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A Review on some Thiazole Containing Heterocyclic Compounds and their Biological Activity

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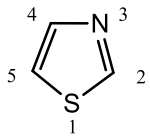
ABSTRACT

Heterocyclic compounds are very important due to their versatile industrial application. there are number of heterocyclic compounds use as medicine in different therapeutic targets. Thiazole is one of the important pharmacophore in drug discovery and development process. there are number of medicine and biologically active molecules those are thiazole substituted heterocyclic compounds covering wide range of therapeutics targets including Anti-Microbial, Anti- cancer, Anti-Imflametry , anti-HIV etc. These reviews collectively get idea about thiazole containing medicines and biological active compounds in recent medicinal chemistry research.
Keywords: Thiazole, Heterocyclic, Biological Activity.

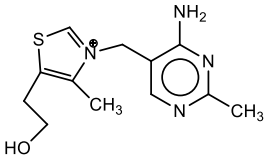
I. INTRODUCTION

Thiazole is five member organic heterocyclic compound containing N and S hetero atom's. thiazole is aromatic as delocalization of alone pair electron of Sulfur atom completing 6π electron to satisfy Huckel rule.

A Thiazole is found naturally in vitamin B1 (Thiamin), **Thiamin** is water soluble vitamin that helps the body to release energy from Carbohydrates during metabolism. and it's enzyme play vital role in decaboxylation of alfa keto acid and as an electron sink respectively. it also helps in the normal functioning of the Nervous system by its role in the synthesis of the acetylcholine a neurotransmitter.



Thiazole



Thiamin

There are number of medicine covering various therapeutic targets are thiazole substituted heterocyclic compounds. like antibiotic Cefidinir the third generation of cephalosporin and antibiotic Abafugin, HIV -1 protease inhibitor Ritonavir, drug use for efficient treatment of hyperuricemia in gout is Febaxostat, dehydrogenase anticancer drug Thiazofurin , anti-depressant drug Pramiperoxale, antineoplastic agent Bleomycin, antiasthamatic drug Cinalukast, antiulcer agent Nizatidine, non-steroidal immunomodulatory drug Fanetizole, antiimflamatory drug Meloxicin, etc.

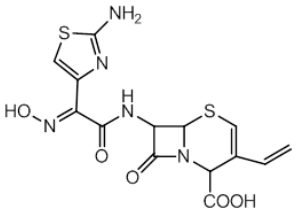
In resent research updates find out that thiazole containing heterocylic compounds are potent Bacterial DNA Gyrase inhibitors, Flavivirus envelope protin inhibitors, anticancer CDK9 inhibitors, p38-MAP, Pan-Src, Spleen-Thyrosin kinase inhibitors. along with that there are number of biologically active thiazole containing heterocyclic compounds show extensive application in medicinal chemistry research as antimicrobial, anti-inflamatory, antiviral, anti-HIV, anticancer, antitumour, antidiabetic, anti-convulscant,anti-depressant [1-28] etc.

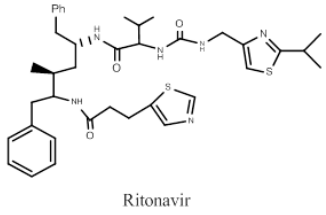
II. THIAZOLE CONTAINING BIOLOGICALLY ACTIVE HETEROCYCLIC COMPOUNDS.

A. Thiazole containing drugs

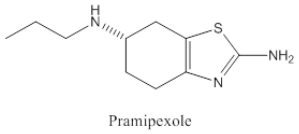
Cefidinir the semi- synthetic third generation cephalosporin, containing amino thiazole with ester and acid moiety it's an orally administrated antibiotic show antibacterial activity against both germ positive and germ negative bacteria. It shows excellent activity against Staphylococcus species.

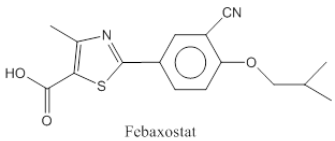
The HIV-1 protease inhibitor **Ritonavir** containing two different substituted Thiazole ring, which achive good bioavailability and long plasma half life in addition, H-bonding of 5-substituted thiazole to back bone of Asp-30 as compare to initially design pyridine ring. It's an earlear candidate for the treatment of AIDS.

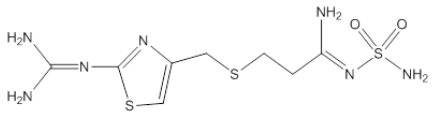

Cefidinir


Ritonavir

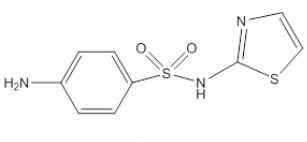
The Dopamine D_2-agoinst **Pramipexole** consist of fused bicyclic tetrahydrobenzothiazole with protected form of 4-amino cyclohexane. Pramiperoxle effectively use as antidepressant agent. **Famotidine** Is an H_2 - receptor antagonist which inhibit isoenzyme of hepatic CYP 450 system and has the additional side effect of increasing the amount of gastric bacteria such as nitrate reduing bacteria. It effectively use in ulcer treatment. It contains Thiazole substituted guanidine and sulfonyl amide. **Febaxostat** The Thiazole containing drug is given in the novel xanthine oxidase in non competitive fashion. Consequently , the amount of the oxidation produce uric acid is reduced. Thus it is an efficient treatment for hyperuricemia in gout.

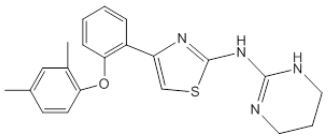

Pramipexole

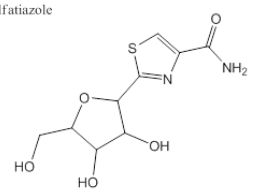

Febaxostat


Famotidine

Sulfatiazole The Thiazole containing sulphonamide effective antimicrobial agent. the drug **Abafugin** amino-thiazole substituted heterocyclic compound use as antibiotic. and **Thiazofurin** Thiazole containing inhibitor of IMP dehydrogenase anticancer drug.


Sulfatiazole

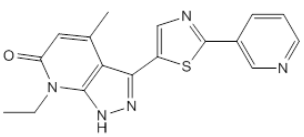

Abafugin


Thiazofurin

B. Thiazole containing biological active molecules in recent drug discovery and development process

a. Antimicrobial activity.

Bacterial DNA gyrase is highly valuable target for antibacterial research, there are number of new biologically active molecules targating over Gyrase-B, DNA gyrase exist as A_2B_2 tetramer that binds dsDNA and catalyzes strand reformation that introducted in negative supercoils. Chemotypes bind to other regions of the protin complex make advantage of avoiding on-target fluroqunolone resistance, inhibition of ATPase activity of GyrB with bacterial DNA replication, resulting potential antibacterial activity. In resent update there are number of researcher find potential DNA Gyrase B inhibitors like- discovery of thiazole substituted pyrazolopyridones [**1]** show potential Gram-positive antibacterial activity and low resistance incidence against clinically important pathogens. thiazole substituted pyrazole esters **[2]** and benzthiazole substituted amid also show potential activity with DNA Gyrase-B.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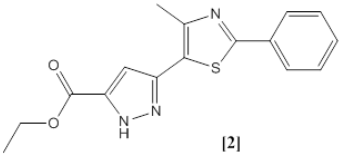
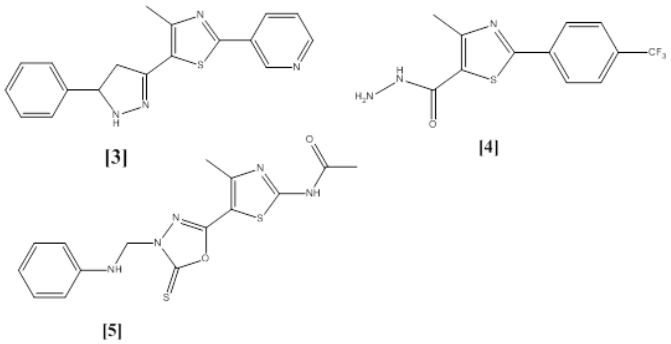
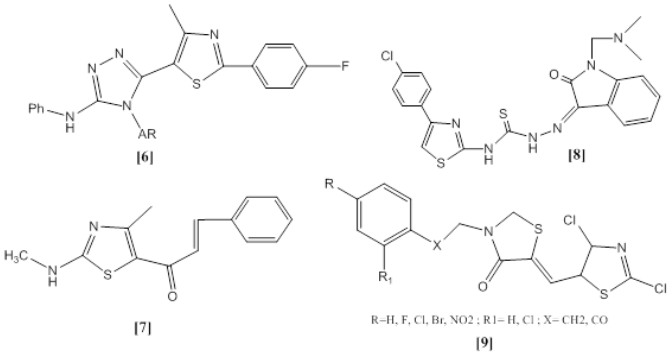

[2]

Synthesis of some new 2-(3-pyridil)-5 pyrazole substituted thiazole **[3]** act as potential antimicrobial agent. new hydrazones bearing thiazole scaffold **[4]** show efficient antimicrobial and antioxidant activity. novel thiazole clubbed 1,3,4-oxadizole with different aromatic substitution like 2F,3F-Ph **[5]** show potential antimicrobial and cytotoxic activity.

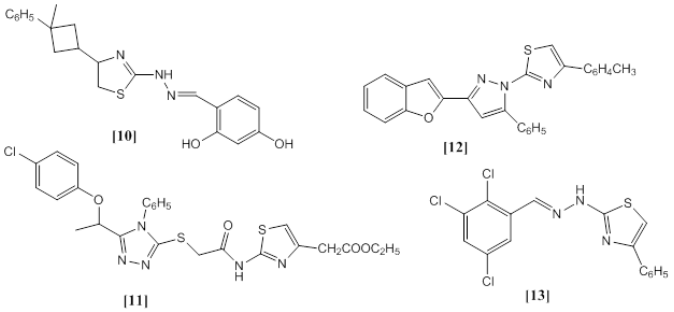


Alog with it number of researcher find various substitution on thiazole show potential antimicrobial activity. like-. Karale et al [6] present new series of Thiazolyl Triazoles analoges and their anti microbial activity. K Liarus et al **[7]** present Thiazole base chalcones as potent anti microbial agents. Pandeya et al **[8]** prepared a series of Schiff and Mannich bases derived from isatin derivatives find out potential antimicrobial activity.



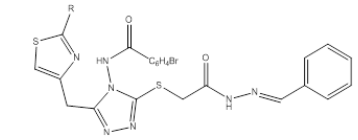
Dundar et al **[9]** presented a set of thiazolyl thiazolidine-2,4-dione derivatives and screened for them for their antibacterial and antifungal activities against methicillin resistant S.aureus, Ecoli and C albicans. All thecompound were found to be modereately potent against screened micro organism.

Cukurovali et al **[10]** reported a synthesis of thiazole substituted series of Schiff bases containing 2, 4 – disubstituted thiazole and cyclobutane rings and hydrazones and evaluated them for antibacterial and antifungal activities. the most effective compound providing a MIC value of 16 μ ml^{-1} was found to be against C..tropicallis and B .subtilis bacterial spaces. Zitouni et al **[11]** reported new thiazole derivatives of triazole and evaluated for antifugal and anti bacterial activity. Their antimicrobial activities Candida albicans,C.glabrata,E. coli,S. aureus,P. aeruginosa were investigated. Abdel – Wahab et al **[12]** synthesized various thiazole containing compounds which show good to modrate antibacterial and antifungal activities. Karegoudar et al **[13]** synthesized a series of novel Thiazole compound. The newly synthesized compounds were screened for their antibacterial and antifungal activities. Shiradkar et al **[14]** reported a series of thiazole substituted amide derivatives were tested for anti bacterial activity



Xin et al **[15]** reported novel oxazolidinone thiazole analogues containing substituted thiazole all the compound were find antibacterial activities. Vicini et al **[16]** reported novel thiazolidinones and assayed in vitro for their antimicrobial activity against Gram positive and Gram negative bacteria, they find potent agent against Gram positive bacteria. Narayana et al **[17]** prepared a series of 5-{2-[(N-substituted aryl) amino]-1, 3-thiazol-5-yl} 2-hydroxy benzamides The newly synthesized compounds were screened for their antifungal activity.

Chimenti et al **[18]** 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 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. Vicini et al **[19]** reported novel thiazolidinones and assayed in vitro for their antimicrobial activity against Gram positive and Gram negative bacteria, yeast and mould. All the compounds exhibited potent against Gram positive bacteria



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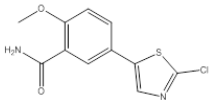

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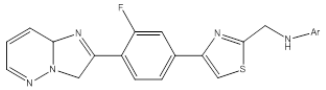

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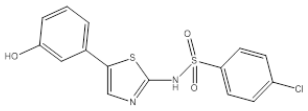

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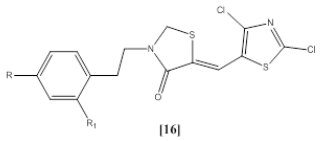

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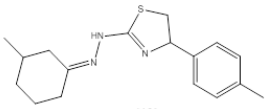
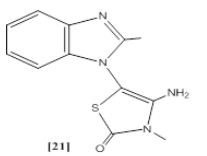


[19]

b. Anticancer activity

Synthesis of substituted 4-(thiazol-5-yl)-2-(phyenylamino)pyrimidines derivatives **[20]** with functional groupattached to the C5 positionof the pyrimidine and investigated there effects on CDK9 potency and selectivity, one of them inhibits CDK9 with IC_{50}= 7nM and shows 80 fold selectivity over CDK-2. Ramla et al **[21]** synthesized a variety of 1-substituted-2-methyl-5-nitrobenzimidazoles and evaluated them for anti-tumor activity. The anti-tumor effect of compound was found to be significant. Popsavin et al **[22]** 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 against K_{562} malignant cells, with IC_{50} ranging from 0.09-0.49 μM. Gulsory et al **[23]** presented a series of thiazole substituted arylidene hydrazides from [6-(4-bromophenyl) imidazol-3yl] acetic acid hydrazide. The synthesized compounds were evaluated one dose primary cytotoxicity assay. Compound demonstrated the most effective agents on a prostate cancer cell lines.



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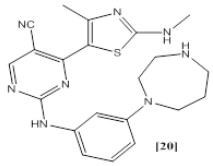

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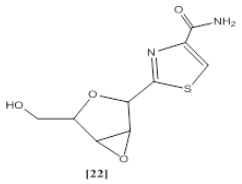

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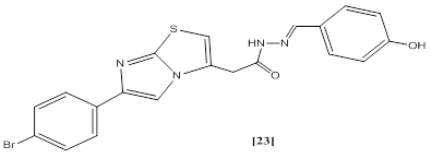
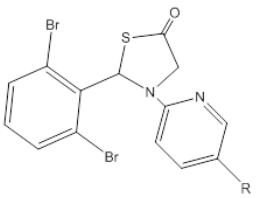


[23]

c. Anti-Viral activity

Synthesis of thiazol -2-(4-Clphenyl)-5-ethyl ester and relevant analogs **[24]** describe over shoe potential antiviral activity targating Flavivirus envelope protins. Many flaviviruses are arthropod-borne, human pathogen that can cause encrphalitis, hemorrhagic fever, shoch syndrome, and jaundice, example of pathogenic flaviviruses include dengue virus, yellow fever virus, west nile virus, tick-bone encephalitis virus, and Japanese encephalitis virus. Rawal et al **[25]** synthesized a series of 2-(2,6-dibromophenyl)-3-heteroaryl-1,3-thiazolidine-4-one and evaluated as selective human immunodeficiency virus type-1 reverse transcriptase (HIV-1, RT) enzyme inhibitors. In vitro cell assay showed that effectively inhibited HIV-1 compounds having isothiourea or thiourea functional group showed high anti-HIV-1 activity.



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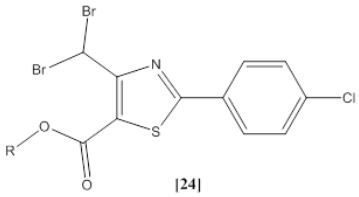

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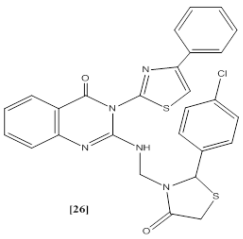
d. Anti-inflammatory activity

Kumar et al **[26]** synthesized a group of 3-[4'(p-chlorophenyl) thiazole-2'-yl]-2-[(substituted azetidinone/thiazolidinone)-aminomethyl]-6-bromoquinazolin-4-ones and screened them for anti-inflammatory and analgesic activities. They found that the presence of thiazolidinone ring have shown much better anti-inflammatory as well as analgesic activity. Holla et al **[27]** reported different series of arylaminothiazoles, and hydrazinothiazoles. screened them for their antibacterial and anti-inflammatory activities. Kalkhambkar et al [**28]** reported triheterocyclic thiazoles containing coumarin and carbostyril. The synthesized compounds were tested for their in vitro analgesic and anti-inflammtory activities.



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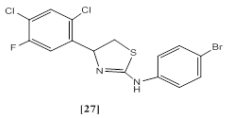

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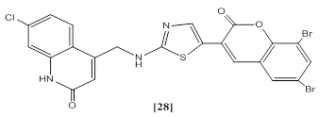

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