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Review Article

A Review on Recent Development and biological applications of benzothiazole derivatives

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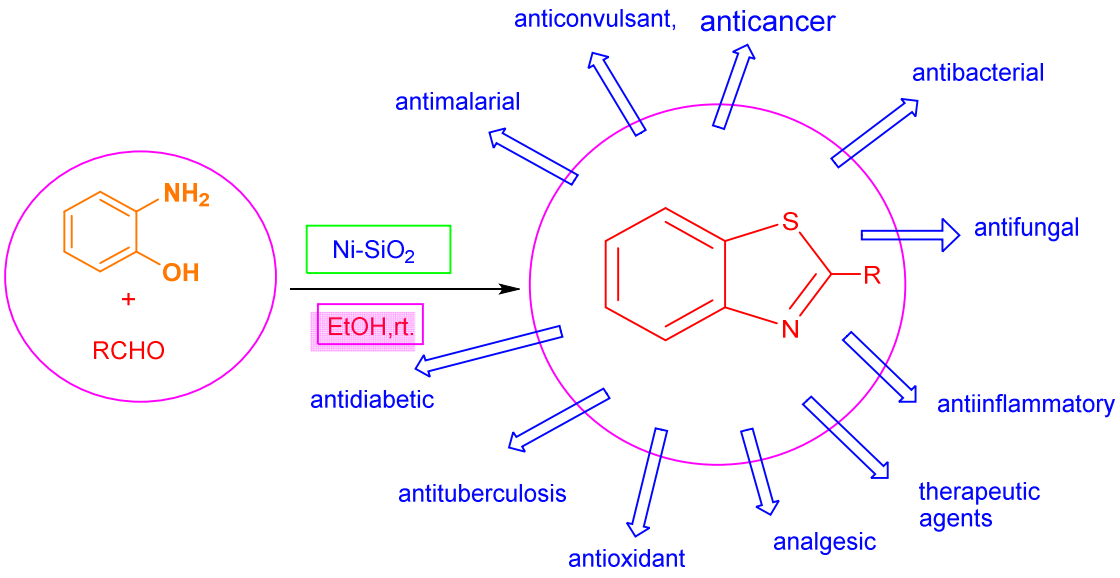
ABSTRACT

Benzothiazole (BTA) and its derivatives are among the most important heterocyclic compounds, widely found in natural commodities and pharmaceutical drugs. It possesses a large number of pharmacological properties, and many of its analogues have structural diversity, to contribute to the production of new medicinal drugs. BTA derivatives possess a broad spectrum of pharmacological activity. The development of medicinal chemistry containing BTA has been rapid and highly active. BTA chemicals are frequently used in medical care to address a wide variety of illnesses with good results. Current advancements in BTA-based compounds such as anticancer, antibacterial, antifungal, anti-inflammatory, analgesic, antioxidant, anticonvulsant, anti-tuberculosis, antidiabetic, antimalarial, and other therapeutic agents are the focus of this review. New ideas are spurring the development of BTA-containing drugs that are more active, less toxic, and more effective for diagnosing diseases.

GRAPHICAL ABSTRACT



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Introduction

Benzothiazoles are heterocyclic dicyclic compounds consisting of a benzene bonded to amembered ring containing nitrogen and sulfur atoms [1] It possesses a number of biological properties, such as anelgesic [2], antiinflammatory [3], antidiabetic [4] and anticancer [5]. Benzothiazoles are found in anumber of natural substances found in the sea and on land with beneficial biological properties. Benzothiazole is used to treat several diseases, such as neurological diseases, local cerebral ischemia, central muscle relaxants, and cancer [6]. It is easy to obtain the biological properties as a drug carrier for the development of new benzothiazoles. Benzothiazoles are used in many dyes, such as theoflavin [7]. (Figure 2) shows a number of commercially available benzothiazole-containing drugs [8-10], Some reviews have recently been published in the literature, finding synthetic and biological methods, synthesis techniques, and biological activities of benzothiazoles [11-14].

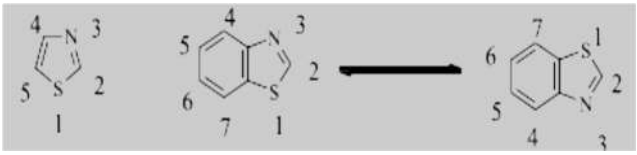


Fig.1. Benzothiazole Toutamerism

BTA is a flavor chemical generated by the fungi Aspergillus clavatus and Polyporus frondosus, and is found in tea leaves and cranberries. [15]. They are also used as appetite suppressants [16], dye intermediates [17], plant protectors [18], B-amyloid plaque imaging agents [19], and photographic inducers [20]. BTA derivatives are heterocyclic compounds used in several fields of chemistry, in polymer chemistry [21], dyes [22], pharmaceuticals [23], and in silver photography, BTA salts are used as sensitive dyes [24,25], Benzothiazole is afungicide.[26] Elastomeric unsaturated polymers of BTA derivatives arise from (lattice) sulfide bonds, and the resulting elastic material is crosslinked(MBT/BTSH) is arubber accelerator and is used in a number of specialty products, such as tire manufacturing [27].

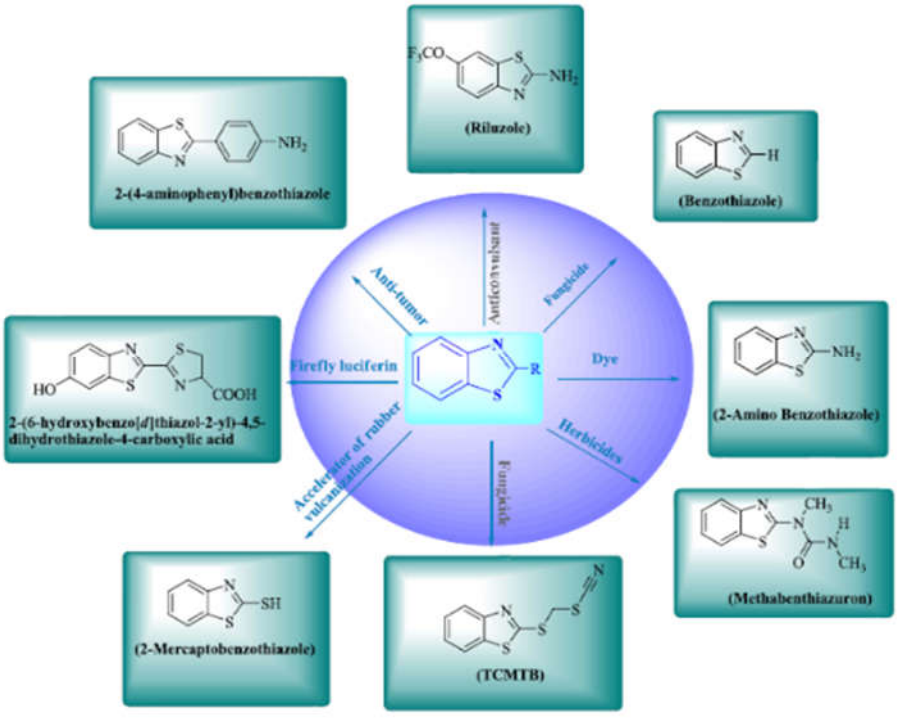
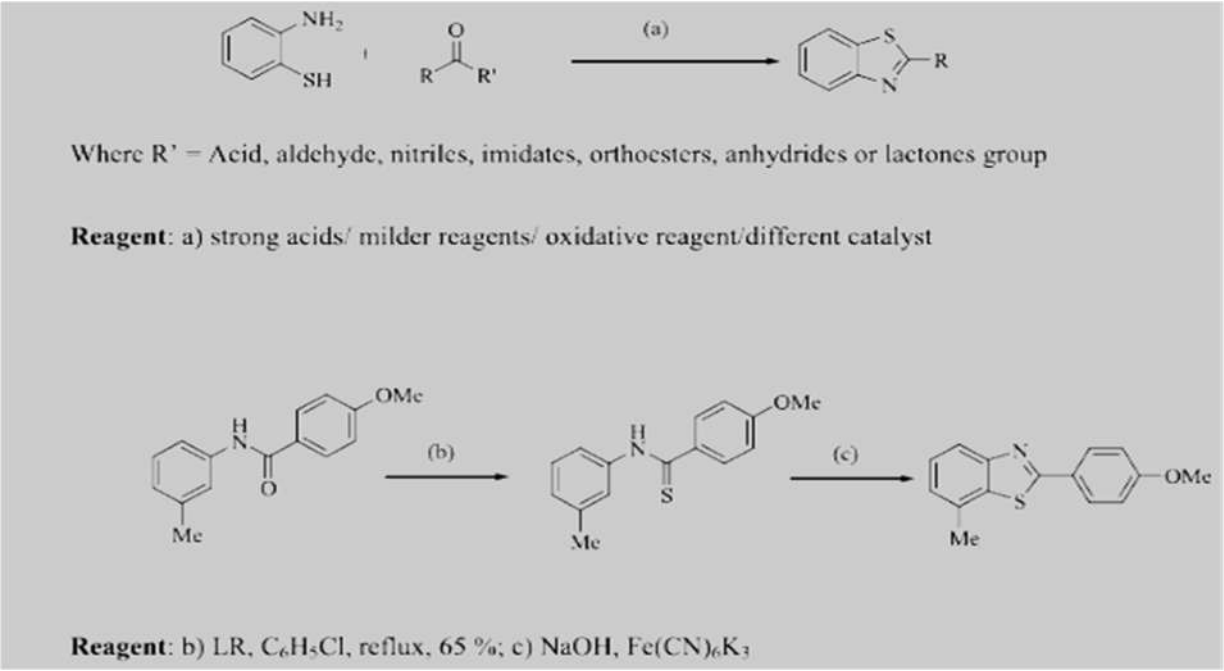


Fig. 2. Benzothiazole, a multifunctional nucleus.

Chemistry of benzothiazole

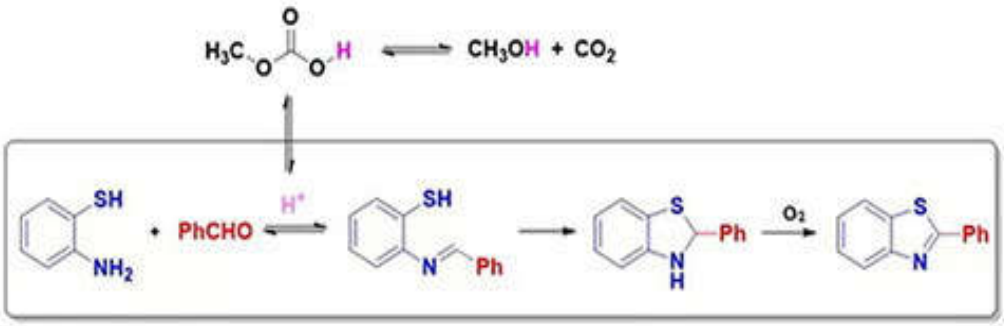
Hoffmann first created and published in 1887 a variety of synthetic methods due to the simple mechanics of the splitting [28]. 2-amino thiophenols condensation reaction with nitrles, aldihydes, carbaxylic acids, acylchlorides, oresters to prepared BTA [29]. On the other hand, it is equivalent to such as the rapid oxidation of 2-amino thiophenols with compensators,

Jacobson's prepared BTA from the ring closure of 2-amino thiophenols [30]. Other methods of preparing it from the reaction of 2-amino thiophenols with p-chlorocinnamaldehydes using a microwave, and BTA is used in several applications such as the formation of biologically active chemicals and more diverse activity Biology, great interest for the synthesis of BTA derivatives such as Grignard arylsothiocyanate methods [31]. Using several catalysts PCC [32],nanoceria (CeO2) [33], boron trifluoride ethers [34], silica-held copper (II) nanoparticles [35]. Scheme.1



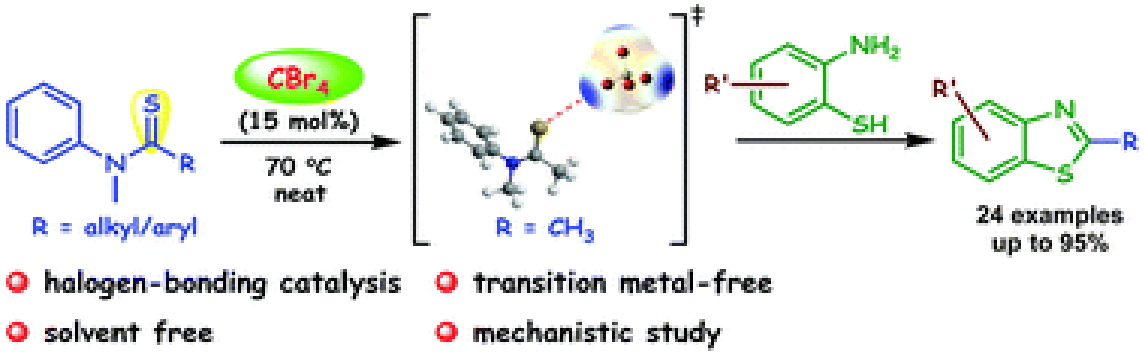
Scheme 1. General synthesis of benzothiazole.

Xiao Li et al., [36] Under minor circumstances, a variety of benzothiazole derivatives were produced via reaction and cyclization of 2-aminthiophenol with aliphatic, heteroaryl, and aryl aldehydes, which was aided by alkyl carbonic acid.



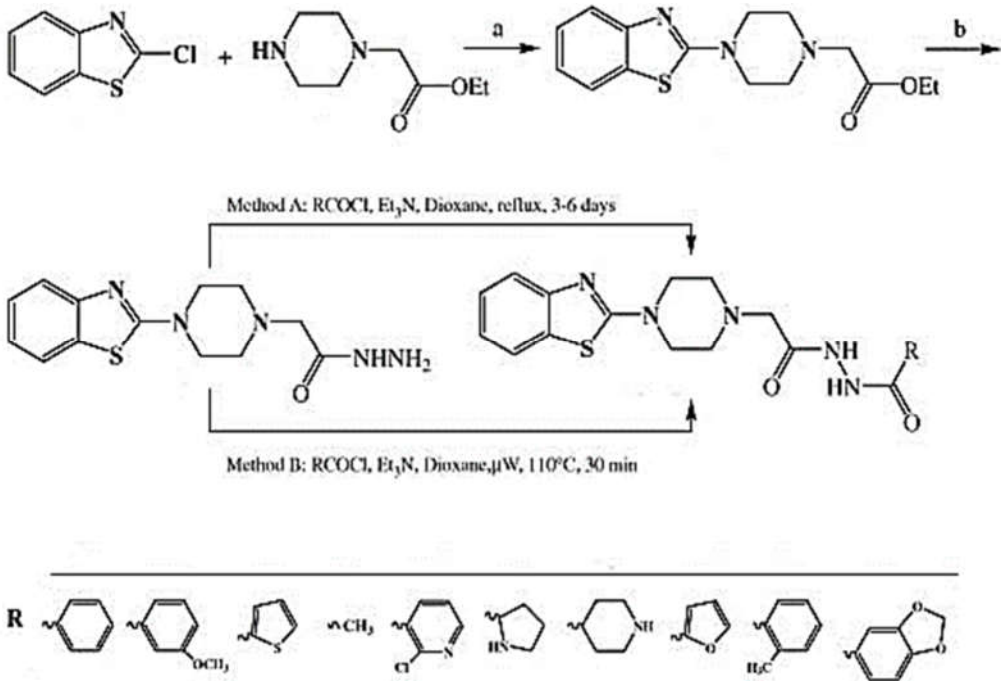
Scheme 2. Synthesis of benzothiazole derivatives

Imran Kazi and Govindasamy Sekar , [37] synthesis of 2-substituted benzothiazole from N-methyl thioamides and tetrabromomethane by CBr_4 as acatalyst, using solvent and metal conditions.



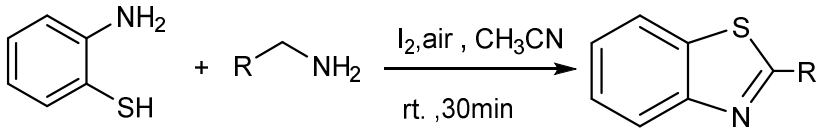
Scheme 3. synthesis of benzothiazole derivetives

MahmoudAl-Talib et al. [38] synthesized of new benzothiazol piperazinderivetives form ethyl 2-(4-(benzothiazol-2yl)piparezin-1-yl)acetate and hydrazinehydrate.



Scheme 4. synthesis of benzothiazole derivatives
(a) EtOH, $NaHCO_3$, ref., 24 h (b) $NH_2NH_2{\cdot}H_2O$, heat.

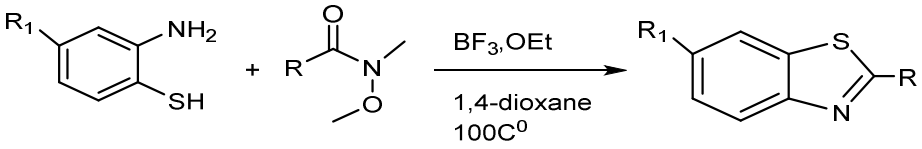
Narender et al, [39] synthesized of benzothiazole derivetives using iodine from amine and 2-mercaptoaniline at room temperature.



R= Ph, 4-OCH_3-Ph , 4-Cl-ph , 3,4-Cl-Ph , 4-F-ph, 4-CH_3-Ph,4-OCF_3-Ph

Scheme 5. synthesis of benzothiazole .

Sadashiva et al, [40] synthesized benzothiazoles via condnsation and cyclzation of amide with oaminothiophenol in $BF_3.OEt_2$ in 1,4-dioxane as
asolvent at 100°C, yielding 75–94% in 60 min.

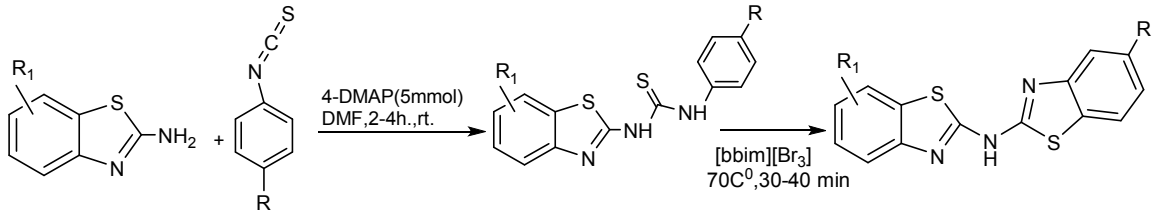


R= Alkyl,Alkenyl,Hetoroaryl

R1 = H,CH_3,Br

Scheme 6. Synthesis of benzothiazoles

Kumbhare et al, [41] Synthesized of benzothiazole by oxidative cyclzation of thiourea with [bbim][Br_3] ionic liquid under mild conditions from reacting 2-aminobenzothiazole and phenylisothiocyanate in 4-DMAP in DMF at 70°C.

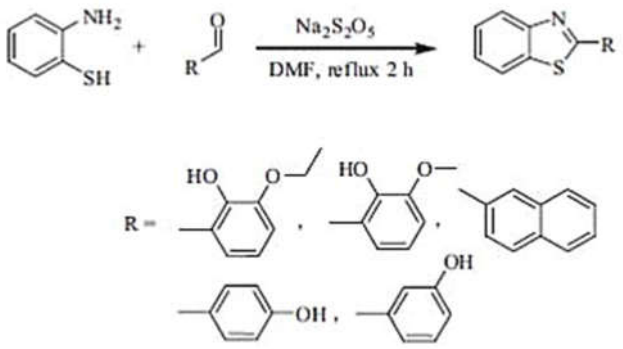


R1=H,6-F,6-OMe,4-Cl,

R= H,F,Cl

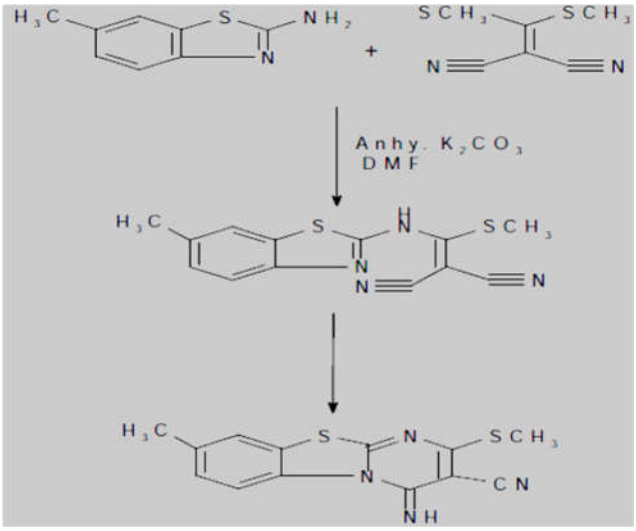
Scheme 7. Synthesis of benzthiazole derivetives

Khan et al, [42] synthezed of benzothiazole derivetives from 2-aminthiophenol with aromotic aldihydes in (DMF) and ($Na_2S_2O_5$) when there is a reflux 2 h., high yield.



Scheme 8. Synthesis of benzothiazoles

Pingle M. S., et al [43] synthesized of 3-cyan-4mino-2methylthio-8methyl4H-pyrimdo[2,1-b],[1,3] benzthiazole from 2-amino6-methylbenzthiazole and bis (methylthio)methylne malonitrile .



Scheme 9. Synthesis of benzothiazole

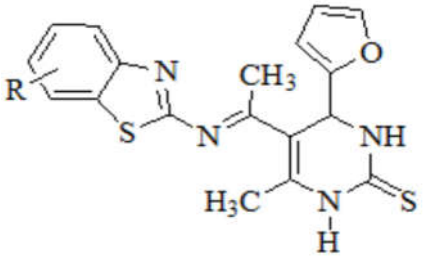
Pharmaclogical actions of BTA

BTA and its analogs are essential pharmacphores and well-known structtures in medicnal chemistry, appearing in a variety of clincally useful medicines.As a result, the current review provides a complete summary of current breakthroughs in BTA-based medicinal chemistry, as well as methods and SAR.

BTA as antimicrobial agents

Most of the treatments used as medicines are an antimicrbial agent to prevent the growth and reproduction of bacteria [44]. When used poorly, it leads to the Antibiotic-resistant diseases are becoming more common. [45] Antimicrbial therapy has advanced a lot, Infectious disorders produced by bacteria or fungus, on the other hand, pose a significant threat.

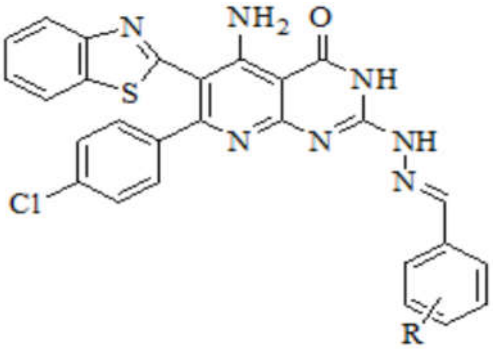
Waghamode KT et al. [46] produced benzothiazole derivatives and tested antibacterial activity against G+ and G- bacterial. The all compounds have excellent antibacterial activity



R=H,4-,5-,6- (NO_2),6-,4- (CH_3),6-OC_2H_5

Fig.3.Structure of benzothiazole derivatives

In 2016, Lavanya P et al [47] Antibacterial and antifungalactivity of benzthiazole pyrimdine derivetives toword Staph. aureus, E. coli, K.pneumoniae, and Strep.pyogenes were examined.



R=H,5 -NO_2,6-,4- $(CH_3)_2$,4-OCH_3

Fig.4: Structure of benzthiazole pyrimdine derivetives

M. Singh et al, [48] identified series of compounds benzthiazolthiazolidin , hich has the most active antimicrobial action versus E. coli and Candida albicans (MIC1 415.6–125 mg/mL)

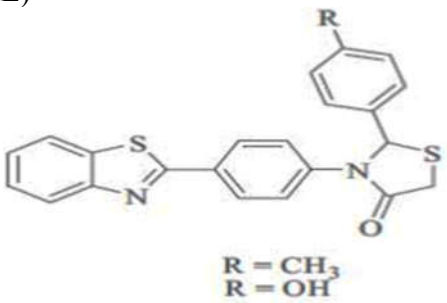


Fig.5: Structure of benzthiazolthiazolidin

Bele et al. [49] synthesized benzthiazole derivetives and S. aureus, S. pyrogens, E. coli, P. mirabilis and A. fumigetus microrgonisms were examined for antibactrial efficacy.

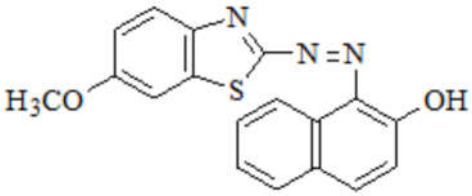
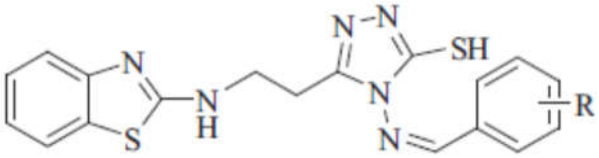


Fig.6: Structure of benzthiazole derivetives

Soni and co-workers [50] synthesized anumber 5-[2-(1,3benzthiazol-2-ylamino)ethyl]-4-(arylidenemino)-3-mercopt-(4H)-1,2,4triazoles, were investigated for antibacterial and antifungal activity



R=4-$N(CH_3)_2$,3,4-OCH_3

Fig.7: Structure of benzthiazole derivetives

H. Al-Tel et al, [51] reported imidaz[2,1-b][1,3]benzothiazoles ,show high inhibitory activity against bacterial and fungal compared with(amoxicilin) and antifungal (fluconzole).

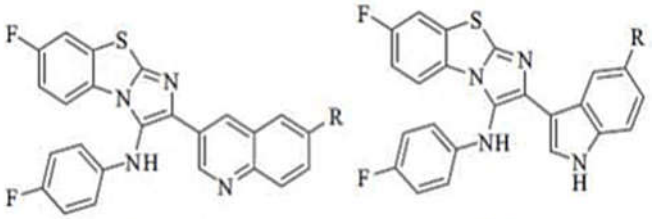


Fig.8: Structure of benzthiazole derivetives

P. K. Sahu et al. [52] identified 4-(4-hydroxyphenyl)-4Hpyrmido-[2,1-b]-[1,3] benzthiazole ,show antibacterial agent against (P. aerug., S. typhi, E. coli and P.rettgeri), campered with slandered ciprofloxacin

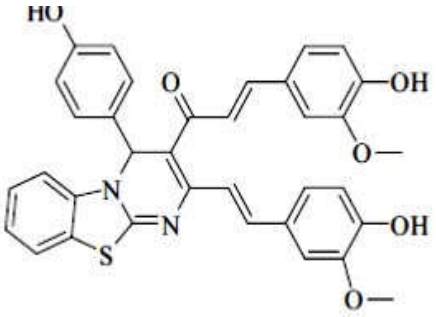
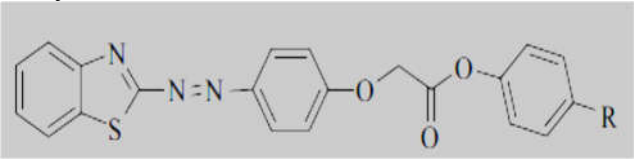


Fig.9: Structure of 4-(4-hydroxyphenyl)-4Hpyrmido-[2,1-b]-[1,3] benzthiazole

H. R. Tomi H.R.et al, [53], study of oxazole and benzothiazole heterocyclic compounds,

were detected benzothiazoles in antibacterial assays, most active than oxzole derivetives.



R=CN,OCH_3,NO_2

Fig.10: Structure of benzthiazole derivetives

BTA as antitubrcular agent

Tubrculosis(TB) is one of the deadly infectious diseases caused by infection Mycobacterium (tubrculosis , bavis and africonum), and it has a great effect on body tissues, such as the lungs, and antibacterial drugs are ineffective because they generate several metabolic directions and drugs leak through the cell wall. Telvekar et al. [62] synthesizednew2-(2(4arylxybenzyldene) hydrzinyl)benzthiazoles from2-hydraznylbenzo-thiazoleand4-(arylxy) benzldehyde, using amolecular hybrdization technique.

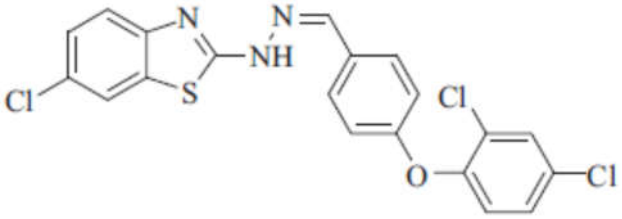
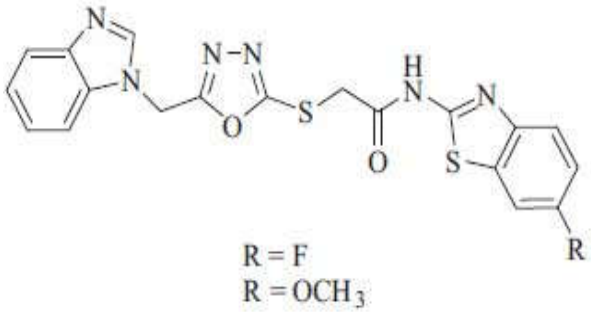


Fig.11: Structure of 2-(2-(4arylxybenzyldene) hydrzinyl)benzthiazole

Patel et al. [55] evaluated many derivatives of benzmidazolyl-1,3,4oxadizol-2-ylthio- N-phenyl-(benzothiazolyl)acetamides for anti-M.tuberculosis H37Rv activity .

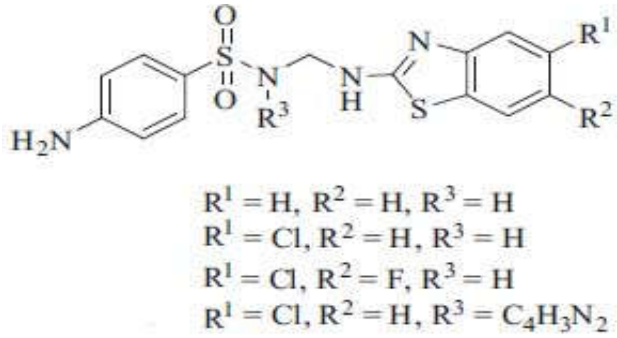


R = F

$R = OCH_3$

Fig.12: Structure of benzthiazole derivetives

N. Nayeemet al [56] synthesized chains of benzthiazole derivetives and the chemicals' potential to fight Mycobacterium



$R^1 = H, R^2 = H, R^3 = H$

$R^1 = Cl, R^2 = H, R^3 = H$

$R^1 = Cl, R^2 = F, R^3 = H$

$R^1 = Cl, R^2 = H, R^3 = C_4H_3N_2$

Fig.13: Structure of benzthiazole derivetives

BTA as Anticancer Activity

Cancer is a global health problem that kills millions of people and has great difficulties in medicine, to produce powerful new drugs against tumors from global research efforts.

Eman A.Abd El-Meguid etal. [57] synthesized of new 2-aryl benzthiazole from 4-oxothiazlidin-2-yldene as well as several aminoacids and ester derivetives.

In combination with doxrubicin, the compounds showed cytotxicity toword cancer cell lines (HepG-2 and MCF-7)

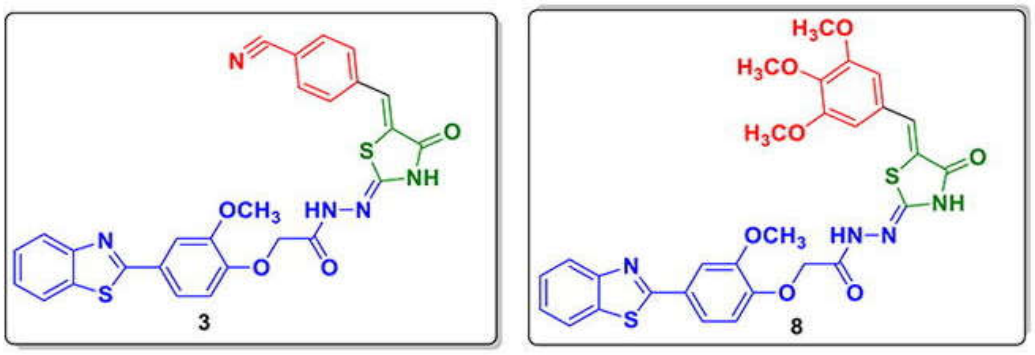


Fig.14: Structure of 2-aryl benzthiazole

Suvarna G Kini and colleagues [58] synthesized two aminobenzothiazoles and tested anticancer action.show N-(6chlor-1, 3benzthiazole-2-yl)-1-(2,5 dimethxyphenyl) methanmine has great action.

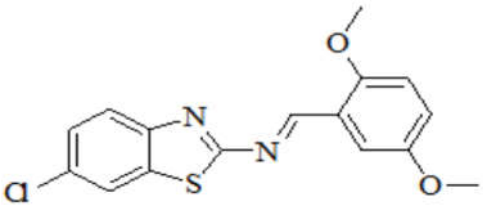


Fig.15: Structure of N-(6chlor-1, 3benzthiazole-2-yl)-1-(2,5 dimethxyphenyl) methanmine

Uremic N et al. [59] The chemicals have excellent anticancer activity and were produced benzthiazole derivatives and assessed anticancer activity versus pancreatic cancer cells.

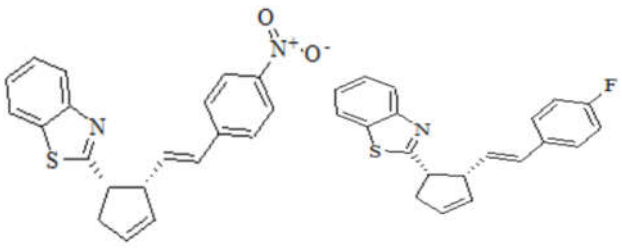


Fig.16: Structure of benzthiazole derivatives

Leal KZ et al [60] synthesized of 2-benzthiazole hydrzonesderivatives. Anticancer activity was also investigated.The anticancer activity of 2-((2-(benzthiazol-2-yl) hydrzono) methyl) benzen1,4-diol has been demonstrated.

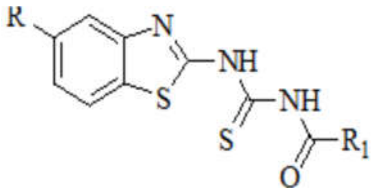
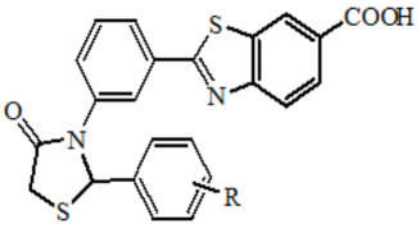


Fig.17: Structure of benzthiazole derivatives

Prabhu et al. [61] produced of thiazldinethi-azolecarbxylic acid derivatives from thioglyclic acid using benzothiazole Schifs bases, showed the more important activity.



R=P-Cl, P-CH_3,P-OH,P-OCH_3

Fig.18: Structure of thiazldinethiazolecarbxylic acid derivatives

Wang et al. [62] New benzothiazolethiol compounds were produced and their antiproliferative properties were tested in HepG2 and MCF-7 cells.

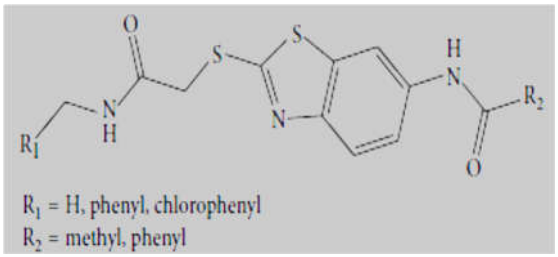


Fig.19: Structure of benzothiazolethiol

Kumbhare et al. [63] synthesized benzothiazolyl-thiocarbamides using acatalytic (DMAP) with [bbim][Br_3]. The cytotxic activity of compounds was tested amousemlnoma cell line and two humen moncytic cell lines (U 937, THP-1).

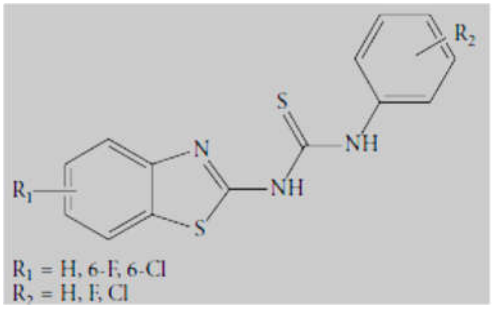


Fig.19: Structure of benzothiazolyl thiocarbamides

Saeed et al. [64] synthesized of benzothiazol derivatives from new 4-thiazolidinones with benzothiazole. Antimicrobial and anticancer activities are also tested.

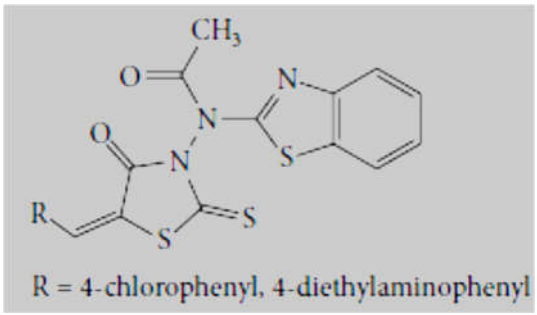


Fig.20: Structure of benzothiazol derivatives

Solomon et al. [65] Asequence of pyrrolbenzo-diazepine with benzthiazole and examined the antibreast cancer effect cell lines, MDAMB231, MDA-MB468, and MCF7.

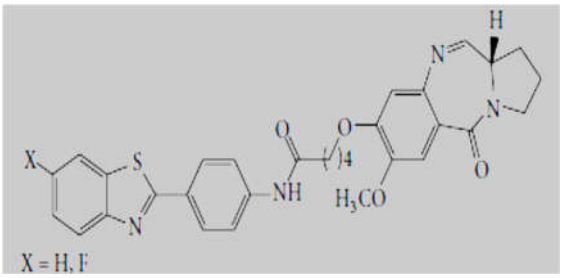


Fig.21: Structure of benzothiazol pyrrol benzodiazepine derivatives

Kamal et al. [66] created 2-(3-(4-oxo2-substtuted phenylthiazlidin- 3-yl)benz[d]thizole-6-carboxyl-icacid derivatives. Anticancer activity was studied in ahumen melanma cell line (A375).

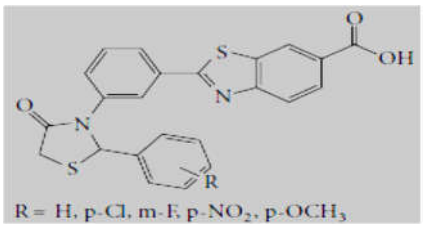


Fig.22: Structure of benzothiazol derivatives

Caputo et al. [67] synthsized of benzothiazole derivatives with anarylamide or an arylurea 60 human tumor cell lines were investigated. in apreliminary anticancer assay.

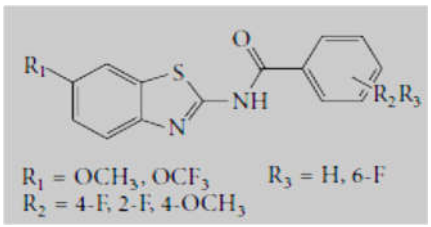


Fig.23: Structure of benzothiazol derivatives

Oanh et al. [68] produced benzothiazole containg analgues of SAHA andtarget Histone deacetylase (HDAC) enzymes of classes I and II.

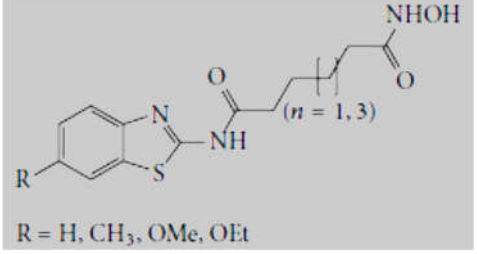


Fig.24: Structure of benzothiazol derivatives

BTA as Antimalarial drug benzothiazoles

Malaria is one of the parasitic diseases transmitted bitten by an infected Anopheles mosquito everywhere in the globe. To avoid it, it is preferable to use antimalarial drugs in a preventive manner and to be in several groups, and some of these drugs are good and resistant to mosquitoes [69].

Sarkar S et al. [70] synthesized and tested benzothiazole derivatives for antimalrial activity found 4-(2-(benzthiazl-2-yl) hydrazon)metthyl) benzen-1, 2-diol has the more action.

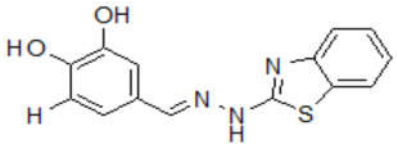


Fig.25- Structure of benzothiazol derivatives

Ongarora et al. [71] developed of amodiaquine correspondents of benzothiazoles Plasmdium falciprum W2 and K1 chlorquinresistant isolteos were used to assess antiplasmodial activity.

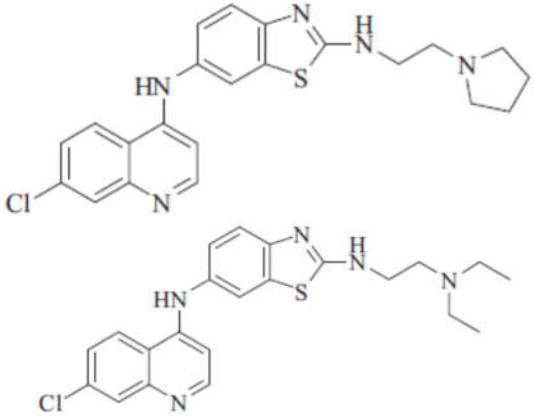
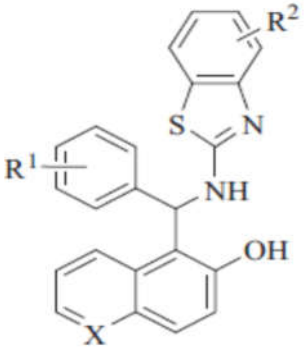


Fig.26: Structure of modiaquine benzothiazol derivatives

Venugopala et al. [72] several benzthiazole derivatives were also studied for their mosquito repellent effects against Anophles crossed.



x=CH,N R1=4-OH,NO_2,H,OCH_3 R2=6-Cl,6-Br,4-CH_3

Fig.27: Structure of benzothiazol derivatives

3.5. BTA as Anti-Inflammatory

Manu Kumar et al. [73] synthesized benzothiazole berberine derivatives and shown the cytopethic effect (CPE) and sulforhdamine B (SRB) assays, the activity against some influenza virus was determined. In 2015, Sadhasivam G et al. [74] created and evaluated benzothiazole for anti-inflammatory action. It was shown that N-(6-[(4-cyclhexylphenyl)sulfnyl] amino-1, 3benz thiazl-2-yl) cetamide has more action.

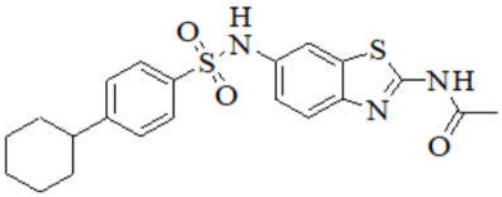


Fig.28-Structure of N-(6-[(4-cyclhexyl phenyl)sulfnyl] amino-1, 3benz thiazl-2-yl) cetamide

In 2013, Kashinath DV et al. [75] produced and evaluated pyrimid [2, 1-b] [1, 3] benzthiazole derivatives and show fairly active for antiinflammatory action.

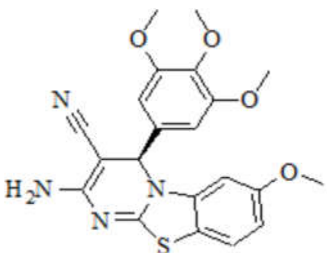
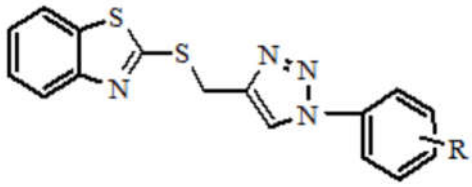


Fig.29: Structure of pyrimid [2, 1-b] [1, 3] benzthiazole

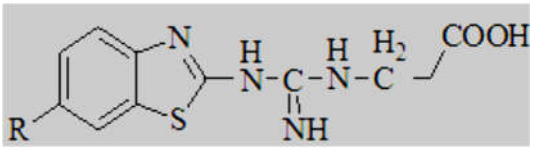
In 2014, Shafi et al. [76] synthesized 2-mercaptbenzothiazole andtriazole derivatives (COX) activity tests and caragenaninduced were used to evaluate antiinflammatory effect of the compound



R=o-Cl, p-Br, p-F,p-NO_2

Fig. 30: Structure of 2-mercaptbenzothiazole riazole derivatives

Venkatesh P et al. [77] prepared 1,3-benzthiazole-2-mines of three compounds, (5-chloro-1, 3-benzthiazole-2-mine), 12b (6-methaxy-1, 3-benzthiazole-2-mine), and (4-methoxy1, 3-benzthiazole-2-mine), were show more anti-inflammatory active.



R=4-Cl,5-OCH_3,6-OCH_3

Fig.31: Structure of 1,3-benzthiazole-2-mines

Gurupadayya et al. [78] synthisezed benzthiazole derivatives azatidin-2ones and thiazline-4ones and investigated them for antiinflammatory activity. Used Diclofnac sodium as acommon medicine.

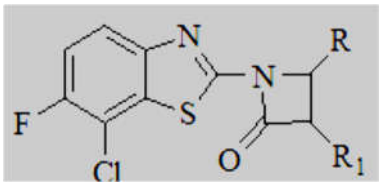


Fig.32: Structure of benzthiazole derivatives

Parmshivappa R et al. [79] synthesized of 2-[(2alkoxy6-pentdcylphenyl) methylthio-1-Hbenz-imdzoles/benzthiazles from (pentadecyl salicy-licacid) and tested to inhibitt human cycloxygenase enzyme230.

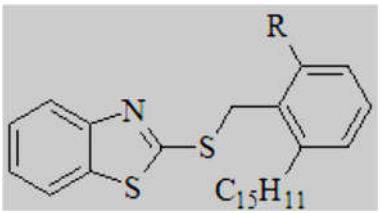


Fig.33: Structure of benzthiazole derivatives

BTA as Anticonvulsant Activity:

Raju GN et al. [80] synthesized benzothiazole derivative and found below compounds, have good anticonvulsant Activity.

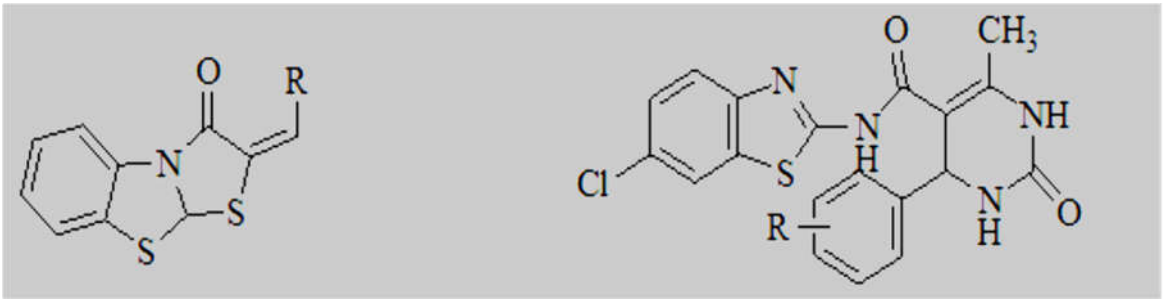


Fig.34-Structure of benzthiazole derivatives

Jin et al. [81] synthesized benzthiazole derivetives and discovered Anticonvulsant properties of 2-((1H-triazolyl)thio)-N(3-fluorbe-nzyl)oxy) benzthiazol-2-yl) acetamide.

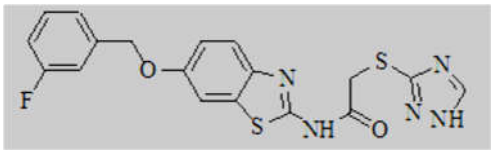
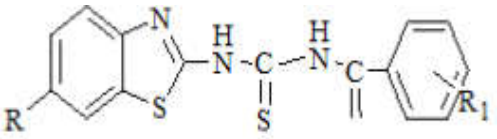


Fig.35-Structure of benzthiazole derivatives

Amnerkar N et al. [82] produced aseries of Nsubsttuted-2-yl)-4-[(substitutedamino) carbnothioyl] aminbenzene sulfonmides from prop-enemido, and 1acetyl-pyrazline derivatives and have high anticanvulsant action.



R=Br,Cl,F,NO_2,CH_3,OCH_3 R1=H,2-Cl,4-Cl, 4-OCH_3

Fig.36-Structure of benzthiazole derivatives

BTA as Antioxidant

Ahmed El-Mekabaty et al. [83] produced aseries of benzothiazole derivatives and found antioxidant action and cytotoxicity against the coloncancer cell line (HCT116)

Fig.37: Structure of benzthiazole derivatives

Amin S et al. [84] produced benzothiazole derivative and show 4-benzthiazole ethoxyphenol .Antioxidant activity is high.

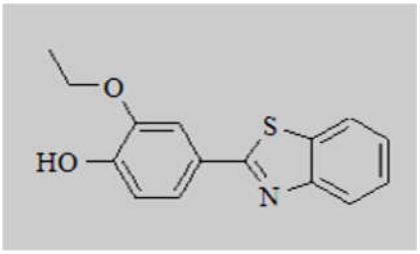


Fig.38: Structure of benzthiazole derivatives

Starcevic K et al. [85] synthesized amidinbenzthiazole derivetives and found 6-Amidnium2-(2, 3, 4-trihydrxyphenyl) benzthiazole chloride have goodantioxidant action.

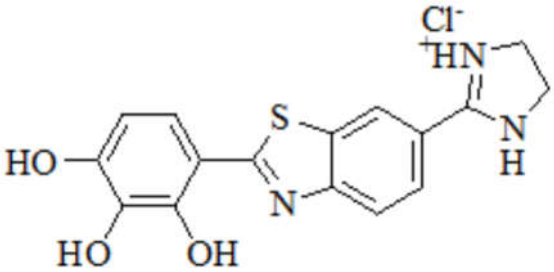


Fig.39: Structure of amidinbenzthiazole derivetives

Rosales-Hernandez MC et al. [86] syntheszed benzthiazole derivatives, found ((benzthiazl-ylimin(methyl) methylmino)-2-hydroxybenzoicacid having a higher level of antioxidant activity

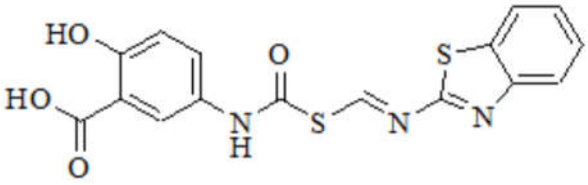


Fig.40: Structure of benzthiazole derivatives

Guzel et al. [87] synthesized group of 3HSpir [benzothiazole-indol]-20(10H)ones and found has more scavnging activties against DPPH and(ABTS+)radicals.

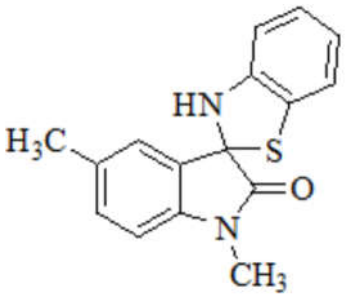


Fig.41: Structure of 3HSpir[benzothiazole-indol]-20(10H)ones

Cressier D et al. [88] synthesized benzothiazoles and thiadiazolderived compounds found 1,5-dimethyl-3H-spir[benz[d]thiazl2,3-indolin]-2-one has a high antioxidant activity.

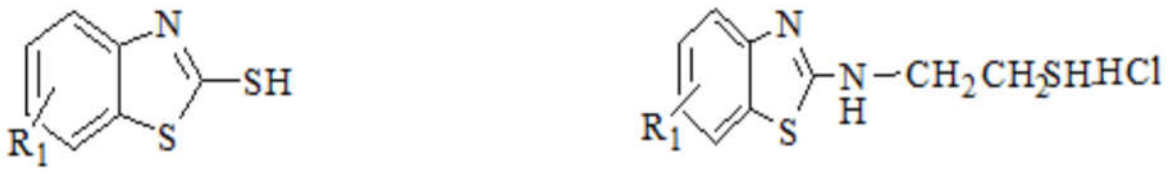


Fig.42: Structure of benzothiazoles derivatives

BTA as AntiDiabetic Activity

Kumar et al. [89] produced 2-((benzthiazole-2ylthio) methyl)-5- and found that they have more antidiabetic eficacy

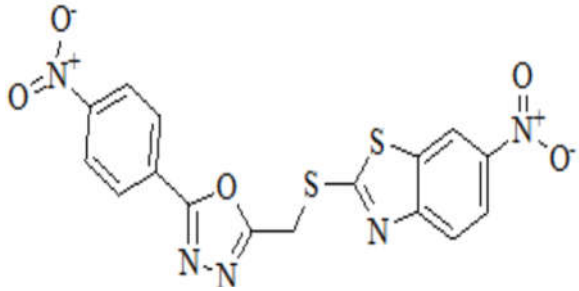


Fig.43: Structure of 2-((benzthiazole-2ylthio) methyl)-5benzthiazole

In 2013, Sasson S et al. [90] produced benzothiazole derivatives and tested antidiabetic ability, show 2- (benz[d] thiazol-2ylmethylthio)-6-ethoxybenz[d]thiazole has moral antidiabetic activity.

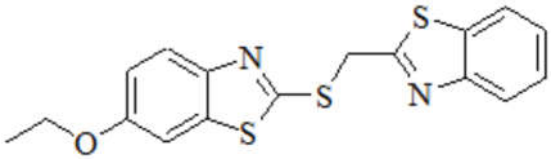


Fig.44: Structure of benzothiazole derivatives

Mariappan G et al. [91] synthesized abenzo-thiazole derivative and show the N-(6-chlorben-zoat[d] thiazol2-yl)-2-morpholinocetamide has antidiabetic action.

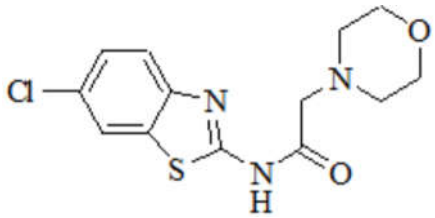


Fig.45: Structure of abenzothiazole derivative

Conclusion

Through the review, we conclude that benzothiazoles are molecules that have several uses and functions with a therapeutic ability in a group of diseases such as cancer, diabetes and others, a diuretic drug (Ethoxolamide), an anti-Parkinson's disease drug (Pramipexole), and a treatment for Alzheimer's disease (Thioflavine). , the production of a good drug by conducting a lot of research, and this indicates the existence of successful conditions for the medicinal substance.

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