoles (**8a-f**) are obtained exclusively in this synthesis.

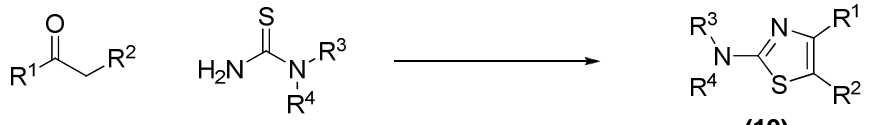


According to Yadav et al. the α-diazaketones smoothly undergo coupling with thiourea in the presence of 10 mol% of copper(II) triflate to afford the 2-aminothiazole in excellent yields with high selectivity.[5] This method offers significant advantages including mild reaction conditions, high conversions, short reaction times, cleaner reaction profiles and high selectivity making it a useful and attractive strategy for the preparation of biologically relevant 2-aminothiazole derivatives (**9**) in a single step operation.



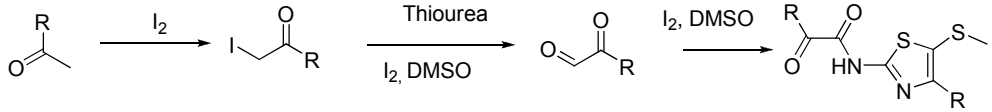
(9)

Zhao et al. reported an efficient procedure for the synthesis of 2-aminothiazoles (**10**) via KI/NH_4NO_3-catalyzed oxidative cyclization of ketones and thioureas using molecular oxygen as a green oxidant.[6]



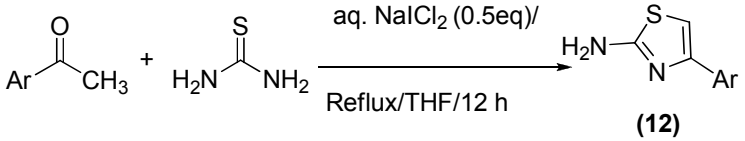
(10)

An-xin Wu and co-workers worked on an iodine-promoted selective synthesis which was developed for the construction of substituted 2- aminothiazoles (**11**) from easily available aryl methyl ketones and thiourea under metal free conditions. This domino process involved the cleavage of C-H, C-O, C-S bonds and the formation of C-N, C-O and C-S bonds.[7]



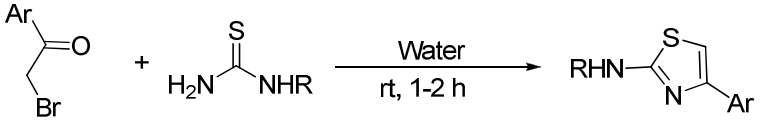
(11)

A simple, novel, concise and highly efficient methodology was developed by Telvekar et al. to synthesize substituted 2-aminothiazoles (**12**) from the corresponding thiourea and substituted ketones using aqueous $NaICl_2$ as catalyst under metal free conditions.[8]



(12)

Srinivasan et al. have reported a highly efficient and facile method has for the synthesis of N-substituted 2-aminothiazoles (**13**) in water without any added catalyst or organic co-solvent. This process is unique as it avoids the use of highly polar and toxic volatile organic solvents such as DMF, dioxane and methanol, and catalyst, with the water itself playing the dual role of a solvent and promoter.[9] This procedure is successfully applied for the development of the anti-inflammatory drug **fentizole**.

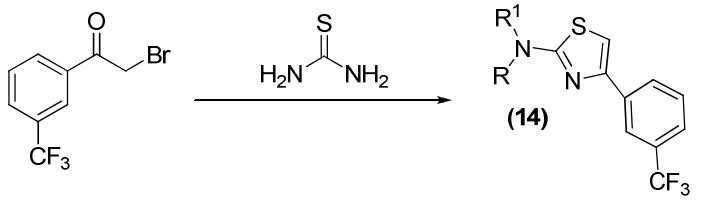


(13)

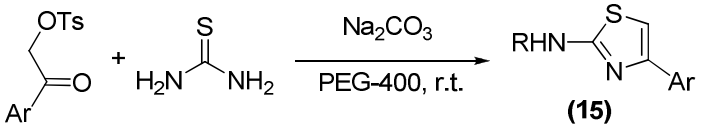
R=H,Me,C_6H_5,$C_6H_5CH_2$
$C_6H_5CH_2CH_2$ (**fanetizole**)

Structurally diverse thiazoles were conveniently synthesised by one pot procedure by the reaction of α-haloketones with thioureas/N,N-disubstituted thioureas by Rao et al. The

desired 2-aminothiazoles (**14**) with alkyl or aryl or halo substitutions was obtained in good yields.[10]

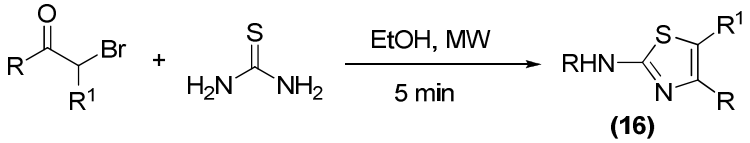


Lina et al. have reported a simple and practical procedure for the synthesis of 2-aminothiazoles (**15**) from α-tosyloxyketones and thiourea was described using PEG-400 [poly(ethylene glycol-400)] at ambient conditions.[11] The enhanced reaction rate, mild reaction condition, high yields and green aspects such as avoiding hazardous organic solvents, toxic catalysts and waste, ease of recovery and reuse of this novel reaction medium are some of the important features of this procedure.

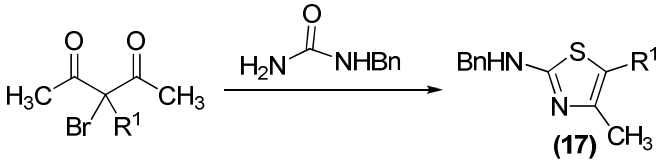


R = H, C_6H_5, $C_6H_5CH_2$, $C_6H_5CH_2CH_2$

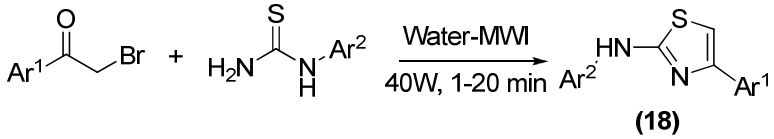
Kabalka et al. reported a microwave irradiated rapid one-pot synthesis of 2-aminothiazoles (**16**) via the condensation of α-bromoketones with thiourea.[12]



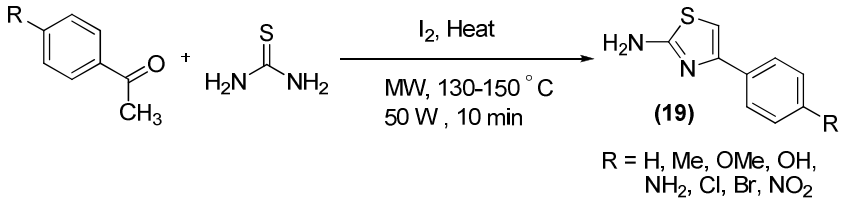
One-pot tandem three-step reaction has been developed by using supported reagents system by Aoyama et al.[13] The synthesis of 2-aminothiazoles (**17**) was selected for confirming the effectiveness of the method using supported reagents system. One-pot three-step reaction effectively proceeded, and the yield of the products is higher than that in step-wise process.



A facile, high yielding green chemical synthetic protocol adaptable to the parallel synthesis of a library of potentially bioactive 2-amino-4-arylthiazoles (**18**) was reported by Jain et.al. The methodology involved the condensation of various aracyl bromides with N-arylthioureas under MWI using water as solvent, to yield pure products (81%-97%) in very short reaction times (1-20 min).[14]



Mena-Rejon et al. have reported the one-pot solvent free procedure for the synthesis of 2-Amino-4-arylthiazoles (**19**) under microwave irradiation.[15]

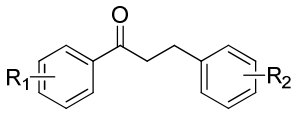


3. Pharmacological importance of 2-amino-4-arylthiazoles

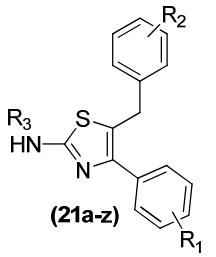
3.1 2-Amino-4-arylthiazoles as anti HIV agents

Three decades have passed since human immunodeficiency virus (HIV) was identified as the causative agent of acquired immunodeficiency syndrome (AIDS). It has been estimated that 35.3 million people were living with HIV globally at the end of 2012. However drug resistant and severe drug-drug interaction limits the clinical efficacy of HIV drugs, thus the search for novel anti-HIV drugs continues. Few of the 2-amino-4-arylthiazole derivatives are reported as HIV inhibitors. The details are described below.

Novel 2,4,5-trisubstituted thiazole derivatives (TSTs) were designed and synthesized as HIV-1 non-nucleoside reverse transcriptase inhibitors (NNRTIs) by Ying Guob et al.[16] Among the thirty-eight synthesized target compounds (**20a-m** and **21a-z**), thirty TSTs showed potent inhibition against HIV-1 replication in wild type HIV-1 at sub micro-molar concentrations (from 0.046 to 9.59 mM). Compounds **20o**, **20q** and **20r** were also tested on seven NNRTI-resistant HIV-1 strains, and all exhibited inhibitory effects with many fold changes in IC50 values ranging from 2.6 to 111, which were better than those of nevirapine (15.6-fold -371-fold).

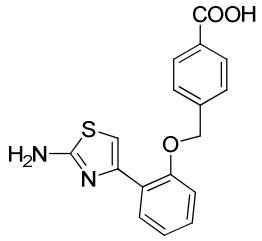


(20a-m)



(21a-z)

Mely et al. have designed AN3 (**22**) as an efficient inhibitor of the HIV-1 NC (nucleocapsid protein) chaperon functions.[17] Although the NC inhibitory activities of A10 and AN3 were comparable, AN3 showed antiviral activities in the infected cells with a mechanism of action clearly indicating NC as the primary target. Structural requirements for AN3 binding to NC were elucidated by NMR, biophysical studies, and MD simulations, showing that the hydrophobic pocket of NC and competes with the nucleic acids for this binding site. In agreement with MD simulations, a direct interaction of AN3 to the key residue Trp37 was observed, whereas NMR chemical shift mapping experiments further highlighted the involvement of Met46, Ala25 and Asn17, thus clearly identifying the hydrophobic pocket of NC as binding site of AN3.



AN3 (22)

3.2 2-Amino-4-arylthiazoles as anti-inflammatory agents

Inflammation is defined as the local response to living mammalian tissues to injury due to any agent. Specifically it is a series of molecular and cellular responses acquired during evolution designed to eliminate foreign agents and promote repair of damage tissues. Recently 2-amino-4-arylthiazoles are emerged as potential anti-inflammatory agents.

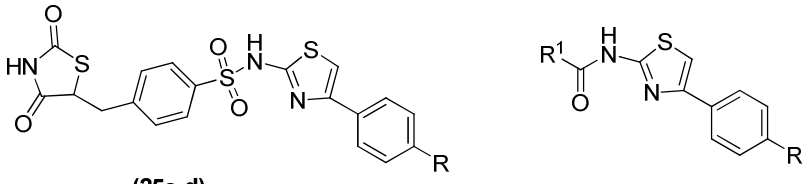
A series of novel 1-phenyl-3-(4-phenylthiazo-2-yl) urea derivatives (**23a-f** and **24a-s**) have been synthesized to meet the structural requirements essential for anti-inflammatory and antimicrobial properties by Ola I. A. Salem et.al.[18] The results shows that most of the target compounds exhibiting potent antibacterial activity that equipotent or higher than ampicillin. Also, they were evaluated for their in vivo anti-inflammatory activities in rats compared to indomethacin. Four compounds **23b**, **24f**, **24k** and **24m** proved to be the most active anti-inflammatory agents with superior GI safety profile and good safety margin compared to indomethacin.

23a-f **24a-s**

X = H, Cl; R^1 = Ph, 4-Cl.Ph, 4-CH_3

R^2 = Ph, 4-Cl.Ph, 4-CH_3Ph, -CH_2CH_2Ph or *cyclo*-C_6H_{11}

Pattan et al. have synthesized some novel substituted phenyl thiazole (**25a-d** & **26a-o**).[19] The fifteen new derivatives of phenyl thiazoles were synthesized during the course of research work. The newly synthesised compounds were evaluated for their anti-inflammatory activity by Carrageenan Induced Rat hind paw method. Out of fifteen compounds **25a**, **25d**, **26b**, **26g**, **26i**, and **26j** shows maximum anti-inflammatory activity.



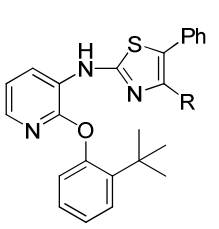
(25a-d) **(26a-o)**

3.3 2-Amino-4-arylthiazoles as anti-platelet agents

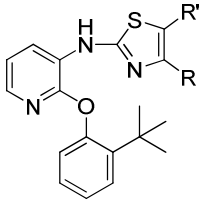
Adenosine-5'-diphosphate (ADP) released from platelet, red blood cells and damaged blood vessels is a key activator of platelates and play a crucial role in generation of arterial thrombi at the site of vascular injury. Two G-protein coupled receptors, P2Y1 and P2Y12 are required

for full ADP-induced plaltelets aggregation but each of these receptors play a different role in this process. 2-amino-4-arylthiazole has identified as potent antiplatelets agents.

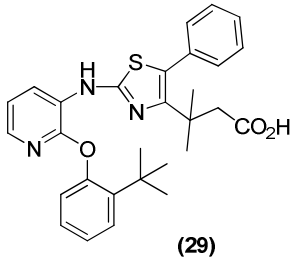
Zulan et. al. have reported that the P2Y1 and P2Y12 receptors are recognised as potential targets for antithrombotic action.[20] A series of P2Y1 antagonists that contain 2-aminothiazoles (**27a-j**, **28a-d** and **29**) as urea surrogates were discovered. They have extensive discussed the SAR of the thiazole ring. The results shows that the most potent compound **27j** showed good P2Y1 binding (Ki = 12 nM), moderate antagonism of platelet aggregation (PA IC50 = 5.2 μM) and acceptable PK in rats.



(27a-j)



(28a-d)

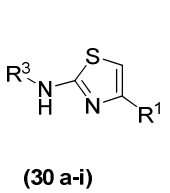


(29)

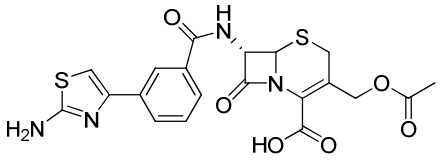
3.4 2-Amino-4-arylthiazoles as anti-microbial agents

The treatment of infectious diseases caused by bacteria, parasites, viruses and fungi always remains a global health problem because of increasing number of multi drug resistant pathogenic microbial strains. Despite of the availability of large number of antibiotics for clinical use, the emergence of antibiotic resistance in recent years against gram positive and Gram negative bacterial and fungal strains constituents an urgent need for the discovery of new class of antimicrobial agents. In these contests the 2-amino-4-arylthiazoles emerges as potential class of antimicrobial agents in recent years.

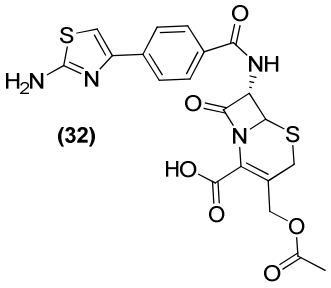
Abou-Gharbia et al. have reported the synthesis and biological screening of a 2-aminothiazole based compound library[21] (**30a-i**, **31a-e** & **32**) to determine their utility as antimicrobials by focusing on MRSA. Several of the compounds in this series demonstrated improved antimicrobial activity as compared to ceftriaxone (CTX), a β-lactam antibiotic. The most potent compound (30i) had MICs in the range of 2- 4 μg/ml across a panel of *Staphylococcus aureus* strains. In addition, trifluoromethoxy substituted aminothiazoles (**30 a** & **30b**) are found to be potent antimicrobials with MICs of 2-16 μg/ml. Compound (**30h**), a pyrrolidine based compound, demonstrated an MIC value of 2 μg/ml against *S. aureus* (UAMS-1).



(30 a-i)

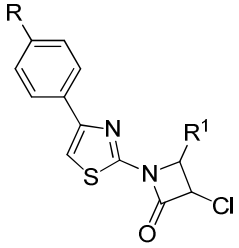


(31 a-e)



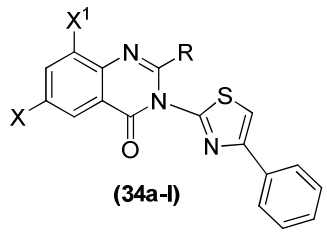
(32)

Novel substituted 2-amino thiazole containing azetidinone derivatives (**33**) were prepared as antimicrobial agents. The synthesized compounds were screened for their antibacterial against *Escherichia coli*, *Staphylococcus aureus* and antifungal activity *Candida albicans* by employing disc diffusion method. The synthesized compounds showed good antibacterial and antifungal activity against all tested organisms.[22]



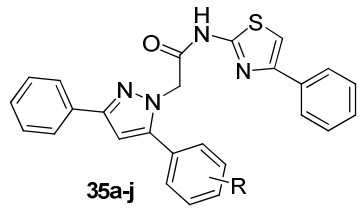
(33)

The novel quinazolin-4-(3*H*)-ones (**34a-l**) were synthesized by condensation of 2-amino-4-phenylthiazole/2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzothiophene with 6,8-(un/mono/di)-bromo-2-(methyl/phenyl)-4*H*-benzo-[1,3]-oxazine-4-ones. The 2-amino-4-phenylthiazole and 2-amino-3-carbethoxy-4,5,6,7-tetrahydrobenzothiophene was synthesized from acetophenone and cyclohexanone respectively. The 6,8- (un/mono/di)-bromo-2-(methyl/phenyl)-4*H*-benzo-[1,3]-oxazine-4-ones were synthesized from 3,5- (un/mono/di)-bromoanthranilic acid. The newly synthesized compounds were screened for antibacterial activity against *Staphylococcus aureus* (ATCC 9144), *Staphylococcus epidermidis* (ATCC 155), *Micrococcus luteus* (ATCC 4698), *Bacillus cereus* (ATCC 11778), *Escherichia coli* (ATCC 25922), *Pseudomonas aeruginosa* (ATCC 2853) and *Klebsiell apneumoniae* (ATCC 11298) and for anti-fungal activities against *Aspergillus niger* (ATCC 9029) and *Aspergillus fumigatus* (ATCC 46645). Most of the synthesized compounds exhibited mild to moderate anti-bacterial and anti-fungal activities. Among the synthesized compounds, 6,8-Dibromo-2-methyl-3-(4-phenylthiazol-2-yl)-quinazolin-4(3*H*)-one (**34c**) was found to exhibit the highest antibacterial activity and 6,8-Dibromo-2-methyl-3-(3-carbethoxy-4,5,6,7-tetrahydrobenzothiophene-2-yl)-quinazolin-4(3*H*)-one (**34f**) exhibited highest anti-fungal activity.[23]



(34a-l)

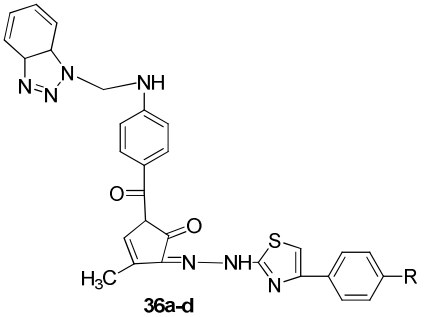
G. Sarvanana have synthesized a series of thiazoles derivatives by incorporation of pyrazole moiety at 2nd position of 2-hydrazinyl-N-(4-phenylthiazol-2-yl)acetamides by treating with chalcones. These compounds (**35a-j**) were screened for their anti-bacterial activity against *Staphylococcus aureus* ATCC 9144, *Staphylococcus epidermidis* ATCC 155, *Micrococcus luteus* ATCC 4698, *Bacillus cereus* ATCC 11778, *Escherichia coli* ATCC 25922, *Pseudomonas aeruginosa* ATCC 2853 and *Klebsiellap neumoniae* ATCC 11298 and for their antifungal activity against *Aspergillus niger* ATCC 9029 and *Aspergillus fumigates* ATCC 46645. Most of the synthesized compounds exhibited significant anti-bacterial and anti-fungal activities. Among the synthesized compounds, 2-(5-(4-hydroxyphenyl)-3-phenyl-4,5-dihydropyrazol-1-yl)-N-(4- phenylthiazol-2-yl)acetamide (**35f**) was found to exhibit the highest antibacterial activity and 2-(5-(4-hydroxy-3-methoxyphenyl)-3-phenyl-4,5-dihydropyrazol-1-yl)-N-(4-phenylthiazol-2-yl)acetamide(**35j**) exhibited highest antifungal activity.[24]



35a-j

R = H**(35a)**, 4-OCH_3**(35b)**, 4-$N(CH_3)_2$**(35c)**, 3-NO_2**(35d)**, 4-CH_3**(35e)**, 4-OH**(35f)**, 4-Cl**(35g)**, 4-NO_2**(35h)**, 3,4,5-OCH_3**(35i)**, 3-OCH_3 -4-OH**(35j)**

A series of 1-(4-((1*H*-benzo[d][1,2,3]triazol-1-yl)methylamino)benzoyl)-4-(2-(4-(4-substitutedphenyl)thiazol-2-yl)hydrazono)-3-methyl-1H-pyrazol-5(4H)-one (**36a-d**) compounds were synthesized as antimicrobial agents. The compounds showed significant anti-microbial activity against various bacteria and fungi.[25]

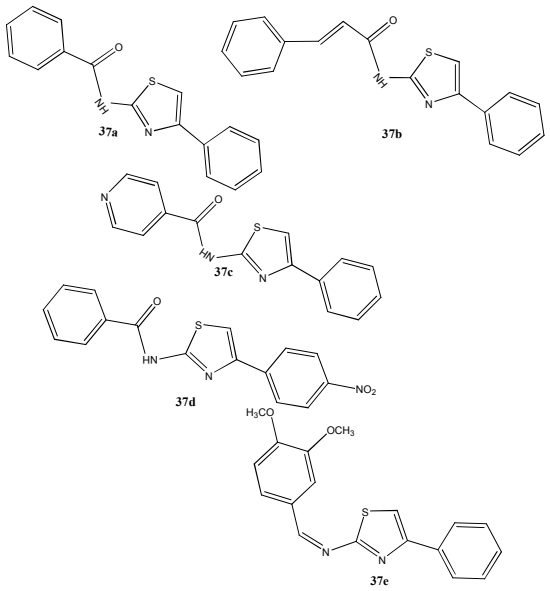


36a-d

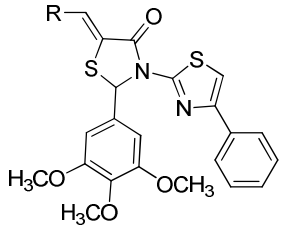
R = H**(a)** , Br**(b)**, OCH_3**(c)**, CH_3**(d)**

Narang et al. have synthesized a series of 2,4-disubstituted thiazole derivatives (**37a-e**) and evaluated for their in vitro antibacterial and antifungal activities against *B. subtilis*, *E. coli*, *S. aureus*, *C. albicans* and *A. niger* by tube dilution method. The analysis of antimicrobial

activity results indicated that the presence of NO_2 and OCH_3groups at para position of phenyl group improved the antimicrobial activity significantly. Molecular docking studies also supported in vitro activity results and showed that NO_2 and OCH_3 groups containing compounds have greater affinity towards the target glucosamine-6-phosphate synthase. QSAR studies indicated that molecular connectivity index (2χv) and Kier's shape index (κα3) are the key parameters for antimicrobial activity of synthesized thiazole derivatives and can be considered as important factors for interaction with target site of different microorganisms.[26]



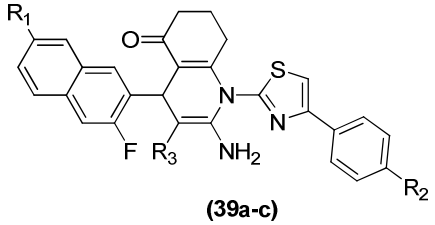
Prakasha et. al described the synthesis and in vitro antimicrobial evaluation of 5-arylidine derivatives of 2-(3, 4, 5-trimethoxyphenyl)-3-(4-phenylthiazol-2-yl) thiazolidin-4-one. The reaction of 2-amino-4-phenylthiazole, 3,4,5trimethoxybenzaldehyde and mercaptoacetic acid in the presence of DCC yielded 2-(3, 4, 5-trimethoxyphenyl)-3-(4-phenylthiazol-2-yl) thiazolidin-4-one and further 5-arylidne derivatives (**38a-k**) were synthesized by the subsequent reaction of 2-(3, 4, 5-trimethoxyphenyl)-3-(4-phenylthiazol-2-yl) thiazolidin-4-one with different aryl aldehydes. The compounds showed some interesting antibacterial activity, the substitution of 5-arylidne groups on new thiazolidinone i.e., 2-(3, 4, 5-trimethoxyphenyl)-3-(4-phenylthiazol-2-yl) thiazolidin-4-one have resulted enhanced antibacterial activity. The compounds showed moderate antifungal activity in a scattered manner.[27]



38a-k
R = various aryl moieties

Raj et al. have carried out a facile one-pot synthesis of heterocyclic derivatives containing 2-aminothaizole moiety (**39a-c**). All the synthesized compounds were screened for their antibacterial activity against Gram positive bacterial species *S. pneumoniae*, *B. subtilus* and

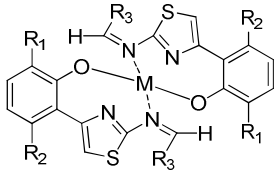
C. tetani and Gram negative bacterial species *E. coli*, *S. typhi* and *V. cholerae* and fungicidal activity against *C. albicans* and *A. fumigates*.[28]



(39a-c)

R_1 = H, Me, C **(39a)**
R_2 = H, OH, Cl **(39b)**
R_3 = CN, $COOC_2H_5$ **(39c)**

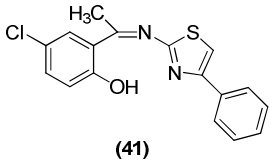
Ghatole et al. have carried out a reaction of heteroaromatic-2-amino-4-arylthiazoles with metal (II) acetate resulted substituted Bis[2-((E)-2-(4-benzylideneamino)thiazol-4-yl)-4-methylphenol] metal complexes (**40a-x**) moiety in a one step process. The representative Schiff base ligand and its metal complex have been tested in vitro for their antibacterial activity against bacteria *E. Coli*, *S. Aureus*, *P. Areuginoso*, *K. Pneumoniae* and fungi *C. Albicans* and *S. Cerevisiae*. Few of these metal complexes exhibited pronounced antimicrobial activity.[29]



(40a-x)

M = Cu, Zn, Co

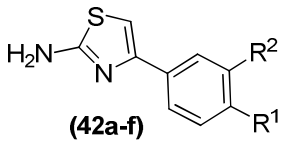
Metal complexes of VO(IV), Zr(IV) and UO_2(VI) with 2-hydroxy-5-chloroacetophenone-2-imino-4-phenylthiazole (**41**) have been synthesized by Sandip R. Kelode.[30] The metal complexes have been examined against the growth of bacteria to assess their antimicrobial potential.



(41)

HCAIPT

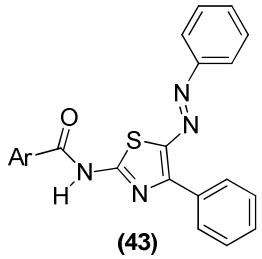
A new series of 2-aminophenylthiazole derivatives (**42a-f**) was synthesized by Dutta et al.[31] The compounds (**42a-f**) were screened for antimicrobial activity in vitro by Kirby-Bauer disc diffusion method and compounds **42b** and **42c** have shown promising activity. The antifungal activity results revealed that all the compounds, except **42b** and **42c** which showed less activity towards *C. albicans* as compared to *A. niger* whereas other compounds were more effective against *C. albicans*.



(42a-f)

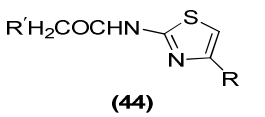
Prajapati et al. have reported the synthesis of a series of amide (**43**) containing 2-aminophenylthaizoles. The newly synthesised amides derivatives are screened for their anti-bacterial activity against *E. coli* and *S. aureusas* as well for their antifungal activity against *A.*

niger and *A. oryzae*. All the synthesized compounds showed moderate to good microbial activity.[32]



(43)

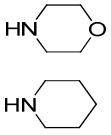
Pattan et al. have synthesized some substituted 2-aminothiazoles derivatives (**44-46**). The newly synthesized compounds were evaluated for their Antibacterial and antifungal activity. The result shows that most of the compound shows moderate to good Antibacterial and antifungal activity against *S. aureus*, *E. coli*, *A. niger* and *C. albicans*.[33]

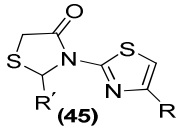


(44)

R = Cl , OCH_3

R′ = $OCOCH_3$, $NHNH_2$

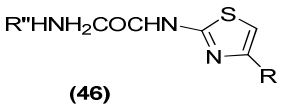




(45)

R = OCH_3, Cl

R′ = C_6H_5

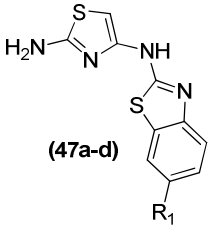


(46)

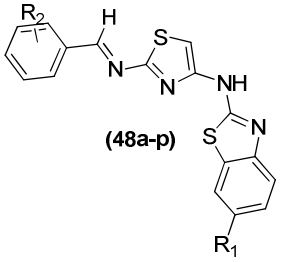
R = Cl , OCH_3

R" = C_6H_5

A series of 4-(6-substituted-1,3-benzothiazol-2-yl)amino-1,3-thiazole-2-amines (**47a-d**) and 4-(6-3-benzothiazole-2-yl)amino-2-(4-substitutedphenyl-methylidiene)amino-1,3-thiazole (**48 a-p**) were synthesised screened for their antibacterial, antifungal and antihelmintic activities by Amnerkar et al.[34] The biological evaluation results revealed that almost all the compounds whosed moderate to excellent antimicrobial activity against two gram negative bacteria i.e., *E. coli*, *P. aurugisona*, two gram positive i.e., *S. aireus* and *B. Subtilis*, and against pathogenic fungal species i.e., *C. albican* and *A. niger* and good anthelmintic activity against earthworm species *P. corethruses*. Among all the compounds tested the compounds **48k** and **48l** showed maximum antibacterial activity against gram negative and gram positive bacteria respectively. Compounds **48j** exhibited good antifungal activity while compound **48n** displayed maximum anthelmintic activity comparable to the standard drugs.



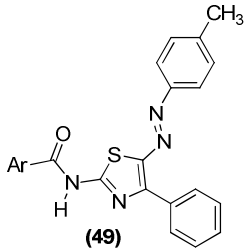
(47a-d)



(48a-p)

Kumar et al. have synthesizes various amides of 2-amino-5-(4-methylphenyl)-diazenyl-4-phenyl-1,3-thiazole (**49**) and evaluated their biological activities.[35] They are screened for anti-bacterial activity against *E. coli* and *S. aureus* as well as screened for antifungal activity

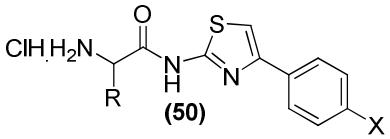
against *A. niger* and *A. oryzae* by cup plate method at 1 µg/ mL concentration in DMF. The biological evaluation results showed that all the compounds exhibited good antimicrobial activity. The results revealed that the chloro and nitro derivatives exhibiting moderate activity against *E.coli*. Similarly all the derivatives show moderate activity against *S. aureus* and *A. niger*, whereas the dichloro and dinitro derivatives have good activity against *A. oryzae*.



(49)

where Ar= phenyl, 2-chlorophenyl,4-chlorophenyl, 2,4-dichlorophenyl, 2-methylphenyl, 3-methylphenyl, 4-methylpheny, 3-nitrophenyl, 3,5-dinitrophenyl, 4-bromophenyl, phenylmethylene, 2-naphthoxymethylene, 4-phenylphenyl, cinnamic acid, nicotin, isonicotin, 4-methoxyphenyl,2-iodophenyl, 2-chlorophenylmethylene, 2,4-dichlorophenoxymethylene, 4-chloro-3-nitrophenyl

Gowda et al. have described the in vitro antimicrobial evaluation of novel amino acid conjugated of 2-aminothiazole (**50**). The antimicrobial activity results show that conjugation of amino acids to the 2-aminothiazole moieties has resulted in the enhanced antibacterial and antifungal activities. Among the two series of amino acid conjugates, chloro substituted analogous has showed better antibacterial and antifungal activities. Tryptophan analogous showed highest antibacterial activity where as lysine and arginine analogous showed highest antifungal activity compares to other amino acid conjugates.[36]

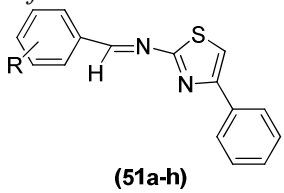


(50)

X = H, Cl

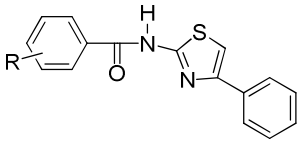
R = side chains of amino acids

Bhuiyan et al. have reported the synthesis of 2-arylideneamino-4-phenylthiazoles (**51a-h**) and N-(thiazol-2-yl)-amides (**52a-d**, **53-55**) and screened for their antimicrobial activity against *B. cereus*, *B. subtilis*, *S. aureus*, *S. dysenteriae*, *S. typhi*, *Pseudomonous* sp. bacteria and *A. niger*, *P. notatum*, *A. funiculosus*, *C. corchori Ikata* (Yoshida) and *C. lunata* fungi respectively. Some of the synthesized compounds exhibited pronounced antimicrobial activities.[37] The antibacterial activity results shows that among all the compounds compound **51b** exhibited highest activity against *B. cereus*. In the case of antifungal activity except compound **51f** and **52c** showed excellent results against *C. lunata*. The compound **51h** revealed highest activity against *A. funiculosus*.



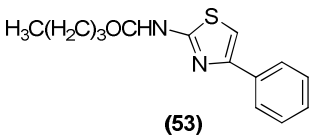
(51a-h)

R=*p*-CH_3,*p*-NO_2, *p*-Cl, *p*-OCH_3, *p*-OH, *m*-OCH_3, *p*-OH, *o*-OH

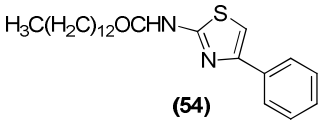


(52 a-d)

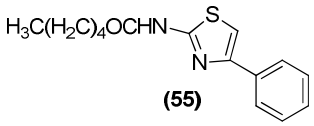
R= *p*-Cl, *p*-OCH_3,*m*-Cl,*p*-NO_2



(53)

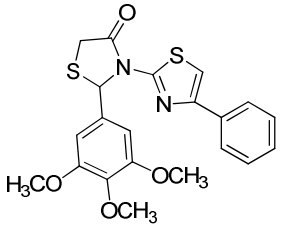


(54)

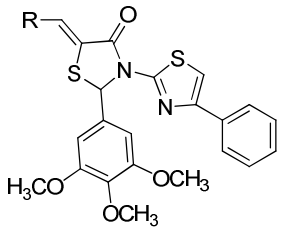


(55)

Patel et al. have reported the synthesis and in vitro antimicrobial evaluation of 5-arylidine derivatives of 2-(3, 4, 5-trimethoxyphenyl)-3-(4- phenylthiazol-2-yl) thiazolidin-4-one (**56**). The reaction of 2-amino-4-phenylthiazole, 3,4,5-trimethoxybenzaldehyde and mercapto acetic acid in presence of DCC yielded 2-(3, 4, 5-trimethoxyphenyl)-3-(4-phenylthiazol-2-yl) thiazolidin-4-one (**56**) and further 5-arylidne derivatives (57a-k) were synthesized by the subsequent reaction of (**56**) with different aryl aldehydes. All the synthesized compounds were evaluated for their antibacterial and antifungal activity. The results showed that the substitution of 5-arylidine groups on new thiazolidinone (**56**) have resulted in the enhanced antibacterial activity. All these compounds showed moderate antifungal activity in a scattered manner.[38]



(56)

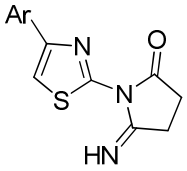


(57a-k)

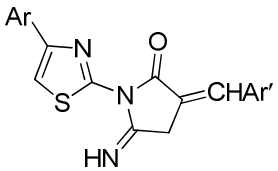
R = various aryl moieties

3.5 2-Amino-4-arylthiazoles as fungicidal agents

Five derivatives of 2-imino-3-(4-arylthiazol-2-yl)-thiazolidin-4-ones (**58a-e**) and a series of their 5-arylidene derivatives(**59a-l**) have been synthesized and tested for their antifungal activity against seven agricultural fungi by Anthonsen et al.[39] all the newly synthesized compounds exhibited higher fungicidal effects than the other compounds prepared. The results showed that the two new compounds (**58d** and **59e**) have higher fungicidal activity than the others, the percentage inhibition of **58d** and **58e** against *Pythiumaphani dermatum* (F1) and of **58d** against *Gaeumanno mycesgraminis* (F4) were higher than 90. The compounds **58a**, **58b**, **58d** and **58e** were more fungicidal against *Pythiumaphani dermatum* than against the other 6 fungi. Introduction of benzylidene group at C-5 decreased the fungicidal activity. The inhibition of all of the 5-arylidene-4-thazolidinones was low. Some of the ortho substituted derivatives (**59b** & **59d**) have showed highest activity than para substituted benzylidene derivatives against certain bacterial strains e.g., **59d** against *Staphylococcus aereus* and *Klebsiellap neumoniae*, **59c** against *Pseudomonas areginosa*. In vitro antifungal activity was performed against *Aspergillus niger* and *Aspergillus flavus*. The starting compound ie 2-(3,4,5-trimethoxyphenyl)-3-(4-phenylthiazol-2-yl) thiazolidin-4-ones (**58a**) has shown some good fungicidal activity.



(58a-e)



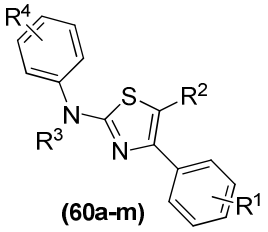
(59a-l)

Jadav et al. have synthesized the ligand complexes of Ni(II), Co(II) and Cu(II) with 2 - amino-4-(p-dihydroxyphenyl)thiazole and evaluated for their fungicidal activity. It is found that the activity decreases with decrease of concentration and the metal complexes are less toxic than the parent ligand.[40]

3.6 2-Amino-4-arylthiazoles as anti-tubercular agents

Tuberculosis (TB) a lung infection mostly caused by mycobacterium tuberculosis (Mtb), is considered one of the threaten diseases for public health. As per WHO report TB is describe a scenario that still frightful, there were an estimated 8.7 million new cases of TB (13% of which co-infected with HIV) and 1.4 million people died from the disease. Although a considerable number of anti-TB agents have been reported over the years only few of them have reached to clinical trials. Therefore, there is an immense need for development of novel anti-TB agents. The 2-amino-4-arylthiazoles have emerges as use full scaffold in the field of development of anti-TB agents.

Pieroni et al. have synthesized 2-aminothiazole scaffold and reported their inhibitory activity towards *Mycobacterium tuberculosis*.[41]

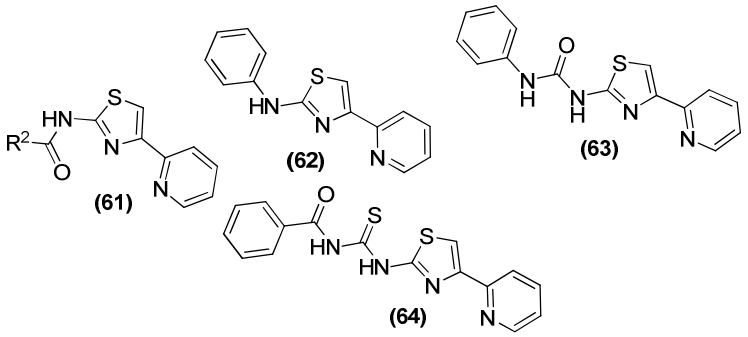


(60a-m)

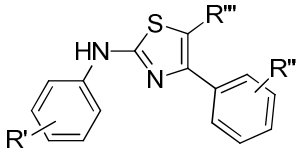
A total of about 38 new 2-aminothiazole derivatives (**60a-m**) were which allowed them to build a reliable SAR with regards to their anti-TB activity. Most notable compounds had MICs ranging in the low micromolar values, and more importantly selected compounds were found to be more active not only towards the replicating mycobacterium strains, but towards the non-replicating persistent phenotype in low oxygen conditions. Moreover, when tested against a panel of single-drug resistant Mtb strains, derivatives **60d** (R^1= 2-F,5-CF_3, R^2=H, R^3=H, R^4=4-Cl) and **60h** (R^1= 2-F,5-CF_3, R^2=H, R^3=H, R^4=3,5-Cl) maintained the same activity as for the wild type, indicating that these derivatives act with a mechanism of action different from those of currently used drugs, although as yet unknown.

Chibale et al. have synthesized a series of compounds derived from the 2-amino-4-(2-pyridyl) thiazole scaffold (**61-64**) and tested for their in vitro anti-mycobacterial activity against the *Mycobacterium tuberculosis* H37Rv strain, anti-plasmodial activity against the chloroquine sensitive NF54 *Plasmodium falciparum* strain and cytotoxicity on a mammalian cell line.[42] Optimal anti-mycobacterial activity was found with compounds with a 2-pyridyl ring at position 4 of the thiazole scaffold, a substituted phenyl ring at the 2-amino position, and an amide linker between the scaffold and the substituted phenyl. The anti-plasmodial activity

was best with compounds that had the phenyl ring substituted with hydrophobic electron withdrawing groups.

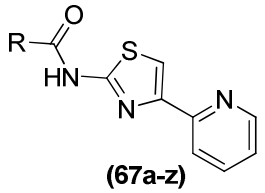


A series of 2-aminothiazole derivatives (**65a-s** and **66a-s**) with a wide range of substitutions at 2-, 4- and 5-positions were designed and synthesized by Kannan et al.[43] The newly synthesised compounds were evaluated for their inhibitory potential against *Mycobacterium tuberculosis* (Mtb), H37Rv. The compound, **65n** showed highest anti-mycobacterial activity with MIC value of 6.25 μM/ml and the succeeding compounds **65b**, **65e** and **65f** also exhibited anti-mycobacterial activity with MIC value of 12.50 μM/ml. Docking studies of these molecules with β-Ketoacyl-ACP Synthase (KasA) protein of Mtb have been carried out to understand the mechanism of anti- mycobacterial action. The compound, **65n** showed good interaction with KasA protein with a Ki value of 0.44 μM/ml.



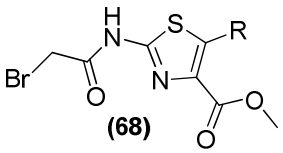
(65a-s and 66a-s)

A series of 2-aminothiazoles (**67a-z**) was synthesized based on a HTS scaffold from a whole-cell screen against *Mycobacterium tuberculosis* (Mtb) by Aldrich et al.[44] The SAR shows that the central thiazole moiety and the 2-pyridyl moiety at C-4 of the thiazole is intolerant to modification. However, the N-2 position of the 2-aminothiazole exhibits high flexibility and successfully improved the antitubercular activity of the initial hit by more than 128-fold through introduction of substituted benzoyl groups at this position. N-(3-Chlorobenzoyl)4-(2-pyridinyl)-1,3-thiazol-2-amine (**67u**) emerged as one of the most promising analogues with a MIC of 0.024μM or 0.008 μM/mL in 7H9 media and therapeutic index of nearly 300.

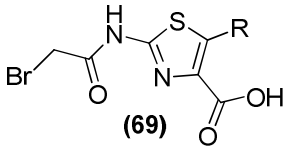


(67a-z)

Coxon et al. have reported the synthesis of 2-Aminothiazole-4-Carboxylate Derivatives (**68** & **69**) and carried out their anti-tubercular activity against Mycobacterium tuberculosis H37Rv and the b-Ketoacyl-ACP Synthase mtFabH.[45] Data clearly indicate that the 2-aminothiazole-4-carboxylate scaffold offers a promising new lead for further development. Methyl 2-amino-5-benzylthiazole-4-carboxylate (**68**) inhibits M. tuberculosis with an MIC of 0.06 mg/ml (240 nM) and is not cytoxic against HS-27 cells at 100 mg/ml concentrations.



(68)

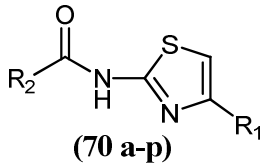


(69)

3.7 2-Amino-4-arylthiazoles as anti-tumour agents

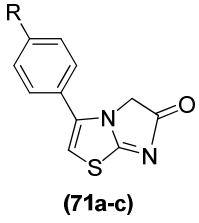
The global burden of cancer continues to increase largely because of aging and growth of the world population. Based on the GLOBOCON estimates, about 12.7 millions cancer cases and 7.6 million cancer deaths have occurred in last year.[46] 2-aminothiazoles have emerges as potential lead compounds for anti-tumour activities.

A number of 2-aminothiazoles were also prepared by Liand et al. in order to investigate the SAR of the inhibitory potency of novel 2-aminothiazoles (**70a-p**).[47] The compounds were evaluated in order to examine the anti-proliferative effects in the Hep3B cell 48h cyto-toxicity assay, the compound 70d exhibiting the best inhibitory potency among the all the compounds.

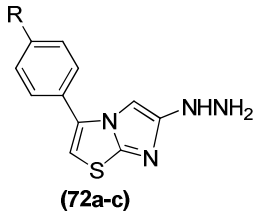


(70 a-p)

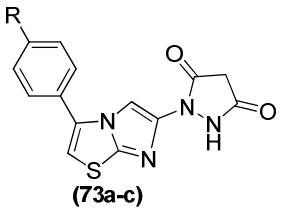
A series of imidazo[2,1-b]thiazoles bearing pyrazole moieties (**71a-c -75a-c**) was synthesized by Ahmed and co-workers.[48] Eleven compounds were screened at the National Cancer Institute (NCI), USA for anticancer activity at a single dose (10 mM). The in vitro anticancer evaluation results revealed that compounds **71a** and **75a** exhibited increased potency towards CNS SNB-75 and Renal UO-31 cancer cell lines.



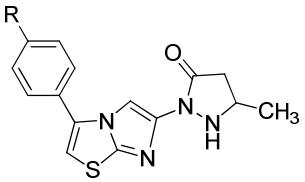
(71a-c)



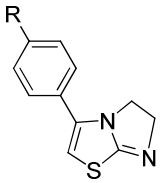
(72a-c)



(73a-c)



(74a-c)

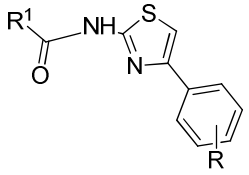


(75a-c)

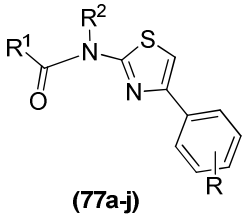
R= H, Cl, CH_3

Shilong et al. have designed and synthesized 40 new 2-aminothiazole derivatives (**76a-p**, **77a-j** & **78a-l**) as novel anti-migration and anti-invasion agents.[49] the results shows that structural modification of the substitution groups on the central 2-aminothiazole ring led to the identification of several potent migration inhibitors that strongly suppressed cell motility in metastatic cancer cells. More importantly, these compounds exhibited no apparent cyto-

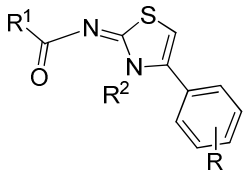
toxicity as they do not inhibit the ability of metastatic cancer cells to form colonies when treated with the migration inhibitors.



(76a-p)

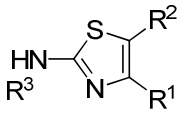


(77a-j)



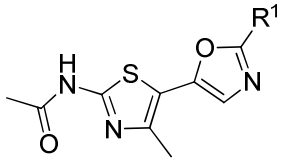
(78a-l)

A novel design and synthesis and evaluation of 2-aminothaizole class of SphK inhibitors (**79$_{1-42}$**) are reported by Dominik et al.[50] They discovered a potent inhibitors through a series of modifications using the known SKI-II scaffold to explain the structure activity relationship. The results shows that the compound 7924 which shows IC50 values of 7.3 μM (SphK1), 6.5 μM (SphK2) is found to be most promising candidate for further in vivo investigations and structural development.



(79$_{1-42}$)

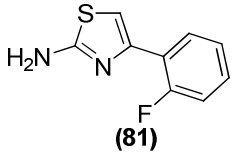
Yusuke et al. have reported the design and synthesis of a novel series of 2-aminothaizoles-oxazoles (**80a-u**) as potent phosphoinositide-3-kinase-γ-(P13Kγ) inhibitors.[51] The results reveals that these compounds shows potent inhibitory activities in enzyme based cell assays, the compounds **80g** (IC50 = 10 nM) and 80l (IC50 = 3 nM) against P13 Kγ.



(80 a-u)

3.8 2-Amino-4-arylthiazoles as miscellaneous agents

4-(2'-fluorophenyl)-2-aminothiazole (FPAT) (**81**) has been synthesized by reacting 2'-fluoroacetophenone, iodine and thiourea under microwave irradiation by a green chemistry approach by Rajmane et al.[52] The compound 81 was evaluated for their in vitro nematicidal and molluscicidal activities on plant parasitic nematode Meloidogynejavanica and freshwater helminthiasis vector snail Lymneaauricularia.

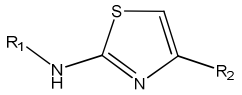


(81)

4-(O-fluorophenyl)-2-aminothiazole

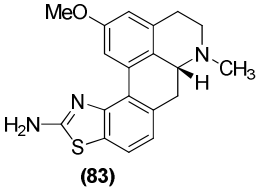
Contini et al. reported the SAR and QSAR study on 2-aminothiazole derivatives (**82**) as modulators of transcriptional repression in Huntington's disease. They identified three 2-aminothiazole derivatives as potent modulators of the RE1/NRSE silencing activity through a cell-based gene reporter assay. The carried out thoroughly the structure–activity relationships (SAR) of a library of commercially available 2-aminoisothiazoles diversely substituted at the amino group or at position 4. They also performed a quantitative structure–activity

relationship analysis using the phase strategy yielded highly predictive 3D-QSAR pharmacophore model for in silico drug screening.[53]

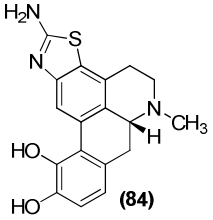


(82)

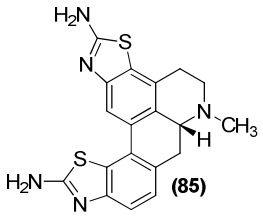
A series of apomorphine ((-)-APO)-derived analogues (**(-)-83-87**), were designed and synthesized by Zhang et al.[54] by hybridizing APO with a privileged 2-aminothiazole functionality which was lent from the orally available anti-parkinsonian drug, pramipexole. The biological assay results shows that among these new hybridized compounds, compound **84** shows good affinity at the D2 receptor with Ki of 328 nM, slightly less potent (3-fold), but more selective against the D1 receptor than that of the parent compound, APO. The compound **86** and **87** are exhibiting significant potency towards both the D1 and 5-HT1A receptors. The compound **86** is equipotent at both receptors (Ki: 116 and 151 nM, respectively), while the compound **87** is 8-fold more potent at the D1 (Ki: 78 nM) than at the 5-HT1A receptors (Ki: 640 nM). The results indicate that the catechol fragment is critical for the D2 receptor binding of the anti-parkinsonian drug apomorphine, but not necessary for binding at the D1 and 5-HT1A receptors.



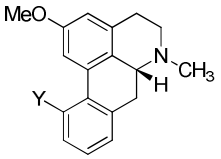
(83)



(84)

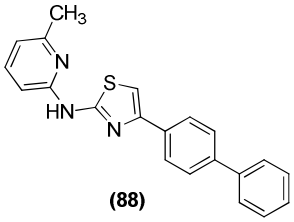


(85)

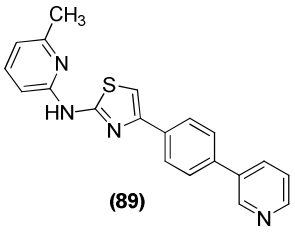


Y= $OCOC_4H_9$ **(86)**
Y= NH_2 **(87)**

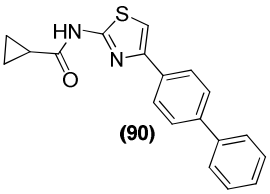
Zhe-Li et. al reported the 2-aminothiazole containing (4-biphenyl-4-yl-thiazol-2-yl)-(6-methyl-pyridin-2-yl)-amine (88) as use-full lead for the treatment of Prion Disease.[55] They identified the analogous of 88 with improved antiprion potency in ScN2a-cl3 cells while retaining comparable or superior properties. The compounds such as (6-methyl-pyridin-2-yl)-[4-(4-pyridin-3-yl-phenyl)-thiazol-2-yl]-amine (**89**) and Cyclopropane carboxylic acid (4-biphenyl-thiazol-2-yl)-amide (**90**) exhibited brain exposure/EC50 ratios at least ten-fold greater than that of 88. The results shows that these two new 2-AMT analogous (**89** & **90**) exhibits substantially (up to 20-fold) improved antiprion potency, while retaining or improving upon the PK properties of **88**.



(88)

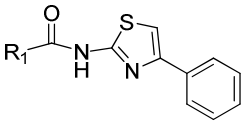


(89)

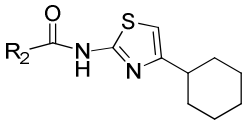


(90)

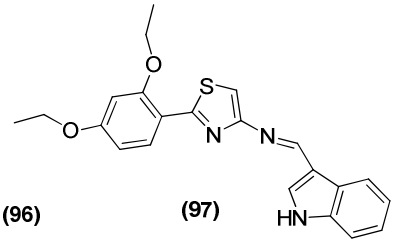
A series of novel poly(ADP-ribose) polymerase-1 (PARP-1) inhibitors were designed within 2-aminothiazole analogues (**91-97**) based on a constructed three-dimensional pharmacophore model by Peng-Fei et al.[56] The inhibitory effect on PARP-1 activity and the cyto-protective action of newly synthesised compounds are tested. The results shows that among newly synthesised compounds **91-93** and **97** appeared to be more potent as PARP-1 inhibitors with IC50 values less than 1μM, which are correlating perfectly the predicted values by pharmacophore model studies. These compounds proved to be highly potent against cell injury induced by H_2O_2 and oxygen-glucose deprivation (OGD) in PC12 cells. Thus these novel 2-aminothiazole analogues are emerged as potentially as neuro-protective agents for the treatment of neurological diseases in future.



R_1= -$CH_2CH_2COOC_2H_5$ **(91)**
4-Pyridyl **(92)**
styryl **(93)**
3,5-diemethoxystyryl **(94)**
-$CH_2CH_2COOC_2H_5$ **(95)**

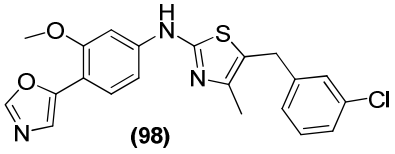


R_2= 3,5-diemethoxystyryl **(96)**

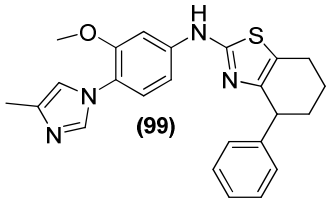


(97)

Thomas et al. reported the discovery of a new γ-secretase modulator class with an 2-aminothiazole core starting from a HTS hit (**98**). These novel compounds demonstrate moderate to good in vitro potency in inhibiting amyloid beta (Ab) peptide production.[57] Overall γ-secretase is not inhibited but the formation of the aggregating, toxic Ab42 peptide is shifted to smaller non-aggregating Ab peptides. Compound (**99**) reduced brain Ab42 in vivo in APPSwe transgenic mice at 30 mg/kg p.o.



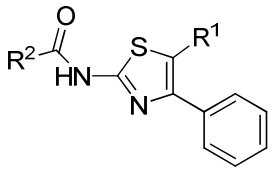
(98)



(99)

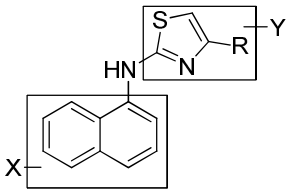
Anette et al. have carried out a hit-to-lead optimization of a series of carboxamides of ethyl-2-amino-4-phenylthaizoles-5-carboxylates (**100a-z**) as novel adenosine A2A receptor antagonists with in vivo efficacy.[58] The compound 100h from the series shown to have effect in a model of PD, and to displace a selective A2A receptor radio-ligand in an in vivo binding experiment with a similar ED50 value. The optimization of the hit (**100a-z**) into a lead series involved the identification of hetero-aromatic replacements for the ester functionality of lead compound. Thus, incorporation of different hetero-aromatics as the R^1 substituent gave compounds with affinities at the hA2A receptor in the same range as the original hit. Interestingly, the observed SAR with respect to the R^2 substituent in the series incorporating hetero-aromatic R^1 substituent's was not parallel to that in the original series, wherein R^1 =

ethyl ester. In general the results show that these compounds display low selectivity toward the hA1receptor affinity.

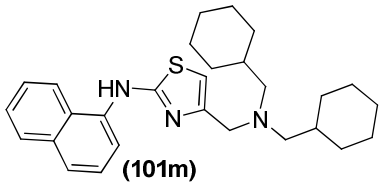


(100a-z)

Medina et al. have reported the synthesis of a novel series of 2-aminothiazole-derived antagonists (**101a-z**) as CCR4 receptor inhibitors.[59] They have evaluated the CCR4 receptor affinity for the by using TARC (CCL17) displacement assay. The results revealed that the bulky hydrophobic substituent's are preferred at the 4-position of the thiazole ring. Thus based on these finding they discovered a compound (**101m**) which displays adequate potency and pharmacokinetics properties to be possible potential candidate for CCR4 receptor antagonist.

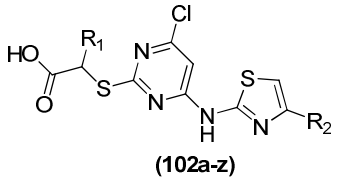


(101a-z)

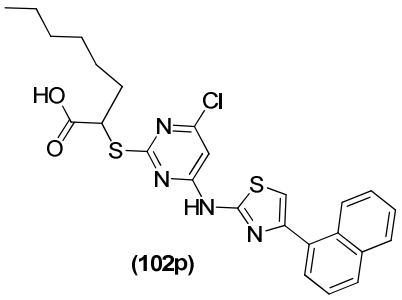


(101m)

Manfred et al. have reported a series of 26 novel 2-aminothiazole-featured pirinixic acid derivatives (**102a-z**) as dual 5-LO/mPGES-1inhibitors with improved potency.[60] The biological assay results revealed that among newly synthesised compounds the compound **102p** i.e., (2-[(4-chloro-6-{[4-(naphthalen-2-yl)-1,3-thiazol-2 yl]amino}pyrimidin-2-yl)sulfanyl]octanoic acid) is a promising candidate as its gives IC50 = 0.3 and 0.4 μM. The Computational analysis presumes binding sites of **102p** at the tip of the 5-LO catalytic domain and within a sub-pocket of the mPGES-1 active site. The results also shows that the compound **102p** reduced vascular permeability and inflammatory cell infiltration in a zymosan-induced mouse peritonitis model accompanied by impaired levels of cysteinyl-leukotrienes and prostaglandin E2.

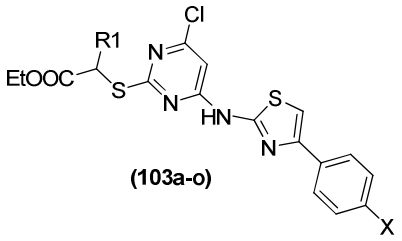


(102a-z)



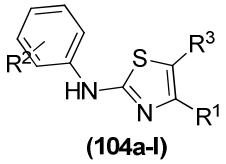
(102p)

Manfred et al. have identified PPAR agonistic activity of a set of 2-aminothiazole-based pirinixic acid derivatives (**103a-o**) as anti-inflammatory or anti-cancer drugs.[61]The most potent derivative regarding PPARc is found to be the compound **103g** which has also shown anti-inflammatory efficacy in vivo. The compound **103g** was also able to reduce the PGE2 and LTC4 levels in vitro and in vivo studies.

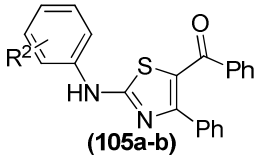


(103a-o)

Christopher et al. have reported the synthesis and biological evaluation of a collection of 2-aminothiazoles (**104a-l** & **105a-b**) as a novel class of compounds with the capability to reduce the production of PGE2 in HCA-7 human adeno carcinoma cells.[62] They synthesised a total of 36 analogous and assayed for PGE2 reduction activity, the compounds with potent cellular activity were taken further for their counter screened for inhibitory activity against COX-2 in a cell free assay techniques. The results revealed that in general, analogs bearing a 4-phenoxyphenyl substituent in the R2 position were highly active in cells while maintaining negligible COX-2 inhibition. Specifically, compound 104l (R^1 = Me, R^2 = 4-OPh-Ph, R^3 = CH(OH)Me) exhibited the most potent cellular PGE2 reducing activity of the entire series (EC50 = 90nM) with an IC50 value for COX-2 inhibition of >5 μM in vitro.

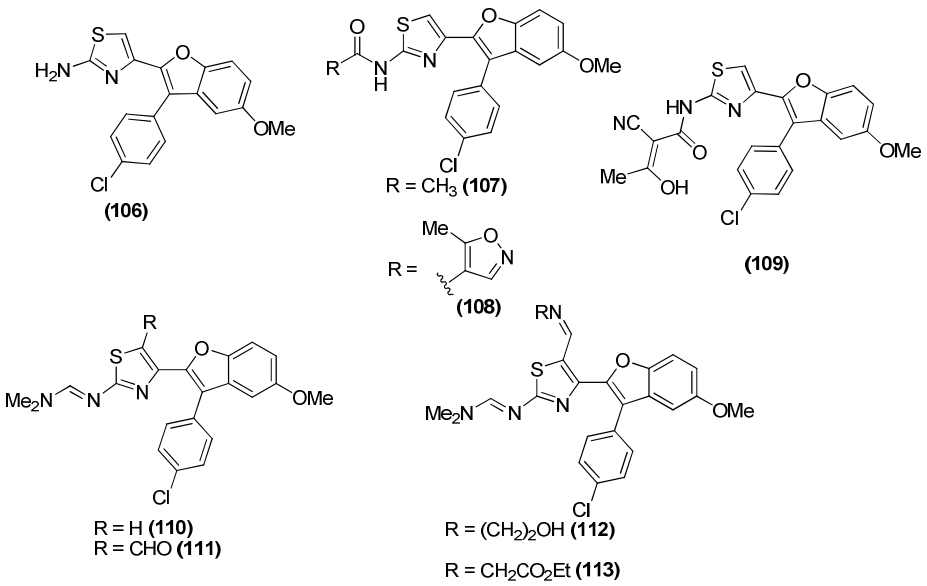


(104a-l)

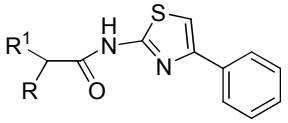


(105a-b)

A series of 3-(4-chlorophenyl)-2-(2-aminothiazol-4-yl)benzo- [b]furan derivatives (**106-113**) were prepared and their leukotriene B4 inhibitory activity was evaluated by Yoshitaka Ohishi et.al.[63] The results revealed that several compounds showed strong inhibition of calcium mobilization in CHO cells over expressing human BLT1 and BLT2 receptors. Among all the compounds 3-(4-chlorophenyl)-2- [5-formyl-2 [(dimethylamino)methyleneamino]thiazol-4-yl]- 5-methoxybenzo[b]furan (**111**) is found to be the most potent and selective inhibitor for the human BLT2 receptor, and its IC50 value was smaller than that of the selected positive control compound, ZK-158252. The compounds **111**, **112**, & **113** were found to potent and selective leukotriene B4 inhibitors. It is noteworthy to note that these compounds inhibitory potencies towards BLT2 were 6.2-3.4 times higher than that of ZK-158252.

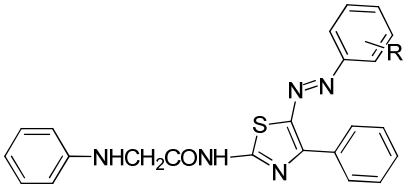


A series of substituted thiazole containing N-methylated amino acids and peptides (**114-118**) were synthesised by solution phase technique and were subjected to evaluation of anthlmintic and insecticidal activity by Himaja et al.[64] The anthelmintic activity results shows that the compound **115** is found to be most potent with compare to standard drug mebendazole (compounds shows paralysing time 50 min with compare to 55 min of mebebndazole).



(114-118)

Malik et al. have reported the synthesis of Azo disperse dyes (**119a-m**) by diazotized aryl amines coupled with N-(phenyl)-2-[(4-phenyl-1,3-thiazol-2-yl)amino] acetamide.[65] The newly synthesised dyes were evaluated for their polyester fabric and their fastness properties by HTHP method. All the dyes gave moderate to excellent fastness properties on polyester fiber. Furthermore, these new dyes compounds (**119a-m**) were tested for their antimicrobial activity at various concentrations using well-known Kirby-Bauer disk diffusion method. All the compounds showed moderate to good antimicrobial activity as compared to standard drugs against *E. coli*, *P. aeruginosa*, *S. Aureues* and *C. Albicans*.



(119a-m)

Conclusion:

The present review article reflects that 2-amino-4-phenylthaizole is a nucleus that can be used potentially in drug discovery area and medicines as it has versatile biological activities. Moreover, existing literature reveal that 2-amino-4-phenylthaizole derivatives can act as alternate medicine to overcome problems pertaining to cancer, TB, infectious diseases etc. Therefore 2-amino-4-phenylthaizole has a great scope for the discovery of new, better safer and more potent chemotherapeutic agents.

Acknowledgements:
All the authors are thankful to the Department of Pharmaceuticals, Ministry of Chemicals and Fertilizers, Govt. of India, New Delhi for the financial support.

REFERENCES

1. J. N. Reshma, *Der Pharmacia Lett.* 6 (5), 134-150 (2014).
2. A. Z. Amrita, *Des Pharma Chemica.* 3(1), 523-537 (2011) and references cited in that.
3. A. Hantzsch, J. H. Weber, *Ber. Dtsch. Chem. Ges.* 20 (2): 3118-3132 (1887).
4. Z. Yan-Ping, J. J. Yaun, Q. Zhao, M. Lian, Q. H. Gao, M. C. Liy, Y. Yang, A. X. Wu, *Tetrahedron.* 68 (1), 173-178 (2012).
5. J. S. Yadav, B. V. Subba Reddy, Y. Gopala Rao, A. V. Narsaiah, *Tetrahedron Lett.* 49 (15), 2381-2383 (2008).
6. J. Zhao, J. Xu, J. Chen, M. He, X. Wang, *Tetrahedron.* 71(4), 539-543 (2015).
7. W. J. Xue, K. L. Zheng, H. Z. Li, F. F. Gao, A. X. Wu, *Tetrahedron Lett.* 55(30), 4212-4215 (2014).
8. S. M. Ghodse, N. T. Vikas, *Tetrahedron Lett.* 56 (2), 472-474 (2015).
9. T. M. Potewar, A. I. Sachin, V. S. Kumar, *Tetrahedron.* 64 (22), 5019-5022 (2008).
10. V. Deepti, M. A. Kumari, N. Harikrishna, G. Ramesh, C. Venkata Rao, *Der Pharma Chemica.* 5 (2), 181-184 (2013).
11. P. Y. Lin, R. S. Hou, H. M. Wang, I. J. Kang, L. C. Chen, *J. of Chin. Chem. Soc.* 56 (3), 455-458 (2009).
12. G. W. Kabalka, R. M. Arjun, *Tetrahedron Lett.* 47 (29), 5171-5172 (2006).
13. T. Aoyama, S. Murata, T. Takido, M. Kodomari, *Tetrahedron.* 63 (48), 11933-11937 (2007).
14. S. J. Kishor, B. B. Jitender, K. K. Muthu, K. R. Vikas, S. W. Gaajanan, A. L. Nitin, N. D. Satish, *Green and Sustainable Chemistry,* 1 (2), 36-40 (2011).
15. C. David, M. C. Ruben, A. R. Jorge, J. M. Gonza, *Tetrahedron Lett.* 53(30), 3934-3936 (2012).
16. X. Zhongliang, B. Mingyu, Z. Hua, C. Yingli, T. Chaojun, Y. Ying, H. Ricai, L. Yu, Z. Xuemei, L. Zhenzhong, Z. Lihong, G. Ying, G. Changbin, *Eur. J. of Med. Chem.* 85, 27-42 (2014).
17. M. Mattia, N. Alessandro, C. D. L. Maria, H. Nicolas, B. Christian, D. Francois, S. C. Sarah, C. Marjorie, S. D. Patricia, D. Ursula, T. Carine, M. Yves, B. Maurizio, *ACS Chemical Biology.* 9(9), 1950-1955 (2014).
18. S. A. Abdel-Aziz, I. A. S. Ola, G. B. Adel, M. S. Ibrahim, *J. Chem. Pharm. Res.* 6 (10), 172-183 (2014).
19. R. P. Shashikant, R. L. Hullolikar, S. D. Nachiket, B. N. Ingalagi, M. B. Hole, V. M. Gaware, P. A. Chavan, *J. Pharm. Sci. & Res.* 1 (4), 96-102 (2009).
20. P. Zulan, S. James, L. John, J. Hua, Q. W. Laura Priice, C. Ming, Z. Joanna, R. Robert, S. H. Christine, R. W. Ruth, Y. S. L. Patrick, *Bio-Org. & Med. Chem. Lett.* 23(14), 4206-4209 (2013).
21. S. Annadurai, R. Martinez, D. J. Canney, T. Eidem, P. M. Dunman, M. Abou Gharbia, *Bio-Org. & Med. Chem. Lett.* 22 (24), 7719-7725 (2012).
22. F. J. Vagadia, D. A. Bhuva, M. A. Jiladia, *Pharma Science Monitor.* 3(4), 2633-2642(2012).

23. G. Saravanan, V. Alagarsamy, C. R. Prakash, S. T. Paneer, V. Kartick, K. P. Dinesh, *RASĀYAN J. Chem.* 2 (3), 746-752 (2009).
24. G. Saravanan, V. Alagarsamy, T. G. V. Pavitra, K. G. Chanukya, Y. Savithri, I. Naresh, P. Avinash, *Intern. J. Pharm. and Bio-Sci*. 1 (3), 1-8 (2010).
25. P. J. Shah, *J. Korean. Chem. Soc.* 58 (1), 57-61 (2014).
26. P. Arora, N. Rakesh, B. Sonam, K. N. Surendra, K. S. Sachin, N. Balasubramanian, *J. Appl. Pharm. Sci.* 5 (2), 028-042 (2015).
27. T. M. Patel, A. M. Patel, *Orient. J. Chem.* 28 (1), 471 (2011).
28. R. Dilpsinh, S. Amish, *J. Saud. Chem. Soc*. 19 (1), 73-82 (2015).
29. G. M. Ajay, R. L. Kushal, M. K. Gaidhane, *Int. J. Pharm. Pharm. Sci*. 6 (2), 142-146 (2014).
30. S. R. Kelode, *Int. J. Chem. Pharm. Sci*., 1 (6), 403-405 (2013).
31. D. Satyajit, G. Mariappan, R. K. Asada, N. R. Bhuyan, J. P. Mohanty, *Pharma Chemica.* 3(1), 507-512 (2011).
32. A. K. Prajapati, P. M. Vishal, *J. Chil. Chem. Soc.* 55 (2), 240-243 (2010).
33. S. R. Pattan, N. S. Dinghe, A. N. Nirmal, A. N. Merekar, R. B. Laware, H. V. Shinde, D. S. Musmade, *Asian. J. Res. Chem.* 2(2), 196-201 (2009).
34. N. D. Amnerkar, B. A. Bhoomendra, B. P. Kishore, *Arab. J. Chem.* 8(4), 545-552 (2015).
35. A. K. K. Prajapati, P. K. M. *Química Nova*. 34 (5), 771-774 (2011).
36. K. C. Prakasha, G. M. Raghvendra, R. Harisha, D. C. Gowda, *Int. J. Pharm. Pharm. Sci.* 3 (3), 120-125 (2011).
37. M. H. Bhuiya, A. F. M. H. Rahman, *J. Sc. Res.* 3 (1), 111-119 (2010).
38. T. M. Patel, A. M. Patel, *Orient. J. Chem.* 28 (1), 471 (2011).
39. L. Hui-Ling, L. Zongcheng, T. Anthonsen, *Molecules*. 5, 1055-1061 (2000).
40. M. Dinkar, Y. Punam, K. Sandeep, *IJPAS*. 2 (2), 8-14 (2015).
41. M. Pieroni, B. Wan, S. Cho, S. G. Franzblau, G. Costantino, *Eur. J. Med. Chem*. 72, 26-34 (2014).
42. F. Mjambili, N. Mathew, N. Krupa, D. K. Carmen, J. S. Peter, M. Valerie, W. Digby, C. Kelly, *Bio-org. Med. Chem. Lett.* 24 (2), 560-564 (2014).
43. P. Makam, K. Tharanikkarasu, *Eur. J. of Med. Chem.* 87, 643-656 (2014).
44. A. Meissner, I. B. Helena, V. Mahalakshmi, P. D. Benjamin, E. B. Clifton, C. A. Courtney *Bio-Org. Med. Chem.* 21 (21), 6385-6397 (2013).
45. Q. Al-Balas, N. G. Anthony, B. Al-Jaidi, A. Alnimr, G. Abbott, A. K. Brown, R. C. Taylor, G. S. Besra, T. D. McHugh, S. H. Gillespie, B. F. Johnston, S. P. Mackay, G. D. Coxon, *PLoS One.* 4 (5), e5617 (2009).
46. A. Jemal, F. Bray, M. M. Center, J. Ferley, E. Ward, D. Forman, *CA Cancer J. Clin*. 61 (2), 69-90 (2011).
47. L. Minghua, S. Yoojin, W. H. Seung, *Bull. Korean Chem. Soc*. 31(6), 1463-1464 (2010).
48. A. R. Ahmed, E. R. El-Bendary, M. A. Ghaly, I. A. Shehata, *Eur. J Med. Chem.* 75, 492-500 (2014).
49. Z. Shilong, Q. Zhong, Q. Jiang, M. Mottamal, Q. Zhang, N. Zhu, M. E. Burow, R. A. Worthylake, G. Wang, *ACS Med. Chem. Lett.* 4(2), 191-196 (2013).
50. V. Dominik, J. Weber, K. Ihlefeld, A. Bruggerhoff, E. Proschak, H. Stark, *Bio-Org. & Med. Chem.* 22 (19), 5354-5367 (2014).
51. O. Yusuke, T. Yabuuchi, Y. Fujii, H. Ohtake, S. Wakahara, K. Matsumoto, M. Endo, Y. Tamura, Y. Sekiguchi, *Bio-Org. & Med. Chem. Lett.* 22, (24), 7534-7538 (2012).
52. S. V. Rajmane, V. P. Ubale, *Int. J. Pharm. Sci. Inven*. 2 (11), 7-13 (2013).

53. S. Leone, C. Mutti, A. Kazantsev, M. Stulese, S. Moro, E. Cattaneo, D. Rigamonti, A. Contini, *Bio-Org. Med. Chem.* 16(10), 5695-5703 (2008).
54. Z. Liu, X. Chen, L. Yu, X. Zhen, A. Zhang, *Bio-Org. Med. Chem.* 16(14), 6675-6681(2008).
55. Z. Li, B. M. Silber, S. Rao, J. R. Gever, C. Bryant, A. Gallardo-Godoy, E. Dolghih, K. Widjaja, M. Elepano, M. P. Jacobson, S. B. Prusiner, A. R. Renslo, *Chem. Med. Chem*. 8 (5), 847-57 (2013).
56. W. T. Zhang, J. L. Ruan, P. F. Wu, F. C. Jiang, L. N. Zhang, W. Fang, X. L. Chen, Y. Wang, B. S. Cao, G. Y. Chen, Y. J. Zhu, J. Gu, J. G. Chen, *J. Med Chem*. 52 (3), 718-725 (2009).
57. L. Thomas, F. Alexander, J. Synese, D. Pascale, J. Helmut, O. Laurence, B. Karlheinz, *Bio-Org. & Med. Chem. Lett*. 21 (21), 6554-6558 (2011).
58. G. S. Anette, K. M. Gitte, L. Mogens, T. Lars, T. B. Lise, J. S. Tenna, B. A. Benny, *Bio-Org. & Med. Chem. Lett.*20 (17), 5241-5244 (2010).
59. W. Xuemei, X. Feng, X. Qingge, M. Hossen, H. Jonathan, Z. Liusheng, A. Michelle, T. George, T. Liang, E. M. Brian, J. D. Daniel, J. S. Thomas, L. C. Tassie, C. M. Julio, *Bio-Org. & Med. Chem. Lett*. 16 (10), 2800-2803 (2006).
60. T. Hanke, F. Dehm, S. Liening, S. D. Popella, J. Maczewsky, M. Pillong, J. Kunze, C. Weinigel, D. Barz, A. Kaiser, M. Wurglics, M. Lammerhofer, G. Schneider, L. Sautebin, M. Schubert-Zsilavecz, O. Werz, *J. Med. Chem*. 56 (22), 9031-9044 (2013).
61. T. Hanke, C. Lamers, R. C. Gomez, G. Schneider, O. Werz, M. Schubert-Zsilavecz, *Bio-org. Med. Chem. Lett*. 24 (16), 3757-3763(2014).
62. B. Smith, H. H. Chang, F. Medda, V. Gokhale, J. Dietrich, A. Davis, E. J. Meuillet, C. Hulme, *Bio-org. Med. Chem. Lett*. 22 (10), 3567-3570 (2012).
63. S. Yoko, K. Mari, A. Kumiko, Y. Mami, K. Ikuo, K. Jun-ichi, Y. Takehiko, O. Yoshitaka, *Org. Biomol. Chem.* 5 (19), 3083-3086 (2007).
64. M. Himaja, G. Nitesh, D. Munirajasekhar, K. Asif, S. S. Mukesh, *JPSI*. 1 (2), 33-36 (2012).
65. S. K. Zadafiya, G. M. Malik, *Fibers and Polymers,* 14 (6), 904-908(2013).

Received on August 21, 2017.